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Feasibility of a prehabilitation program dedicated to older cancer patients before complex medico-surgical procedures: the PROADAPT pilot study protocol

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4 1 **Feasibility of a prehabilitation program dedicated to older cancer**
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6 2 **patients before complex medico-surgical procedures: the PROADAPT**
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8 3 **pilot study protocol**
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25 **Abstract**

26 **Background:** Aging is associated with an increased prevalence of co-morbidities and sarcopenia and
27 with a decline of functional reserve of multiple organ systems, eventually leading in the context of the
28 disease- and/or treatment-related stress to functional deconditioning or organ failure. The
29 multicomponent intervention “PROADAPT” was built multi-professionally to implement
30 prehabilitation in older cancer patients.

31 **Methods:** PROADAPT-pilot study is an interventional, non-comparative, prospective, multicenter
32 study. It will include 122 patients oriented to complex medico-surgical curative procedures (major
33 surgery or radiation therapy +/- chemotherapy). After informed consent, patients will undergo a
34 comprehensive geriatric assessment and will be offered a prehabilitation kit “PROADAPT” including an
35 advices booklet with personalized objectives and respiratory rehabilitation devices. Patients will then
36 be called weekly and monitored for physical and respiratory rehabilitation, pre-operative re-nutrition,
37 motivational counseling, and iatrogenic prevention. Six outpatient consultations will be planned at
38 inclusion, few days before the procedure, at 1, 3, 6 and 12 months after the end of the procedure. The
39 main outcome of the study is the feasibility of the intervention, defined as the ability to perform at
40 least one of the components of the program. Clinical data collection will include patient-specific and
41 cancer-specific characteristics.

42 **Discussion:** PROADAPT program was designed to be implemented pragmatically in the centers
43 according local habits and in different tumor contexts. Based on the results of this feasibility study,
44 two randomized study are planned, that will evaluate the impact of PROADAPT program after cancer
45 treatment for ovarian cancer (NCT04284969) or susmesocolic cancers.

46 **Ethics and dissemination:** Study protocol and several amendments were ethically approved. The
47 results of the primary and secondary objectives will be published in peer-reviewed journals.
48 ClinicalTrials registration: NCT03659123.

49 **Keywords:** oncogeriatrics, prehabilitation, motivation, sarcopenia, older cancer patients, care
50 pathway.

52 **Article summary**

53 Strengths and limitations of this study

- 54 - PROADAPT program is a prehabilitation program specifically tailored for older cancer patients
- 55 - The program was designed according a multidisciplinary analysis of available evidence and
56 according a multistep validation process involving patients.

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- 57 - PROADAPT pilot trial is a prospective and multicenter trial designed to evaluate the feasibility
- 58 of the intervention, next leading to future 2 randomised trials
- 59 - The construct of the trial includes lots of secondary outcomes, to better adapt the program to
- 60 patients' specificities

61

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63 Introduction

64 Many oncological situations involve complex medical-surgical procedures at risk of patient's
65 deconditioning. Surgery or complex medico-surgical procedures can be considered as one proof-of
66 principle of such risks, since major cancer surgery exposes the older population to a higher risk of
67 morbi-mortality and unplanned hospitalization for geriatric events (1). Outpatient treatments and
68 rapid post-operative rehabilitation strategies are used to decrease post-operative deconditioning but
69 do not take geriatric risk factors into account. The deconditioning of older patients, not anticipated,
70 can thus lead to prolonged and iatrogenic hospitalizations, generating frustration, appeals by patients
71 and their families and additional hospital costs.

72 In order to reduce complications after surgery, prehabilitation has often been considered, and 71 % of
73 the surgeons would accept a 4 weeks delay before surgery to improve older patients' outcomes if
74 shown to be beneficial (2). However, the actual level of evidence depends on the interventions: high
75 for pre-operative nutrition (3), but low for physical exercise, due to heterogeneous programs with
76 often bad adherence (4). In addition, geriatric validated interventions, in order to prevent iatrogenic
77 event, may be added in a multi-interventional model of intervention.

78 To date, the interventions likely to prevent geriatric deconditioning include nutritional care, pre-
79 therapeutic (prehabilitation) and post-therapeutic (rehabilitation) physical reconditioning, iatrogenic
80 prevention (drug and care system-related) and hospital-to-home transition to limit the risk of early
81 readmission of patients. Nevertheless, the level of evidence for each of these care segments remains
82 limited, and not specific to the oncogeriatric population. Indeed, studies about more specific care have
83 already been carried out but do not consider all of the above interventions (5). Moreover, cancer in
84 the older patient is often associated with comorbidities, particularly cardiovascular disease (6,7). The
85 older population also has a higher risk of loss of autonomy and cognitive impairment, which can be
86 increased with surgery (8–10). In response to the growing population of older cancer patients, a
87 modification of oncological care and the implementation of specific geriatric interventions have been
88 developed (11–13).

89 PROADAPT (Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning risk and
90 Accompaniment of Patients' Trajectories) is a geriatric intervention program constructed on a multi-
91 professional and multi-disciplinary basis after a systematic analysis of published data. It includes: 1)
92 before surgery: prehabilitation of patients, including nutritional, physical, respiratory and motivational
93 counselling; 2) during hospitalisation for surgery (if performed): optimization of their treatment by
94 pharmaceutical reconciliation, educational interventions, standardization of surgical interventions and
95 improved rehabilitation after surgery; 3) bridging and post-discharge interventions for hospital-to-
96 home transition (table 1).

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3 974
5 98 **Methods and analysis**6
7 99 **Objectives**8
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10 100 *Primary objective*

11
12 101 The primary objective of the PROADAPT pilot study is to assess the feasibility of the program, defined
13
14 102 as the achievement of at least one item of the program during patient's follow up.

15 103

16
17 104 *Secondary objectives*

18
19 105 The secondary objectives of the study are:

- 20
21
22 106 1) To assess the achievement of each item of the program independently of each other (rate of
23
24 107 achievement of all or part of the instructions);
25 108 2) To assess patients' satisfaction with the program;
26
27 109 3) To estimate the rate of adherence to items during the various visits;
28
29 110 4) To appreciate the longitudinal evolution over 1 year.

30
31 111 In addition to these secondary objectives, a series of parameters will be measured and monitored
32
33 112 in this order:

- 34
35 113 5) To assess patients' post treatment complications according Clavien Dindo and NCI-CTC version
36
37 114 4 scoring systems;
38 115 6) To estimate the rate and the nature of post-operative complications according to the CCI index
39
40 116 at 30 and 90 days;
41
42 117 7) To estimate the post-operative mortality at 30 and 90 days;
43
44 118 8) To estimate the costs of treatments (health system, patients);
45 119 9) To study the therapeutic strategies (treatment completion rate);
46
47 120 10) To estimate the progression-free survival rate at one year (PFS);
48
49 121 11) To estimate the overall survival rate at one year (OS);
50 122 12) To study the physical performance tests and the evolution of these performances through the
51
52 123 proposed exercises;
53
54 124 13) To study the other dimensions of quality of life relating to health at 3 months;
55 125 14) To estimate the longitudinal evolution of QoL;
56
57 126 15) To estimate the tolerance of treatments;
58
59 127 16) To estimate the evolution of geriatric covariates.
60

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3 128 **Study design**
4

5 129 PROADAPT - pilot phase is a second category interventional study involving the human person with
6
7 130 minimal risks and constraints excluding health products. It is a prospective, non-comparative
8
9 131 multicenter opened in different centers of Auvergne-Rhône-Alpes region, France (n=7).

10
11 132 **Study sites and participants**
12

13 133 The study population will include older patients identified during multidisciplinary consultation
14
15 134 meetings and oriented to complex medico-surgical curative procedures in the including centers (Lyon
16
17 135 Sud Hospital, Croix Rouse Hospital and Edouard Herriot Hospital from the Hospices Civils de Lyon,
18
19 136 Nord-Ouest Villefranche-sur-Saône Hospital, Annecy-Genevois Hospital, Chambéry Hospital, Lyon-
20
21 137 Villeurbanne Médipôle).

22 138 Inclusion criteria are: patient aged 70 and over or 60 and over with significant comorbid condition
23
24 139 (modified Charlson index ≥ 3) or disability (ADL score $< 6/6$), histologically or cytologically proven
25
26 140 cancer, life expectancy > 3 months planned for a complex medico-surgical procedure in a curative
27
28 141 intent.

29 142 Exclusion criteria are: patient with other malignancy within the last 5 years (except for adequately
30
31 143 treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled
32
33 144 limited basal cell skin cancer), unable to be regularly followed for any reason (geographic, familial,
34
35 145 social, psychologic) or with any mental or physical handicap at risk of interfering with the appropriate
36
37 146 treatment.
38

39 147
40 148 **Intervention**
41

42 149 PROADAPT intervention program was built according to a multi-dimensional and multidisciplinary
43
44 150 basis. From January 2016 to April 2018, nine regional meetings were organized, gathering 40
45
46 151 representatives of the following medical and paramedical specialties: geriatricians, nutritionists,
47
48 152 surgeons (subspecialties: gynaecology, digestive surgery, urology), oncologists, anaesthesiologists,
49
50 153 nurses, physiotherapists, occupational therapists, adapted physical activity monitors. A systematic
51
52 154 review of published data was done in the following axes, in order to provide a graded state-of-the-art:
53
54 155 nutrition, physical activity, patient education, medication rationalization, cardiovascular optimization,
55
56 156 transition and standardization of surgical procedures. Based on the qualitative grading of existing data,
57
58 157 a modified DELPHI method was performed, in order to co-validate the content of the standardized
59
60 158 intervention checklist, and the feasibility of the implementation of each point of this checklist (Table
159
160 1).

1
2
3 160 A PROADAPT booklet was built, in order to propose a standardized, adapted and evolutive tool
4
5 161 designed to explain physical exercise and nutrition counselling and to insure a follow-up of patients'
6
7 162 day-to-day achievements. This first version was tested by candidate patients during two turns of
8
9 163 validation before the validation of the current version 3 of the booklet.

10 164 *PROADAPT standardized geriatric intervention program includes:*

- 11
12
13 165 - Pre-operative physical activity including strength and endurance exercise +/- group activities
14
15 166 during 4 +/-2 weeks. Interventions with high level of evidence were retained, according to an ongoing
16
17 167 systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42020100110; (14,15));
18
19 168 - Nutrition: nutrition before and after physical activity, pre-postoperative immuno-nutrition +/-
20
21 169 artificial nutrition according international guidelines (3);
22
23 170 - Patient (and caregiver) education and coaching (on nutrition, physical exercise) according to a
24
25 171 weekly schedule with the activation of integrated supports by hetero- and self-management (16);
26
27 172 - Standardized intervention procedures, according to a checklist established in consensus with
28
29 173 surgeons' representatives;
30
31 174 - Enhanced rehabilitation will be promoted according to international guidelines (17);
32
33 175 - Pharmaceutical medication conciliation, treatment optimization, according a centralized
34
35 176 process with pharmaceutical expertise;
36
37 177 - Bridging interventions for hospital-to-home transition, according to a proposed standardized
38
39 178 procedure including training of dedicated nurses, and post-discharge phone-calls follow-up during 12
40
41 179 weeks after surgery. Interventions with high level of evidence were retained, according to an ongoing
42
43 180 systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42017055698).

44 181 The intervention is designed to be implemented at different times of patients' care (table 1).

45 182

46 183 *During the prehabilitation time:*

- 47 184 • A dedicated nurse, trained in patient education ("coaching nurse") presents him/herself to the
48
49 185 patient for:
50
51 186 - Presentation of the program to the patient and his/her caregiver(s)
52
53 187 - Personalization of the PROADAPT book (see after) to the patient's characteristics
54
55 188 - Collection of personal data, nutritional and functional habits
56
57 189 - Evaluation of psycho-cognitive context
58
59 190 - Gathering of the information needed: comorbidities, comedications (for transmission
60
191 to the centralized pharmaceutical expertise)
192
193 - Anticipation and organization of the future appointments (anesthesiologist,
stomatherapist, ...)

- 1
2
3 194 - A weekly visit or phone call according to a structured interview for health education
4 and transmission of nutritional and functional advices (see after)
5 195
6 196 • Nutritional care is based on:
7
8 197 - A personalized evaluation of nutritional balance and nutritional needs of the patient
9 according to dietician diagnosis based on measured intake and international
10 198 recommendations
11 199
12
13 200 - A weekly follow-up of weight and nutritional intake
14
15 201 - Artificial nutrition if needed according ESPEN recommendations (3)
16
17 202 - Pre-operative immune-nutrition during 7 days before surgery
18
19 203 • Total-body rehabilitation:
20 204 - 2 to 3 times a week: strength exercise (each time with dedicated exercises for upper
21 members, legs and abs, 20 to 45 minutes each sequence)
22 205
23 206 - 2 to 3 times a week: endurance exercise (walk or cycle ergometer), 20 to 45 min each
24 sequence
25 207
26 208 - 3 times a day: respiratory physiotherapy
27
28 209 - Once a week (if possible): group activities (according to the center organization and
29 home-hospital distance)
30 210
31 211 • Pharmaceutical conciliation and optimization according to STOPP/START criteria and
32 international recommendations about peri-operative care (18): to be transmitted to the surgical and
33 anesthesia team without any obligation.
34
35 213
36
37 214

38 215 *During peri-operative time*

- 40 216 • The coaching nurse contacts the surgical team for transmission of:
41
42 217 o patient's personal data
43 218 o physical (nutritional, functional and/or comorbidities) as well as psychological
44 219 difficulties
45
46 220 o medication conciliation results
47
48 221

50 222 *During rehabilitation time*

- 51 223 • The coaching nurse contacts the rehabilitation team for transmission of:
52
53 224 o patient's personal data and care course
54 225 o physical (nutritional, functional and/or comorbidities) as well as psychological
55 226 difficulties
56
57 227 o medication conciliation results
58
59 228 • The rehabilitation program is left at the discretion of the rehabilitation team
60

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3 229 • A weekly phone call of the coaching nurse to the rehabilitation team for nutritional and
4 functional follow-up as well as medication conciliation
5 230

6 231

8 232 *During hospital-home transition time*

- 9
10 233 • The coaching nurse contacts the patient's general practitioner for transmission of:
11 234 o patient's personal data and care course
12 235 o physical (nutritional, functional and/or comorbidities) as well as psychological
13 236 difficulties
14 237 o medication conciliation results
15
16 238 • Bi-weekly phone call of the coaching nurse to the patient for nutritional and functional follow-
17
18 239 up
19
20 240 • Advices for optimization of symptoms management: abdominal pain, nausea, vomiting...
21
22 241

23
24
25 242 **Participant timeline**

26
27
28 243 Six successive evaluations are planned for the participants.

29
30 244 *The inclusion visit* is planned during a geriatric consultation planned before the start day of the complex
31
32 245 medico-surgical procedure, at least 7 days before start date. If the start date is delayed for any reason
33
34 246 or the patient is included into a neo-adjuvant treatment, the prehabilitation time may be prolonged
35
36 247 until 9 months. In that case, the frequency of the phone calls is decreased (from 1/week to 1/month)
37
38 248 after 4 weeks. During the inclusion visit, lasting about 1 hour, the following steps are planned:

- 39 249 - Clinic (blood pressure, heart rate, WHO score, patient's comorbidities), biologic (albumin,
40 prealbumin, C-reactive protein) and paraclinic (year of birth, gender, weight, height, body
41 250 mass index, weight evolution over the last 3 and 6 months) data collection
42
43 251 - All concomitant treatments and drug conciliation
44
45 252 - The history of the disease (primitive site, metastasis, histology of the initial tumor, presence
46 253 of tumor markers)
47
48 254 - Radiological disease assessments (date and nature)
49
50 255 - A standardized geriatric assessment using validated questionnaires with a particular attention
51 256 on physical activity and nutrition (**Error! Reference source not found.** tables 2 and 3).
52
53 257 - Delivery of the "PROADAPT kit" device during a meeting with a dedicated paramedic (nurse,
54 258 physiotherapist, ergotherapist...) in order to:
55
56 259 o Provide to the patient VOLDYNE® and TRIFLO® devices for inspiratory training
57
58 260

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2
3 261 ○ Present the PROADAPT notebook that includes a battery of exercises and nutritional
4
5 262 counselling specifically designed for this older population:
6
7 263 ▪ muscle strengthening of upper limbs (6 exercises, 3 difficulty levels), lower
8 264 limbs (6 exercises, 3 difficulty levels), abdominal wall (4 exercises, 3 difficulty
9
10 265 levels) (objective: 2 to 3 sessions per day for a total time between 20 and 45
11 266 minutes)
12
13 267 ▪ endurance/aerobic activities (7 exercises, 3 difficulty levels with 3 duration
14 268 objectives, objective: every day)
15
16 269 ▪ inspiratory training with VOLDYNE® and TRIFLO® devices (objective: 3 sessions
17 270 per day for a total time of 30 minutes)
18
19 271 ▪ general nutritional counselling adapted to the older population: food
20 272 enrichment, inter-meals collations, oral nutritional supplements.
21
22 273 ○ A fulfilling of 3-day food statement allows, in the 7 days after inclusion, to deliver a
23 274 dietician-driven personalized nutritional counseling. If needed, in case of unfavorable
24 275 nutritional parameters, artificial nutrition is introduced.
25
26
27 276 - Delivery, if needed, of medical prescription:
28
29 277 ○ for home physiotherapy according PROADAPT program for respiratory training
30 278 sessions and physical activity training sessions
31
32 279 ○ For oral nutritional supplements
33
34 280 ○ For usual medicines, including pharmaceutical review
35
36 281 - For patients requiring inpatient follow-up, hospital admission for a few days in a rehabilitation
37 282 unit for a physiotherapeutic program and/or artificial nutrition (enteral preferred).
38
39
40
41 283 During pre-intervention time, phone calls are planned by a dedicated paramedic (once a week for the
42 284 first 4 weeks and then once a month until the intervention). Calls are semi-directed interviews focused
43 285 on the patient's autonomy, physical activity, appetite and sleep over the last period (week/month). A
44 286 special attention is paid on encouraging patient's motivation and adherence to the program (figure 1)
45
46
47 287 *The pre-therapeutic visit* is scheduled when possible between 5 days and the day of the intervention.
48
49 288 This visit is performed in the surgery or radiotherapy unit only if the visit is necessary before the
50 289 intervention still without modifying the standard therapeutic care for:
51
52
53 290 - Clinic, biologic and paraclinic data collection
54
55 291 - All concomitant treatments and drug conciliation
56
57 292 - Questionnaires about pain, nutrition, fitness and physical tests (table 2 and 3)
58
59 293 - Therapeutic care data collection (date, nature, entitled, reason)
60

294 During post-intervention time, paramedics trained in clinical research will resume follow-up calls as
295 before the intervention once a week during 12 weeks after D0 and once a month up to 12 months after
296 D0. The D0 date is determined as the last day of surgery (day of the last resumption of surgery in the
297 limit of 30 days after the first intervention) or the last day of the radiotherapy. For weekly calls, a
298 margin of +/- 2 days is allowed and for monthly calls, a margin of +/- 7 days is allowed.

299 *Visits at 1, 3 and 6 months after the intervention (+/- 7 days):* The patient may have started an
300 antineoplastic treatment according to standard of care. The visit could be performed with the surgeon,
301 the radiotherapist or the oncologist according local habits:

- 302 - Clinic (blood pressure, heart rate, WHO score), biologic (albumin, prealbumin, C-reactive
303 protein) and paraclinic (weight, body mass index) data collection
- 304 - All concomitant treatments and drug conciliation
- 305 - Patient care data (surgery and complications, treatment for the cancer)
- 306 - Radiological disease assessments (date and nature)
- 307 - Questionnaires about quality of life, pain, nutrition, fitness and physical tests (table 2 and 3)
- 308 - Socio-economic assessment with patient's care data (date, nature of acts, designation, reason)

309 *The end of study visit* is planned at 12 months (per-protocol) or at the date of trial premature
310 discontinuation (+/- 7 days) for a final assessment of the same outcomes as previously listed. When
311 requested, if previous visits were omitted, a final assessment of all the complications during the post-
312 therapeutic period is performed.

313 **Outcomes and measurements**

314 ***Primary outcome***

315 The main outcome measure will be the percentage of patients who have completed at least one item
316 in the PROADAPT program after 12 months after the start of therapeutic treatment. The start of
317 treatment is defined in this study by the last day of surgery (date of the last recovery within the limit
318 of 30 days after the date of the initial intervention) or the last day of radiotherapy. The workshops of
319 the program are:

- 320 - Physical and respiratory rehabilitation
- 321 - Re-nutrition session
- 322 - Telephone nurse follow-up

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325 ***Secondary outcomes***

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3 326 The secondary outcomes of the study are:
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5 327 - To evaluate the feasibility of each stage of the program independently of each other (rate of
6 achievement of all or part of the instructions)
7 328

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9 329 ○ Pre-operative physical rehabilitation including (figure 2):

10 330 ● Muscle strengthening

11 331 ● Respiratory rehabilitation

12 332 ● Endurance work

13
14 333 ○ Pre-operative nutrition counselling (figure 2)

15 334 ○ Drug reconciliation / iatrogenic prevention

16 335 ○ Pre-therapeutic follow-up calls (figure 1)

17 336 ○ Post-surgery or post-radiotherapy follow-up calls (figure 1)
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23
24 338 - To estimate patients' satisfaction with the overall program, at the end of the study (**Error! Reference**
25 **source not found.**table 2).
26 339

27
28 340 - To estimate the rate of adherence to the items (physical activity, nutrition and nursing follow-up)
29 during follow-up time. To evaluate this criterion, various parameters will be recorded: physical activity
30 341 duration (in h/week), kinetics (duration (% increase), level of difficulty), respiratory activity, food intake
31 342 during phone calls.
32 343

33
34
35 344 - To assess the longitudinal evolution over 1 year of:

36 345 ○ patient's physical performance (SPPB, gate speed, TUG test) and functional independence on
37 ADL (19), IADL (20), AIPVQ (21)
38 346

39 347 ○ nutritional parameters of the patient (weight, albuminemia, appetite)

40 348 ○ health-related quality of life for patients based on QLQ-C30 and ELD14 (5 dimensions: mobility,
41 disease burden, emotional and physical functioning, tiredness) (22,23)
42 349

43 350 ○ pharmaceutical conciliation
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48
49 352 In parallel to these secondary objectives, a series of parameters will be measured and monitored in
50 order to:
51 353

52 354 - Estimate the rate and nature of post-operative complications at 30 days (NCI-CTCAE)

53 355 - Estimate the rate and nature of post-operative complications according to the CCI at 30 and 90 days

54 356 - Estimate post-operative mortality at 30 and 90 days

55 357 - Estimate the overall one-year survival rate (OS)

56 358 - Estimate the one-year progression-free survival rate (PFS)
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3 359 - Estimate the longitudinal evolution of QoL according to QLQ C30, ELD14, EQ-5D

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5 360 - Estimate treatment costs (health system, patients)

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7 361 - Study therapeutic strategies (treatment completion rate)

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9 362 - Estimate the evolution of geriatric covariates.

10 363

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12 364 **Sample size calculation**

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14 365 The program will be considered feasible, at the patient level, if all or part of the program is
15 366 implemented in at least 50 % of the included patients (= alternative hypothesis).

16
17
18 367 The calculation of the number of subjects needed was done as follows: to reject the null hypothesis of
19 368 the program feasibility rate lower than 35 %, with a first alpha species risk of 5 % and a power of 90 %
20 369 (beta=10 %, bilateral test), the number of subjects to be analyzed is 111. Including 10 % non-treatable
21
22 370 patients, a total of 122 patients should be included. The included patients will be analyzed with
23
24 371 intention-to-treat.

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26
27 372 **Data management and statistical analyses**

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29
30 373 Data are monitored by a clinical research associate (CRA). Inconsistencies will be reported to the study
31 374 investigators in order to decide whether the data should be corrected or considered as missing data.

32
33 375 Any changes in the data will be reported.

34
35 376 Data analyses will be performed by the data management and analysis centre. The analyses will be
36 377 carried out by an independent statistician with the latest version of the R software environment.

37
38 378 All of the characteristics collected will be subjected to a descriptive analysis.

39
40 379

41
42 380 ***Descriptive analyses***

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44
45 381 A flow-chart diagram will describe the data available for the patient population at baseline, and during
46 382 each follow-up visit. Eligibility criteria for treated patients will be verified, as well as follow-up and end
47 383 of study visits. Reasons for premature end of study will be provided.

48
49
50 384 Characteristics of the study population and proportions of missing values will be reported. Patient
51 385 characteristics will be described using mean and standard deviation or median and interquartile range
52 386 for quantitative variables, and frequencies and distribution for categorical variables. A comparison of
53
54 387 baseline characteristics between patients with complete follow-up and those with attrition will be
55 388 performed. If needed, methods for handling missing data (multiple imputation, mixed model or
56
57 389 auxiliary variable) will be used when appropriate.

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5 391 **Primary analysis**

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8 392 The percentage of patients who have completed at least one PROADAPT program activity at the end
9 393 of 12 months after the start of treatment will be estimated using mean and standard deviation.

10
11
12 394 **Secondary analyses**13
14 395 **Time-to-event variables: follow-up, overall survival, progression free survival**

15
16 396 The proportion of events at specific measurement times will be estimated according to the Kaplan-
17 397 Meier curve. Medians of event-free survival will be reported by treatment arm with its 95 % confidence
18 398 interval (95 % CI), if the number of events allows estimation of the median.

19
20
21 399 Overall survival rate and progression free survival rate at 12 months (after the day of the last revision
22 400 of surgery or the last day of radiotherapy) will be provided with 95 % CI.

23
24
25 401 **Quality of life**

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28 402 Analyses of the QoL data will be performed with modified intention to treat (mITT): all included
29 403 patients, regardless of compliance with the eligibility criteria and whether or not they were followed
30 404 up and for whom the QoL scores at inclusion will be included in the analysis. Patients' quality of life,
31 405 linked to health, will be analysed after 3 months through 5 dimensions: mobility, disease burden,
32 406 emotional and physical functioning, tiredness.

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37 40738
39 408 **Data monitoring**

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41 409 The successful completion of the database is ensured by the hospital CRA. The hospital CRA also
42 410 ensures compliance with the study protocol. The sponsor CRA verifies that the rights of the participants
43 411 are respected.

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46 41247
48 413 **End of protocol**

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50 414 Patients leave the study either on a per-protocol basis during the "end of study visit" on month 12
51 415 after the intervention or at any time during the conduct of the study if they no longer wish to
52 416 participate. However, as indicated in the information letter to the patients/caregivers, the data
53 417 collected before exclusion may be used as part of the study.

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56 41857
58 419 **Confidentiality**59
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3 420 Correspondence tables will be kept in a separate file that does not contain clinical data. The access to
4
5 421 the nominative information is protected by a password and confidentiality is guaranteed by the study.

6 422

7
8 423 ***Protocol amendments***

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10 424 Any important modifications requiring a new ethics committee approval will be communicated in
11
12 425 future publications. Any potential impact of protocol modifications on the results will be discussed as
13
14 426 appropriate.

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17 428 ***Trial status***

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19 429 Patient enrolment began on July 3, 2018. Data are collecting.

20 430

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23 431 ***Patients' and public involvement***

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25 432 Patients were involved at different steps of the trial: (i) during PROADAPT booklet conception, several
26
27 433 (30) patients were asked to answer an anonymous questionnaire in order to improve its ergonomics;
28
29 434 (ii) the information note and consent form of the protocol have been re-read by the patients' review
30
31 435 committee of the Ligue Nationale de Lutte contre le Cancer (a French association of cancer patients).

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34 437 **Discussion**

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36 438 **Discussion of the intervention**

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39 439 Prehabilitation has long been conceptualized as an effective means of improving the functional
40
41 440 capacity of the individual to enable him to resist various stressors. Originally developed in the military
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43 441 as the association of physical training to improve strength and endurance, improving nutritional intake
44
45 442 and general education (24), it has been transposed into medicine and major surgery – initially when
46
47 443 an ICU admission is planned - at the beginning of this century (25).

48 444 Despite a growing interest in the medical community for prehabilitation and particularly cancer
49
50 445 prehabilitation, the level of evidence for specific interventions stays too low to be implemented in
51
52 446 common care. Among the main disadvantages of published data include the heterogeneity of
53
54 447 programs, sometimes poor patient adherence and the fact that most studies were small pilot studies
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56 448 developed for patients more fit and younger than those who should make the best part of
57
58 449 prehabilitation. Another point to emphasize is that most programs include only one intervention -
59
60 450 physical, nutritional, or psychological rehabilitation - when multimodal interventions are often
451 considered to be more effective in older populations.

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3 452 Considering these points, the PROADAPT intervention was developed according to an innovative
4
5 453 management strategy since it started in 2016 by multi-professional meetings conceived as
6
7 454 brainstorming sessions in order to develop a multidisciplinary program dedicated to prehabilitation
8
9 455 and follow-up of older patients. The multidisciplinary conception of the intervention, the particular
10
11 456 attention paid to older patients' specificities and the previous experience of the participants in as
12
13 457 various fields as patients' education, cognition, physiotherapy were hopefully the warrants of the most
14
15 458 tailored approach to the target population. For example, the booklet typography was of big character
16
17 459 font and the illustrations highly schematic with high contrast. Each sentence was verified by a panel of
18
19 460 patients in order to insure proper understanding. Finally, the booklet was evaluated by 30 patients,
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21 461 with a high rate of satisfaction (Ravot et al, PROADAPT Pilot trial: A survey on patients' expectations
22
23 462 and satisfaction, unpublished data).

24
25 463 This pilot study is the first step towards an ambitious program, since PROADAPT program will be
26
27 464 declined in the future into two randomized studies, PROADAPT-ovary/EWOC-2 (NCT04284969) and
28
29 465 PROADAPT sus-mesocolic, designed to evaluate the impact of PROADAPT program on post-treatment
30
31 466 complications versus common care. In order to favor patients' compliance and follow-up, an eHealth
32
33 467 tool has been developed that will help supervising patients' care courses.

34 468 **Discussion of the study design**

35
36 469 In line with the previous points, this pilot study was designed in order to answer to this critical
37
38 470 question: is a multidomain prehabilitation program feasible in an older cancer population? This
39
40 471 question encompasses several points: (i) Is the program physically adapted to an older population? (ii)
41
42 472 Is such a program applicable in ambulatory care? (iii) How to build pedagogic tools adapted for such
43
44 473 ambulatory use? (iv) Are such pedagogic tools understandable? (v) What is the compliance of the
45
46 474 patients for each domain of the intervention program?... Another point is to know whether the
47
48 475 patient's care team is expected to accept such intervention, but this point was previously evaluated by
49
50 476 Ghignone et al. They demonstrated through an international survey that surgeons are generally in
51
52 477 favor for such programs since 71 % of them would accept to prehabilitate their elderly patients 4 weeks
53
54 478 before surgery, if such intervention is proven to be effective (2). Nevertheless, the participation of
55
56 479 surgeons and anesthesiologists during initial brainstorming sessions was of major interest since they
57
58 480 enriched a lot the structure of the program.

59
60 481 Thus, the construct of this trial may appear as highly complex with overabundant secondary endpoints,
482
483 but this design encompasses as much as possible the complexity of prevention care in an older
484
485 population, which has to mix the adaptation to the target population and the ability to maintain
486
487 compliance over time.

485

486 Ethics and dissemination

487 The study sponsor is the Hospices Civils de Lyon, responsible for study insurance and
488 pharmacovigilance. The study protocol was approved by the Ile de France 8 Ethics Committee on May
489 3, 2018 and cover all sites involved in this study. Several amendments have been added to the first
490 version of the protocol. The initial approved version was V2 of May 28, 2018, then the amended
491 versions were as follows: V3 of October 23, 2018 (change in the recruitment period, addition of new
492 investigation centers), V4 of May 17, 2019 (request for an additional 12 months extension, update with
493 the GDPR and update of the patient book). Current version is the V4 of May 17, 2019, authorized on
494 June 27, 2019. The research will be carried out on accordance with the Helsinki Declaration and ICH
495 GCP Guidelines. Trial protocol fulfills SPIRIT 2013 checklist (Supplementary table 1) and World Health
496 Organization Trial Registration Data Set (Supplementary table 2). The study complies with the
497 principles of the data protection act in France and with the General Data Protection Regulations in
498 force in Europe. Each investigator must collect a written consent at the beginning of the procedure.
499 This consent is retained in the patient's medical chart. The patient can stop the study at any time with
500 an oral information at his investigator or clinical research assistant. Patients will be informed on
501 additional amendments according the law in force.

502 The results of the primary and secondary objectives will be published in peer-reviewed journals. All
503 authors of future publications will have to meet the criteria for authorship stated in the Uniform
504 Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of
505 Medical Journal Editors.

506

507 Total words count : 4547

508

509 Abbreviations

510 ADL: Activities of Daily Living; AIPVQ: Physical Instrumental activities of daily living (in French: Activités
511 Instrumentales Physiques de la Vie Quotidienne); CRA: Clinical Research Assistant; ESPEN: European
512 Society for Clinical Nutrition and Metabolism; FSS: Fatigue Severity Scale; GDS: Geriatric Depression
513 Scale; IADL: Instrumental Activities of Daily Living; ICU: Intensive Care Unit; mITT: Modified Intention
514 To Treat; MNA: Mini Nutritional Assessment; QLQ: Quality of Life Questionnaire; QoL: Quality of Life;
515 RAPA: Rapid Assessment of Physical Activity; SF: Short Form; SPPB: Short Physical Performance Battery

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3 517 **Declarations**
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7
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9

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20

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23

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31

32 538 **Availability of data and materials**
33

34 539 The final dataset of the PROADAPT pilot study will be available on reasonable request after publication

35 540 of the primary objective. Data requests can be submitted to the corresponding author.
36

37 541 **Competing interest**
38

39 542 The authors declare that they have no competing interests.
40

41 543 **Consent for publication**
42

43 544 Not applicable
44

45 545 **Author contributions**
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546 All authors participated to the PROADAPT intervention conception. Study protocol was conceived by
547 DD, CF, CG, OLS, AM, VP and CR. DD and CF assumed fundraising and grant follow-up. MR led the
548 drafting of the manuscript. All authors critically reviewed and approved the final version of the
549 protocol.

550

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3 620 **Illustrations' legends**
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6 621 Figure 1: PROADAPT program: follow-up visits and phone calls
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8 622 Figure 2: PROADAPT program: interventions at the patient's level
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10 623 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
11 624 steps (before, during and after complex medico-surgical procedure)
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13 625 Table 2: PROADAPT pilot trial: questionnaires and screening tests
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15 626 Table 3: PROADAPT pilot trial: flow diagram
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629 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
630 steps (before, during and after complex medico-surgical procedure)

Nurse coaching & education Bridging interventions	Coaching nurse self-presentation Delivery of a personalized patient book Care according best practice guidelines: - Confirm and document patient goals and treatment preferences, including advance directives. - Confirm and document patient's health care proxy or surrogate decision-maker. - In patients with existing advance directives, discuss new risks associated with the surgical procedure and an approach for potentially life-threatening problems consistent with the patient's values and preferences ("required reconsideration"). Weekly phone calls	Coaching nurse visits / phone calls Communication of patient's preference to the staff	Coaching nurse visit in the rehabilitation ward Communication of patient's preference and care difficulties to the staff (checklist): - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - pressure ulcers prevention	Coaching nurse bi-weekly phone call Communication of patient's care difficulties to the staff
Nutrition	W-4 : nutritional evaluation Nutritional plan based on measured intake W-3 : nutritional follow up - weight W-2 : nutritional follow up-weight W-1 : nutritional follow up-weight + pre-operative immunonutrition	If surgery: Care according best practice guidelines: - Consider shortened fluid fast (clear liquids up to 2 hours before anaesthesia). - Normal food intake or enteral feeding should start as early as possible	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain
Physical activity	W-4 : physical performances evaluation Physical activity plan W-3 : group physical activity W-2 : + W-1 : functional follow-up	If surgery: care according best practice guidelines: - Early physical and/or occupational therapy. - Check for orthostatic hypotension. - Review physical environment to reduce injury risk. - Assistive walking devices (eg walkers) at bedside if used as outpatient	(to the discretion of the rehabilitation unit)	Pursuing of the pre-operative physical activity plan
Medication conciliation	Centralized medication conciliation and treatment optimization (STOPP/START guidelines)	Centralized medication conciliation Advices for care according best practice guidelines (16): - Adhere to existing best practices regarding antibiotic and venous thromboembolism prophylaxis. - Ensure nonessential medications have been stopped and essential medications have been taken.	Centralized medication conciliation	Centralized medication conciliation
Standardization of surgical procedures		If surgery: consider antiseptic toothpaste If surgery: care according best practice Guidelines (16): - Consideration of regional techniques to avoid postoperative complications and improve pain control. - Directed pain history. - Multi-modal or opioid-sparing techniques. - Postoperative nausea risk stratification and prevention strategies. - Strategies to avoid pressure ulcers and nerve damage. - Prevention of postoperative pulmonary complications and hypothermia. - Judicious use of intravenous fluids. - Appropriate hemodynamic management. - Continuation of indicated cardiac medications. - Daily post-operative rounding checklist: - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - Pressure ulcers prevention If surgery: consider IV iron supplementation		

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633 Table 2: PROADAPT pilot trial: questionnaires and screening tests

Domain	
Autonomy	Activity of Daily Living Scale (ADL)
	Instrumental Activities of Daily Living scale (IADL)
Geriatric screening	G8
Physical activity	RAPA (Rapid Assessment of Physical Activity), AIPVQ
Quality of life	QLQ-C30, QLQ-ED14, EQ-5D-3L, SF-36
Locomotion and balance	Time Up and Go, SPPB (Short Physical Performance Battery)
Pain	Pain scale evaluation
Nutrition	Nutrition scale evaluation
Tiredness severity	FSS
Depression/anxiety	MNA, GDS4/GDS15
Cognitive assessment	MINI-COG
Fall risk assessment	Tinetti test
Breathlessness	Borg scale

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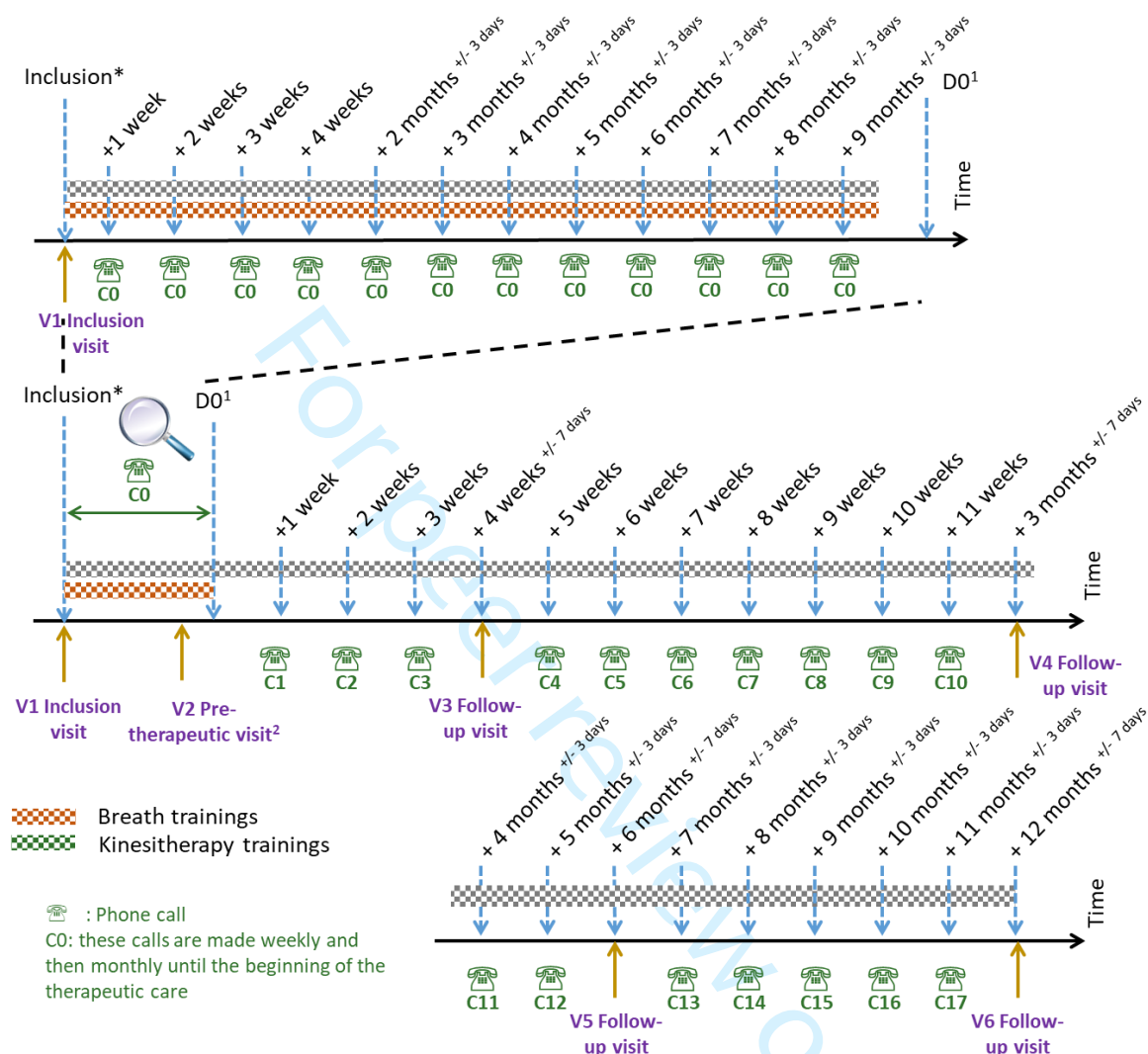
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636 Table 3: PROADAPT pilot trial: flow diagram

	Baseline	Pre-therapeutic visit (0-5 days before intervention)	M1, M3, M6	M12	End of study visit
<i>Complex geriatric assessment</i>					
G8	X			X	X
ADL/IADL	X			X	X
GDS4/GDS15	X			X	X
MINI COG	X			X	X
MNA	X			X	X
QLQ-C30	X		X	X	X
QLQ-ELD14	X		X	X	X
EQ-5D-3L	X		X	X	X
Pain scale evaluation	X	X	X	X	X
Nutrition scale evaluation	X	X	X	X	X
Socio-economic evaluation	X	X	X	X	X
<i>Physical and respiratory assessments</i>					
FSS	X		X	X	X
SF-36	X		X	X	X
Time and Go	X			X	X
SPPB	X		X	X	X
Borg scale	X			X	X
RAPA questionnaire	X		X	X	X
AIPVQ scale	X		X	X	X
Tinetti test	X			X	X
Equimog evaluation	X			X	X
Triflo	X	X			
Voldyne	X	X			
Physical activity data collection		X	X	X	X
<i>Patients' satisfaction</i>					
Standardized questionnaire					X

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Figure 1: PROADAPT program: follow-up visits and phone calls



*Inclusion is made at least 7 days before the date of surgery or the date of the first day of radiotherapy. The duration of pre-habilitation may not exceed 9 months after inclusion.

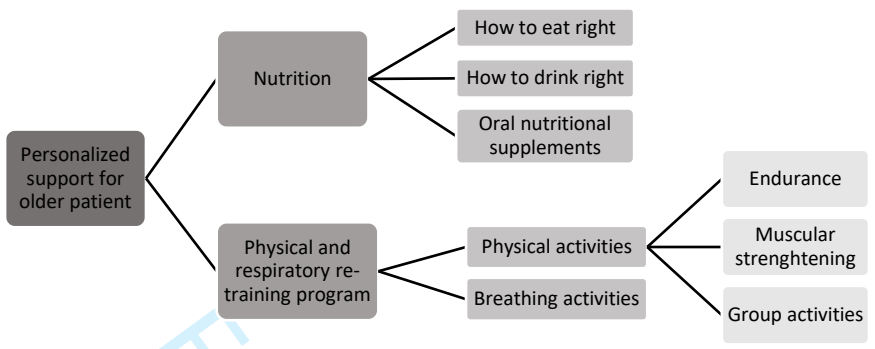
¹ D0 corresponds to the last day of radiotherapy or the last day of the revision of the surgery within 30 days after the initial operation

² Visit should be performed between 5 days before and J0

➔ Weekly calls or visits have no margin, monthly calls have a margin of +/- 3 days and visits have a margin of +/- 7 days.

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Figure 2: PROADAPT program: interventions at the patient's level





Supplementary table 1: SPIRIT 2013 checklist of the trial

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Reported on page #
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary table 2 Ref 24
Protocol version	3	Date and version identifier	17 (Ethics and Consent to participate)
Funding	4	Sources and types of financial, material, and other support	17-18 (Funding)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1 (Authors' list) 18 (Authors' contributions)
	5b	Name and contact information for the trial sponsor	Supplementary table 2 Ref 24

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	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	10 (Ethical and legal considerations) 17 (Funding)
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13 (Data management and statistical analyses) 14 (Data monitoring)
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5

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4	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
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8	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
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11		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14 (End of protocol) And N/4 (no dose modifications)
12				
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15		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	6 (two turns of validations of the PROADAPT booklet by candidate patients)
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21		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
22				
23				
24	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
25				
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31	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8-9
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36	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12-13 (Sample size calculation)
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Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A (no problem for accrual)
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Methods: Assignment of interventions (for controlled trials) N/A

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	-
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial	-

Methods: Data collection, management, and analysis

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4	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 3
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12		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
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16	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13 (Data management and statistical analyses)
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22	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13-14 (Data management and statistical analyses)
23				
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26		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
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28		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
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Methods: Monitoring

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Data monitoring

21a

Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

14 (Data Monitoring)

21b

Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial

N/A

Harms

22

Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

11 (Secondary outcomes: NCI CTCAE, QOL)

Auditing

23

Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

N/A

Ethics and dissemination

Research ethics approval

24

Plans for seeking research ethics committee/institutional review board (REC/IRB) approval

10 (Ethical and legal considerations)

Protocol amendments

25

Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)

10 (Ethical and legal considerations)
14 (Protocol amendments)

Consent or assent

26a

Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)

10-11 (Ethical and legal considerations)

26b

Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable

N/A

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4	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14 (Confidentiality)
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8	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17 (Competing interests)
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11	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17 (Availability of data and materials)
12				
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14	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
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18	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15 (Dissemination policy)
19				
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24		31b	Authorship eligibility guidelines and any intended use of professional writers	15 (Dissemination policy), N/A
25				
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27		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
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30	Appendices			
31				
32	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Annex 1 (in French)
33				
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35	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

For peer review only

Supplementary table 2: All items from the World Health Organization Trial Registration Data Set (SPIRIT item 2b)

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT03659123
Date of registration in primary registry	September 6, 2018
Secondary identifying numbers	69HCL16_0701 ID RCB N° 2018-A001026-49
Source(s) of monetary or material support	Agence Régionale de Santé Auvergne Rhône Alpes
Primary sponsor	Hospices Civils de Lyon
Secondary sponsor(s)	
Contact for public queries	David Dayde, +33.4.78.86.37.74, david.dayde@chu-lyon.fr
Contact for scientific queries	Claire Falandry, +33.4.78.86.66.34, claire.falandry@chu-lyon.fr
Public title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer
Scientific title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer, a Multicenter Pilot Study
Countries of recruitment	France
Health condition(s) or problem(s) studied	Old Injury
Intervention(s)	Behavioral: standardized geriatric intervention Nutritional care is based on: <ul style="list-style-type: none"> • A personalized evaluation of nutritional balance and nutritional needs of the patient • A weekly follow-up of weight and nutritional intake Total-body rehabilitation is based on: <ul style="list-style-type: none"> • 2 to 3 times a week: strength exercise • 2 to 3 times a week: endurance exercise, 20 to 45 min each sequence • 2 times a week: respiratory physiotherapy Pharmaceutical conciliation and optimization according STOPP/START criteria During peri-operative time, the nurse contacts the surgical team for transmission of patient's personal data, physical medication conciliation results During rehabilitation time and hospital-home transition time, the nurse contacts

Data category	Information
	the rehabilitation team for transmission of patient's personal data and care course, physical (nutritional, functional and/or comorbidities), medication conciliation results.
Key inclusion and exclusion criteria	<p>Inclusion Criteria:</p> <p>Patient ≥ 70 year old OR patient ≥ 60 years with significant comorbid condition (modified Charlson index ≥ 3) or disability (ADL score $< 6/6$);</p> <p>Histologically or cytologically proven cancer.</p> <p>Life expectancy > 3 months.</p> <p>Written informed consent obtained</p> <p>Covered by a Health System where applicable.</p> <p>Exclusion Criteria:</p> <p>Other malignancy within the last 5 years, except for adequately treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled limited basal cell skin cancer.</p> <p>Patient unable to be regularly followed for any reason (geographic, familial, social, psychological).</p> <p>Any mental or physical handicap at risk of interfering with the appropriate treatment.</p> <p>Any administrative or legal supervision where applicable</p>
Study type	<p>Interventional</p> <p>Allocation: N/A</p> <p>Intervention model: Single Group Assignment</p> <p>Masking: None (Open Label)</p> <p>Primary purpose: Health Services Research</p> <p>Phase II</p>
Date of first enrolment	July 3rd, 2018
Target sample size	122
Recruitment status	Recruiting
Primary outcome(s)	<p>Implementation of at least one item of PROADAPT standardized geriatric intervention of the program PROADAPT pilot study [Time Frame: 12 months]:</p> <ul style="list-style-type: none"> • Preoperative physical activity including strength and endurance exercise assessed by physical exercises accomplished under the supervision of a physiotherapist. Number of patients with at least 1 intervention achieved in the domain. • Nutrition guidelines before and after physical activity assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain.

Data category	Information
	<ul style="list-style-type: none"> • Patient education and coaching assessed by questionnaires and visits. Number of patients with at least 1 intervention achieved in the domain • Achievement of standardized intervention procedures, according to the checklist established in consensus with surgeons. Number of patients with at least 1 intervention achieved in the domain • Rehabilitation assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain • Accomplishment of pharmaceutical medication conciliation and treatment optimization. Number of patients with at least 1 intervention achieved in the domain • Bridging interventions for hospital-to-home transition. Number of patients with at least 1 intervention achieved in the domain
Key secondary outcomes	<ul style="list-style-type: none"> • Post operative morbidity [Time Frame: 30 and 90 days] according Clavien-Dindo classification • Post-operative morbidity [Time Frame: 90 days] according to NCI CTC v4.4 • Therapeutic strategy [Time Frame: 12 months]: Treatment plan completion rate: Number of patients for whom the treatment plan was completed. • Progression-free Survival [Time Frame: 12 months] • Post-treatment complication [Time Frame: 12 months]: Post-treatment complication grade\geq3 according the National Cancer Institute Common Toxicity Criteria version 4 (NCI-CTC-v4)



Supplementary table 1: SPIRIT 2013 checklist of the trial

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Reported on page #
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary table 2 Ref 24
Protocol version	3	Date and version identifier	17 (Ethics and Consent to participate)
Funding	4	Sources and types of financial, material, and other support	17-18 (Funding)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1 (Authors' list) 18 (Authors' contributions)
	5b	Name and contact information for the trial sponsor	Supplementary table 2 Ref 24

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4		5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities
5			10 (Ethical and legal considerations)
6			17 (Funding)
7			
8			
9		5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)
10			13 (Data management and statistical analyses)
11			14 (Data monitoring)
12			
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14			
15	Introduction		
16			
17	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention
18			3
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22		6b	Explanation for choice of comparators
23			N/A
24	Objectives	7	Specific objectives or hypotheses
25			4
26	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
27			5
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32	Methods: Participants, interventions, and outcomes		
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34	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained
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Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14 (End of protocol) And N/4 (no dose modifications)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	6 (two turns of validations of the PROADAPT booklet by candidate patients)
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8-9
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12-13 (Sample size calculation)

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4 Recruitment 15 Strategies for achieving adequate participant enrolment to reach target sample size N/A (no problem for accrual)
5
6

7 **Methods: Assignment of interventions (for controlled trials)**

N/A

8
9 Allocation:

10 Sequence generation 16a Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions -
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17 Allocation concealment 16b Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned -
18 mechanism
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22 Implementation 16c Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions -
23
24
25 Blinding (masking) 17a Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how -
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28 17b If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial -
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32 **Methods: Data collection, management, and analysis**

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Data collection methods

18a

Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

Table 3

18b

Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

N/A

Data management

19

Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

13 (Data management and statistical analyses)

Statistical methods

20a

Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

13-14 (Data management and statistical analyses)

20b

Methods for any additional analyses (eg, subgroup and adjusted analyses)

N/A

20c

Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

N/A

Methods: Monitoring

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4	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	14 (Data Monitoring)
5				
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11		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
12				
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14				
15	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11 (Secondary outcomes: NCI CTCAE, QOL)
16				
17				
18				
19	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
20				
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22				
23	Ethics and dissemination			
24				
25	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	10 (Ethical and legal considerations)
26				
27				
28	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	10 (Ethical and legal considerations) 14 (Protocol amendments)
29				
30				
31				
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34	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11 (Ethical and legal considerations)
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37				
38		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14 (Confidentiality)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17 (Competing interests)
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17 (Availability of data and materials)
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15 (Dissemination policy)
	31b	Authorship eligibility guidelines and any intended use of professional writers	15 (Dissemination policy), N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Annex 1 (in French)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

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3 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on
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BMJ Open

Feasibility of a prehabilitation program dedicated to older cancer patients before complex medico-surgical procedures: the PROADAPT pilot study protocol

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	Lyon, CarMeN Laboratory, Inserm U1060, INRA U1397, Université Claude Bernard Lyon 1, INSA Lyon, Charles Mérieux Medical School
Primary Subject Heading :	Oncology
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Keywords :	Adult oncology < ONCOLOGY, GERIATRIC MEDICINE, REHABILITATION MEDICINE, Adult surgery < SURGERY





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4 1 **Feasibility of a prehabilitation program dedicated to older cancer**
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6 2 **patients before complex medico-surgical procedures: the PROADAPT**
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8 3 **pilot study protocol**
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25 **Abstract**

26 **Background:** Aging is associated with an increased prevalence of co-morbidities and sarcopenia and
27 with a decline of functional reserve of multiple organ systems, eventually leading in the context of the
28 disease- and/or treatment-related stress to functional deconditioning or organ failure. The
29 multicomponent intervention “PROADAPT” was built multi-professionally to implement
30 prehabilitation in older cancer patients.

31 **Methods:** PROADAPT-pilot study is an interventional, non-comparative, prospective, multicenter
32 study. It will include 122 patients oriented to complex medico-surgical curative procedures (major
33 surgery or radiation therapy +/- chemotherapy). After informed consent, patients will undergo a
34 comprehensive geriatric assessment and will be offered a prehabilitation kit “PROADAPT” including an
35 advices booklet with personalized objectives and respiratory rehabilitation devices. Patients will then
36 be called weekly and monitored for physical and respiratory rehabilitation, pre-operative re-nutrition,
37 motivational counseling, and iatrogenic prevention. Six outpatient consultations will be planned at
38 inclusion, few days before the procedure, at 1, 3, 6 and 12 months after the end of the procedure. The
39 main outcome of the study is the feasibility of the intervention, defined as the ability to perform at
40 least one of the components of the program. Clinical data collection will include patient-specific and
41 cancer-specific characteristics.

42 **Ethics and dissemination:** Study protocol and several amendments were ethically approved by Ile de
43 France 8 Ethics Committee on May 3, 2018. The results of the primary and secondary objectives will
44 be published in peer-reviewed journals. ClinicalTrials registration: NCT03659123.

45 **Keywords:** oncogeriatrics, prehabilitation, motivation, sarcopenia, older cancer patients, care
46 pathway.

48 **Article summary**

49 Strengths and limitations of this study

- 50 - PROADAPT program is a prehabilitation program specifically tailored for older cancer patients
- 51 - The program was designed according a multidisciplinary analysis of available evidence and
52 according a multistep validation process involving patients
- 53 - PROADAPT pilot trial is a prospective and multicenter trial designed to evaluate the feasibility
54 of the intervention
- 55 - Different secondary outcomes including quality of life will be collected to better adapt the
56 program to patients’ specificities

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57 A specific attention will be paid on program safety and patients' adherence to the program.

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60 Introduction

61 Many oncological situations involve complex medical-surgical procedures at risk of patient's
62 deconditioning. Surgery or complex medico-surgical procedures can be considered as one proof-of
63 principle of such risks, since major cancer surgery exposes the older population to a higher risk of
64 morbi-mortality and unplanned hospitalization for geriatric events (1). Outpatient treatments and
65 rapid post-operative rehabilitation strategies are used to decrease post-operative deconditioning but
66 do not take geriatric risk factors into account. The deconditioning of older patients, not anticipated,
67 can thus lead to prolonged and iatrogenic hospitalizations such as immobilization syndrome, acute
68 confusion, undernutrition, falls, de novo urinary incontinence and adverse drug events, generating
69 frustration, appeals by patients and their families and additional hospital costs.

70 In order to reduce complications after surgery, prehabilitation has often been considered, and it can
71 be estimated that a majority of surgeons would accept a 4 weeks delay before surgery to improve
72 older patients' outcomes if shown to be beneficial (2–9). However, the actual level of evidence
73 depends on the interventions: high for pre-operative nutrition (10), but low for physical exercise, due
74 to heterogeneous programs with often bad adherence (11). In addition, geriatric validated
75 interventions, in order to prevent iatrogenic event, may be added in a multi-interventional model of
76 intervention.

77 To date, the interventions likely to prevent geriatric deconditioning include nutritional care, pre-
78 therapeutic (prehabilitation) and post-therapeutic (rehabilitation) physical reconditioning, iatrogenic
79 prevention (drug and care system-related) and hospital-to-home transition to limit the risk of early
80 readmission of patients. Nevertheless, the level of evidence for each of these care segments remains
81 limited, and not specific to the oncogeriatric population. Indeed, studies about more specific care have
82 already been carried out but do not consider all of the above interventions (12). Moreover, cancer in
83 the older patient is often associated with comorbidities, particularly cardiovascular disease (13,14).
84 The older population also has a higher risk of loss of autonomy and cognitive impairment, which can
85 be increased with surgery (15–17). In response to the growing population of older cancer patients, a
86 modification of oncological care and the implementation of specific geriatric interventions have been
87 developed (18–20).

88 PROADAPT (Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning risk and
89 Accompaniment of Patients' Trajectories) is a geriatric intervention program constructed on a multi-
90 professional and multi-disciplinary basis after a systematic analysis of published data. It includes: 1)
91 before surgery: prehabilitation of patients, including nutritional, physical, respiratory and motivational
92 counselling; 2) during hospitalisation for surgery (if performed): optimization of their treatment by
93 pharmaceutical reconciliation, educational interventions, standardization of surgical interventions and

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3 94 improved rehabilitation after surgery; 3) bridging and post-discharge interventions for hospital-to-
4 home transition (table 1).

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8 97 **Methods and analysis**

10 98 **Objectives**

11 99 *Primary objective*

12
13 100 The primary objective of the PROADAPT pilot study is to assess the feasibility of the program, defined
14 as the achievement of at least one item of the program during patient's follow up.
15 101
16 102

17 103 *Secondary objectives*

18 104 The secondary objectives of the study are:

- 19 105 1) To assess the achievement of each item of the program independently of each other (rate of
20 achievement of all or part of the instructions);
- 21 106 2) To assess patients' satisfaction with the program;
- 22 107 3) To estimate the rate of adherence to items during the various visits;
- 23 108 4) To appreciate the longitudinal evolution over 1 year.

24 109
25 110 In addition to these secondary objectives, a series of parameters will be measured and monitored
26 in this order:
27 111

- 28 112 5) To assess patients' post treatment complications according Clavien Dindo and NCI-CTC version
29 4 scoring systems(21);
- 30 113 6) To estimate the rate and the nature of post-operative complications according to the CCI index
31 at 30 and 90 days;
- 32 114 7) To estimate the post-operative mortality at 30 and 90 days;
- 33 115 8) To estimate the costs of treatments (health system, patients);
- 34 116 9) To study the therapeutic strategies (treatment completion rate);
- 35 117 10) To estimate the progression-free survival rate at one year (PFS);
- 36 118 11) To estimate the overall survival rate at one year (OS);
- 37 119 12) To study the physical performance tests and the evolution of these performances through the
38 proposed exercises;
- 39 120 13) To study the other dimensions of quality of life relating to health at 3 months;
- 40 121 14) To estimate the longitudinal evolution of QoL;
- 41 122 15) To estimate the tolerance of treatments;

1
2
3 126 16) To estimate the evolution of geriatric covariates.
4

5 127 **Study design**
6

7
8 128 PROADAPT - pilot phase is a second category interventional study involving the Human Person with
9 129 minimal risks and constraints excluding health products. It is a prospective, non-comparative
10 130 multicenter opened in different centers of Auvergne-Rhône-Alpes region, France (n=7).
11
12

13 131 **Study sites and participants**
14

15
16 132 The study population will include older patients identified during multidisciplinary consultation
17 133 meetings and oriented to complex medico-surgical curative procedures in the including centers (Lyon
18 134 Sud Hospital, Croix Rousse Hospital and Edouard Herriot Hospital from the Hospices Civils de Lyon,
19 135 Nord-Ouest Villefranche-sur-Saône Hospital, Annecy-Genevois Hospital, Chambéry Hospital, Lyon-
20 136 Villeurbanne Médipôle).
21
22

23
24 137 Inclusion criteria are: patient aged 70 and over or 60 and over with significant comorbid condition
25 138 (CIRS-G ≥ 3 (22)) or disability (ADL score $< 6/6$ (23)), histologically or cytologically proven cancer, life
26 139 expectancy > 3 months planned for a complex medico-surgical procedure in a curative intent. Complex
27 140 medico-surgical procedures are defined as major abdominal surgery (breast excluded) either minimally
28 141 invasive or open.
29

30 142 Exclusion criteria are: patient with other malignancy within the last 5 years (except for adequately
31 143 treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled
32 144 limited basal cell skin cancer), unable to be regularly followed for any reason (geographic, familial,
33 145 social, psychologic) or with any mental or physical handicap at risk of interfering with the appropriate
34 146 treatment.
35

36 147 A screening of older patients will be systematically performed during multidisciplinary meetings and
37 148 described in the CONSORT diagram of the study.
38
39

40 149 **Intervention**
41

42 150 PROADAPT intervention program was built according to a multi-dimensional and multidisciplinary
43 151 basis. From January 2016 to April 2018, nine regional meetings were organized, gathering 40
44 152 representatives of the following medical and paramedical specialties: geriatricians, nutritionists,
45 153 surgeons (subspecialties: gynaecology, digestive surgery, urology), oncologists, anaesthesiologists,
46 154 nurses, physiotherapists, occupational therapists, adapted physical activity monitors. A systematic
47 155 review of published data was done in the following axes, in order to provide a graded state-of-the-art:
48 156 nutrition, physical activity, patient education, medication rationalization, cardiovascular optimization,
49 157 transition and standardization of surgical procedures. Based on the qualitative grading of existing data,
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3 158 a modified DELPHI method was performed, in order to co-validate the content of the standardized
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5 159 intervention checklist, and the feasibility of the implementation of each point of this checklist (Table
6
7 160 1).

8
9 161 A PROADAPT booklet was built, in order to propose a standardized, adapted and evolutive tool
10
11 162 designed to explain physical exercise and nutrition counselling and to insure a follow-up of patients'
12
13 163 day-to-day achievements. This first version was tested by candidate patients during two turns of
14
15 164 validation before the validation of the current version 3 of the booklet.

16 165 PROADAPT standardized geriatric intervention program includes:

- 17
18 166 - Pre-operative physical activity including strength and endurance exercise +/- group activities
19
20 167 during 4 +/-2 weeks. Interventions with high level of evidence were retained, according to an ongoing
21
22 168 systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42020100110; (24,25));
23
24 169 - Nutrition: nutrition before and after physical activity, pre-postoperative immuno-nutrition +/-
25
26 170 artificial nutrition (ie enteral or parenteral nutrition) according international guidelines (10);
27
28 171 - Patient (and caregiver) education and coaching (on nutrition, physical exercise) according to a
29
30 172 weekly schedule with the activation of integrated supports by hetero- and self-management (26);
31
32 173 - Standardized intervention procedures, according to a checklist established in consensus with
33
34 174 surgeons' representatives;
35
36 175 - Enhanced rehabilitation will be promoted according to international guidelines (27);
37
38 176 - Pharmaceutical medication conciliation, treatment optimization, according a centralized
39
40 177 process with pharmaceutical expertise;
41
42 178 - Bridging interventions for hospital-to-home transition, according to a proposed standardized
43
44 179 procedure including training of dedicated nurses, and post-discharge phone-calls follow-up during 12
45
46 180 weeks after surgery. In practice, only 2 or 3 people from the coordination team are in charge of
47
48 181 coaching for all patients. In the future, a "special nurse coach" will be trained in each center and
49
50 182 responsible of patients' coaching. Interventions with high level of evidence were retained, according
51
52 183 to an ongoing systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42017055698).

53 184 The intervention is designed to be implemented at different times of patients' care (table 1).

54 185

55 186 *During the prehabilitation time:*

- 56 187 • A dedicated nurse, trained in patient education by the coordination team ("coaching nurse")
57
58 188 presents him/herself to the patient for:
59
60 189 - Presentation of the program to the patient and his/her caregiver(s)
190
- Personalization of the PROADAPT booklet (see after) to the patient's characteristics

- 1
2
3 191 - Collection of personal data, nutritional and functional habits
4
5 192 - Evaluation of psycho-cognitive context using questionnaires (GDS4/GDS15, MNA,
6 193 MINI-COG)
7
8 194 - Gathering of the information needed: comorbidities, comedications (for transmission
9 to the centralized pharmaceutical expertise)
10 195
11 196 - Anticipation and organization of the future appointments (anesthesiologist,
12 stomatherapist, ...)
13 197
14
15 198 - A weekly visit or phone call according to a structured interview for health education
16 199 and transmission of nutritional and functional advices (see after)
17
18 200 • Nutritional care is based on:
19
20 201 - A personalized evaluation of nutritional balance and nutritional needs of the patient
21 according to dietician diagnosis based on measured intake and international
22 202 recommendations
23 203
24
25 204 - A weekly follow-up of weight and nutritional intake. If the coaching nurse identifies an
26 205 unfavorable nutritional trend, she reports it to the referring physician and nutritionist
27
28 206 - Artificial nutrition if needed according ESPEN recommendations (10,28,29)
29
30 207 - Pre-operative immune-nutrition during 7 days before surgery (29)
31
32 208 • Total-body rehabilitation:
33 209 - 2 to 3 times a week: strength exercise (each time with dedicated exercises for upper
34 members, legs and abs, 20 to 45 minutes each sequence)
35 210
36 211 - 2 to 3 times a week: endurance exercise (walk or cycle ergometer), 20 to 45 min each
37 212 sequence
38
39 213 - 3 times a day: respiratory physiotherapy
40
41 214 - Once a week (if possible): group activities (according to the center organization and
42 215 home-hospital distance)
43
44 216 • Pharmaceutical conciliation and optimization according to STOPP/START criteria and
45 217 international recommendations about peri-operative care (30): to be transmitted to the surgical and
46 218 anesthesia team without any obligation.
47
48
49 219
50
51
52 220 *During peri-operative time*
53
54 221 • The coaching nurse contacts the surgical team for transmission of:
55 222 o patient's personal data
56 223 o physical (nutritional, functional and/or comorbidities) as well as psychological
57 224 difficulties
58
59 225 o medication conciliation results
60

226

227 *During rehabilitation time*

- 228 • The coaching nurse contacts the rehabilitation team for transmission of:
 - 229 o patient's personal data and care course
 - 230 o physical (nutritional, functional and/or comorbidities) as well as psychological
 - 231 difficulties
 - 232 o medication conciliation results
- 233 • The rehabilitation program is left at the discretion of the rehabilitation team (standard care
- 234 and local habits).
- 235 • A weekly phone call of the coaching nurse to the rehabilitation team for nutritional and
- 236 functional follow-up as well as medication conciliation

237

238 *During hospital-home transition time*

- 239 • The coaching nurse contacts the patient's general practitioner for transmission of:
 - 240 o patient's personal data and care course
 - 241 o physical (nutritional, functional and/or comorbidities) as well as psychological
 - 242 difficulties
 - 243 o medication conciliation results
- 244 • Bi-weekly phone call of the coaching nurse to the patient for nutritional and functional follow-
- 245 up
- 246 • Advices for optimization of symptoms management: abdominal pain, nausea, vomiting...

247

248 Participant timeline

249 Six successive evaluations are planned for the participants.

250 *The inclusion visit* is planned during a geriatric consultation planned before the start day of the complex
251 medico-surgical procedure, at least 7 days before start date. If the start date is delayed for any reason
252 or the patient is included into a neo-adjuvant treatment, the prehabilitation time may be prolonged
253 until 9 months. In that case, the frequency of the phone calls is decreased (from 1/week to 1/month)
254 after 4 weeks. During the inclusion visit, lasting about 1 hour, the following steps are planned:

- 255 - Clinic (blood pressure, heart rate, ECOG scale(31), patient's comorbidities), biologic (albumin,
256 prealbumin, C-reactive protein) and paraclinic (year of birth, gender, weight, height, body
257 mass index, weight evolution over the last 3 and 6 months) data collection
- 258 - All concomitant treatments and drug conciliation

- 1
2
3 259 - The history of the disease (primitive site, metastasis, histology of the initial tumor, presence
4 of tumor markers)
5 260
6 261 - Radiological disease assessments (date and nature)
7
8 262 - A standardized geriatric assessment using validated questionnaires with a particular attention
9 on physical activity and nutrition (ADL(23)/iADL(32), G8 (33), RAPA (34), AIPVQ (35), QLQ-C30
10 263 (36), QLQ-ED14 (37), EQ-5D-3L (38), SF-36 (39), SPPB (40), FSS (41), MNA (42), GDS4/GDS15
11 264 (43), MINI-COG (44), Tinetti test (45), Borg scale (46), Pain scale (47), Nutrition scale (48))
12
13 265 **(Error! Reference source not found.tables 2 and 3) .**
14 266
15 267 - Delivery of the “PROADAPT kit” device during a meeting with a dedicated paramedic (nurse,
16 268 physiotherapist, ergotherapist...) in order to:
17
18 269 ○ Provide to the patient VOLDYNE® and TRIFLO® devices for inspiratory training
19 270 ○ Present the PROADAPT booklet that includes a battery of exercises and nutritional
20 271 counselling specifically designed for this older population:
21
22 272 ▪ muscle strengthening of upper limbs (6 exercises, 3 difficulty levels), lower
23 273 limbs (6 exercises, 3 difficulty levels), abdominal wall (4 exercises, 3 difficulty
24 274 levels) (objective: 2 to 3 sessions per day for a total time between 20 and 45
25 275 minutes)
26 276 ▪ endurance/aerobic activities (7 exercises, 3 difficulty levels with 3 duration
27 277 objectives, objective: every day)
28 278 ▪ inspiratory training with VOLDYNE® and TRIFLO® devices (objective: 3 sessions
29 279 per day for a total time of 30 minutes)
30 280 ▪ general nutritional counselling adapted to the older population: food
31 281 enrichment, inter-meals collations, oral nutritional supplements.
32 282 ○ A fulfilling of 3-day food statement allows, in the 7 days after inclusion, to deliver a
33 283 dietician-driven personalized nutritional counseling. If needed, in case of unfavorable
34 284 nutritional parameters, artificial nutrition is introduced.
35
36 285 - Delivery, if needed, of medical prescription:
37
38 286 ○ for home physiotherapy according PROADAPT program for respiratory training
39 287 sessions and physical activity training sessions
40 288 ○ For oral nutritional supplements
41 289 ○ For usual medicines, including pharmaceutical review
42
43 290 - For patients requiring inpatient follow-up, hospital admission for a few days in a rehabilitation
44 291 unit for a physiotherapeutic program and/or artificial nutrition (enteral preferred).
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292 During pre-intervention time, phone calls are planned by a dedicated paramedic (once a week for the
293 first 4 weeks and then once a month until the intervention). Calls are semi-directed interviews focused
294 on the patient's autonomy, physical activity, appetite and sleep over the last period (week/month). A
295 special attention is paid on encouraging patient's motivation and adherence to the program.

296 *The pre-therapeutic visit* is scheduled when possible between 5 days and the day of the intervention.
297 This visit is performed in the surgery or radiotherapy unit only if the visit is necessary before the
298 intervention still without modifying the standard therapeutic care for:

- 299 - Clinic, biologic and paraclinic data collection
- 300 - All concomitant treatments and drug conciliation
- 301 - Questionnaires about pain, nutrition, fitness and physical tests (table 2 and 3)
- 302 - Therapeutic care data collection (date, nature, entitled, reason)

303 During post-intervention time, paramedics trained in clinical research will resume follow-up calls as
304 before the intervention once a week during 12 weeks after D0 and once a month up to 12 months after
305 D0. The D0 date is determined as the last day of surgery (day of the last resumption of surgery in the
306 limit of 30 days after the first intervention) or the last day of the radiotherapy. For weekly calls, a
307 margin of +/- 2 days is allowed and for monthly calls, a margin of +/- 7 days is allowed.

308 *Visits at 1, 3 and 6 months after the intervention (+/- 7 days):* The patient may have started an
309 antineoplastic treatment according to standard of care. The visit could be performed with the surgeon,
310 the radiotherapist or the oncologist according local habits:

- 311 - Clinic (blood pressure, heart rate, ECOG scale(31)), biologic (albumin, prealbumin, C-reactive
312 protein) and paraclinic (weight, body mass index) data collection
- 313 - All concomitant treatments and drug conciliation
- 314 - Patient care data (surgery and complications, treatment for the cancer)
- 315 - Radiological disease assessments (date and nature)
- 316 - Questionnaires about quality of life, pain, nutrition, fitness and physical tests (table 2 and 3)
- 317 - Socio-economic assessment with patient's care data (date, nature of acts, designation, reason)

318 *The end of study visit* is planned at 12 months (per-protocol) or at the date of trial premature
319 discontinuation (+/- 7 days) for a final assessment of the same outcomes as previously listed. When
320 requested, if previous visits were omitted, a final assessment of all the complications during the post-
321 therapeutic period is performed.

322 **Outcomes and measurements**

1
2
3 323 **Primary outcome**
4

5 324 The main outcome measure will be the percentage of patients who have completed at least one item
6
7 325 in the PROADAPT program after 12 months after the start of therapeutic treatment. The start of
8
9 326 treatment is defined in this study by the last day of surgery (date of the last recovery within the limit
10
11 327 of 30 days after the date of the initial intervention) or the last day of radiotherapy. The workshops of
12
13 328 the program are:

- 14 329 - Physical and respiratory rehabilitation
- 15 330 - Re-nutrition session
- 16
17 331 - Telephone nurse follow-up
18

19 332

20 333

21 334 **Secondary outcomes**
22
23

24 335 The secondary outcomes of the study are:
25

26
27 336 - To evaluate the feasibility of each stage of the program independently of each other (rate of
28
29 337 achievement of all or part of the instructions)

30 338 ○ Pre-operative physical rehabilitation including (figure 1):

- 31
32 339 • Muscle strengthening
- 33
34 340 • Respiratory rehabilitation
- 35
36 341 • Endurance work

37 342 ○ Pre-operative nutrition counselling (figure 1)

38 343 ○ Drug reconciliation / iatrogenic prevention

39 344 ○ Pre-therapeutic follow-up calls

40 345 ○ Post-surgery or post-radiotherapy follow-up calls
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44 346

45 347 - To estimate patients' satisfaction with the overall program, at the end of the study (end of follow-up
46
47 348 or study discontinuation) using a questionnaire (Supplemental material).

48
49 349 - To estimate the rate of adherence to the items (physical activity, nutrition and nursing follow-up)
50
51 350 during follow-up time. To evaluate this criterion, various parameters will be recorded: physical activity
52
53 351 duration (in h/week), kinetics (duration (% increase), level of difficulty), respiratory activity, food intake
54
55 352 during phone calls.

56
57 353 - To assess the longitudinal evolution over 1 year of:

- 58 354 ○ patient's physical performance (SPPB, gait speed, TUG test) and functional independence on
59
60 355 ADL (23), IADL (32), AIPVQ (49)

- 356 ○ nutritional parameters of the patient (weight, albuminemia, appetite)
- 357 ○ health-related quality of life for patients based on QLQ-C30 and ELD14 (5 dimensions: mobility,
- 358 disease burden, emotional and physical functioning, tiredness) (50,51)
- 359 ○ pharmaceutical conciliation

360

361 In parallel to these secondary objectives, a series of parameters will be measured and monitored in
362 order to:

- 363 - Estimate the rate and nature of post-operative complications at 30 days (NCI-CTCAE)
- 364 - Estimate the rate and nature of post-operative complications according to the CCI at 30 and 90 days
- 365 - Estimate post-operative mortality at 30 and 90 days
- 366 - Estimate the overall one-year survival rate (OS)
- 367 - Estimate the one-year progression-free survival rate (PFS)
- 368 - Estimate the longitudinal evolution of QoL according to QLQ C30, ELD14, EQ-5D
- 369 - Estimate treatment costs (health system, patients)
- 370 - Study therapeutic strategies (treatment completion rate)
- 371 - Estimate the evolution of geriatric covariates.

372

373 **Sample size calculation**

374 The program will be considered feasible, at the patient level, if all or part of the program is
375 implemented in at least 50 % of the included patients (= alternative hypothesis). This threshold was
376 defined in line with previous studies on prehabilitation for older cancer patients, that showed
377 compliance rates between 16 and 95% (52,53). Considering that PROADAPT program is highly complex
378 even if tailored for older patients, we anticipate modest compliance rates.

379 The calculation of the number of subjects needed was done as follows: to reject the null hypothesis of
380 the program feasibility rate lower than 35 %, with a first alpha species risk of 5 % and a power of 90 %
381 (beta=10 %, bilateral test), the number of subjects to be analyzed is 111. Including 10 % non-treatable
382 patients, a total of 122 patients should be included. The included patients will be analyzed with
383 intention-to-treat.

384 **Data management and statistical analyses**

385 Data are monitored by a clinical research associate (CRA). Inconsistencies will be reported to the study
386 investigators in order to decide whether the data should be corrected or considered as missing data.
387 Any changes in the data will be reported.

1
2
3 388 Data analyses will be performed by the data management and analysis centre. The analyses will be
4
5 389 carried out by an independent statistician with the latest version of the R software environment.
6
7 390 All of the characteristics collected will be subjected to a descriptive analysis.
8
9 391

392 ***Descriptive analyses***

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11
12
13 393 A flow-chart diagram will describe the data available for the patient population at baseline, and during
14
15 394 each follow-up visit. Eligibility criteria for treated patients will be verified, as well as follow-up and end
16
17 395 of study visits. Reasons for premature end of study will be provided.

18
19 396 Characteristics of the study population and proportions of missing values will be reported. Patient
20
21 397 characteristics will be described using mean and standard deviation or median and interquartile range
22
23 398 for quantitative variables, and frequencies and distribution for categorical variables. A comparison of
24
25 399 baseline characteristics between patients with complete follow-up and those with attrition will be
26
27 400 performed. If needed, methods for handling missing data (multiple imputation, mixed model or
28
29 401 auxiliary variable) will be used when appropriate.
30
31 402

31 403 ***Primary analysis***

32
33 404 The percentage of patients who have completed at least one PROADAPT program activity at the end
34
35 405 of 12 months after the start of treatment will be estimated using mean and standard deviation.

36 37 406 ***Secondary analyses***

38 39 407 **Time-to-event variables: follow-up, overall survival, progression free survival**

40
41
42 408 The proportion of events at specific measurement times will be estimated according to the Kaplan-
43
44 409 Meier curve. Medians of event-free survival will be reported by treatment arm with its 95 % confidence
45
46 410 interval (95 % CI), if the number of events allows estimation of the median.

47
48 411 Overall survival rate and progression free survival rate at 12 months (after the day of the last revision
49
50 412 of surgery or the last day of radiotherapy) will be provided with 95 % CI.

51 413 **Quality of life**

52
53
54 414 Analyses of the QoL data will be performed with modified intention to treat (mITT): all included
55
56 415 patients, regardless of compliance with the eligibility criteria and whether or not they were followed
57
58 416 up and for whom the QoL scores at inclusion will be included in the analysis. Patients' quality of life,
59
60

1
2
3 417 linked to health, will be analysed after 3 months through 5 dimensions: mobility, disease burden,
4
5 418 emotional and physical functioning, tiredness.
6

7 419

8 9 420 ***Data monitoring***

10
11 421 The successful completion of the database is ensured by the hospital CRA. The hospital CRA also
12
13 422 ensures compliance with the study protocol. The sponsor CRA verifies that the rights of the participants
14
15 423 are respected.
16

16 424

17 18 425 ***End of protocol***

19
20 426 Patients leave the study either on a per-protocol basis during the “end of study visit” on month 12
21
22 427 after the intervention or at any time during the conduct of the study if they no longer wish to
23
24 428 participate. However, as indicated in the information letter to the patients/caregivers, the data
25
26 429 collected before exclusion may be used as part of the study.
27

27 430

28 29 431 ***Confidentiality***

30
31 432 Correspondence tables will be kept in a separate file that does not contain clinical data. The access to
32
33 433 the nominative information is protected by a password and confidentiality is guaranteed by the study.
34

34 434

35 36 435 ***Protocol amendments***

37
38 436 Any important modifications requiring a new ethics committee approval will be communicated in
39
40 437 future publications. Any potential impact of protocol modifications on the results will be discussed as
41
42 438 appropriate.
43

43 439

44 45 440 ***Trial status***

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47 441 Patient enrolment began on July 3, 2018. Data are collecting.
48

49 442

50 51 443 ***Patients' and public involvement***

52
53 444 Patients were involved at different steps of the trial: (i) during PROADAPT booklet conception, several
54
55 445 (30) patients were asked to answer an anonymous questionnaire in order to improve its ergonomics;
56
57 446 (ii) the information note and consent form of the protocol have been re-read by the patients' review
58
59 447 committee of the Ligue Nationale de Lutte contre le Cancer (a French association of cancer patients).
60

60 448

449 **Discussion**

450 **Discussion of the intervention**

451 Prehabilitation has long been conceptualized as an effective means of improving the functional
452 capacity of the individual to enable him to resist various stressors. Originally developed in the military
453 as the association of physical training to improve strength and endurance, improving nutritional intake
454 and general education (54), it has been transposed into medicine and major surgery – initially when
455 an ICU admission is planned - at the beginning of this century (55).

456 Despite a growing interest in the medical community for prehabilitation and particularly cancer
457 prehabilitation, the level of evidence for specific interventions stays too low to be implemented in
458 common care. Among the main disadvantages of published data include the heterogeneity of
459 programs, sometimes poor patient adherence and the fact that most studies were small pilot studies
460 developed for patients more fit and younger than those who should make the best part of
461 prehabilitation. Another point to emphasize is that most programs include only one intervention -
462 physical, nutritional, or psychological rehabilitation - when multimodal interventions are often
463 considered to be more effective in older populations.

464 Considering these points, the PROADAPT intervention was developed according to an innovative
465 management strategy since it started in 2016 by multi-professional meetings conceived as
466 brainstorming sessions in order to develop a multidisciplinary program dedicated to prehabilitation
467 and follow-up of older patients. The multidisciplinary conception of the intervention, the particular
468 attention paid to older patients' specificities and the previous experience of the participants in as
469 various fields as patients' education, cognition, physiotherapy were hopefully the warrants of the most
470 tailored approach to the target population. For example, the booklet typography was of big character
471 font and the illustrations highly schematic with high contrast. Each sentence was verified by a panel of
472 patients in order to insure proper understanding. Finally, the booklet was evaluated by 30 patients,
473 with a high rate of satisfaction (Ravot et al, PROADAPT Pilot trial: A survey on patients' expectations
474 and satisfaction, unpublished data).

475 This pilot study is the first step towards an ambitious program, since PROADAPT program will be
476 declined in the future into two randomized studies, PROADAPT-ovary/EWOC-2 (NCT04284969) and
477 PROADAPT sus-mesocolic, designed to evaluate the impact of PROADAPT program on post-treatment
478 complications versus common care. In order to favor patients' compliance and follow-up, an eHealth
479 tool has been developed that will help supervising patients' care courses.

480 **Discussion of the study design**

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2
3 481 In line with the previous points, this pilot study was designed in order to answer to this critical
4 question: is a multidomain prehabilitation program feasible in an older cancer population? This
5 482 question encompasses several points: (i) Is the program physically adapted to an older population? (ii)
6 483 Is such a program applicable in ambulatory care? (iii) How to build pedagogic tools adapted for such
7 ambulatory use? (iv) Are such pedagogic tools understandable? (v) What is the compliance of the
8 484 patients for each domain of the intervention program?... Another point is to know whether the
9 patient's care team is expected to accept such intervention, but this point was previously evaluated by
10 485 Ghignone et al. They demonstrated through an international survey that surgeons are generally in
11 486 favor for such programs since 71 % of them would accept to prehabilitate their elderly patients 4 weeks
12 before surgery, if such intervention is proven to be effective (2). Nevertheless, the participation of
13 487 surgeons and anesthesiologists during initial brainstorming sessions was of major interest since they
14 enriched a lot the structure of the program.
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24 493 Thus, the construct of this trial may appear as highly complex with overabundant secondary endpoints,
25 but this design encompasses as much as possible the complexity of prevention care in an older
26 494 population, which has to mix the adaptation to the target population and the ability to maintain
27 495 compliance over time.
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34 498 **Ethics and dissemination**

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36 499 The study sponsor is the Hospices Civils de Lyon, responsible for study insurance and
37 pharmacovigilance. The study protocol was approved by the Ile de France 8 Ethics Committee on May
38 500 3, 2018 and cover all sites involved in this study. Several amendments have been added to the first
39 501 version of the protocol. The initial approved version was V2 of May 28, 2018, then the amended
40 502 versions were as follows: V3 of October 23, 2018 (change in the recruitment period, addition of new
41 503 investigation centers), V4 of May 17, 2019 (request for an additional 12 months extension, update with
42 504 the GDPR and update of the patient booklet), V5 of July 17, 2020 (addition of a cohort of 30 patients
43 505 to test the follow-up program with an e-health interface, request for an additional 8 months
44 506 extension). Current version is the V5 of July 17, 2020, authorized on September 10, 2020. The research
45 507 will be carried out on accordance with the Helsinki Declaration and ICH GCP Guidelines. Trial protocol
46 508 fulfills SPIRIT 2013 checklist (Supplementary table 1) and World Health Organization Trial Registration
47 509 Data Set (Supplementary table 2). The study complies with the principles of the data protection act in
48 510 France and with the General Data Protection Regulations in force in Europe. Each investigator must
49 511 collect a written consent at the beginning of the procedure. This consent is retained in the patient's
50 512 medical chart. The patient can stop the study at any time with an oral information at his investigator
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2
3 514 or clinical research assistant. Patients will be informed on additional amendments according the law
4
5 515 in force.

6
7 516 The results of the primary and secondary objectives will be published in peer-reviewed journals. All
8
9 517 authors of future publications will have to meet the criteria for authorship stated in the Uniform
10
11 518 Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of
12
13 519 Medical Journal Editors.

14 520

15 521 Total words count : 4791

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18 522

19
20 523 **Abbreviations**

21
22 524 ADL: Activities of Daily Living; AIPVQ: Physical Instrumental activities of daily living (in French: Activités
23
24 525 Instrumentales Physiques de la Vie Quotidienne); CRA: Clinical Research Assistant; ESPEN: European
25
26 526 Society for Clinical Nutrition and Metabolism; FSS: Fatigue Severity Scale; GDS: Geriatric Depression
27
28 527 Scale; IADL: Instrumental Activities of Daily Living; ICU: Intensive Care Unit; mITT:Modified Intention
29
30 528 To Treat; MNA: Mini Nutritional Assessment; QLQ: Quality of Life Questionnaire; QoL: Quality of Life;
31
32 529 RAPA: Rapid Assessment of Physical Activity; SF: Short Form; SPPB: Short Physical Performance Battery

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35
36 531 **Declarations**

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38 532

39
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41
42
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60
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4
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6
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8

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16
17 551 dieticians, physiotherapists, and clinical research assistants.

18
19 552 **Availability of data and materials**

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21 553 The final dataset of the PROADAPT pilot study will be available on reasonable request after publication
22
23 554 of the primary objective. Data requests can be submitted to the corresponding author.

24
25 555 **Competing interest**

26
27 556 The authors declare that they have no competing interests.

28
29 557 **Consent for publication**

30
31
32 558 Not applicable

33
34 559 **Author contributions**

35
36 560 All authors participated to the PROADAPT intervention conception. Study protocol was conceived by
37
38 561 DD, CF, CG, OLS, AM, VP and CR. DD and CF assumed fundraising and grant follow-up. MR led the
39
40 562 drafting of the manuscript. All authors (MR, CR, AM, CG, VP, MT, BR, BG, MG, CBa, CBo, EG, LS, MH,
41
42 563 ECK, IMS, VC, OLS, DD and CF) critically reviewed and approved the final version of the protocol.

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3 704 **Illustrations' legends**
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6 705 Figure 1: PROADAPT program: interventions at the patient's level

7 706 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
8 707 steps (before, during and after complex medico-surgical procedure)

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10 708 Table 2: PROADAPT pilot trial: questionnaires and screening tests

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12 709 Table 3: PROADAPT pilot trial: flow diagram

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712 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
713 steps (before, during and after complex medico-surgical procedure)

Nurse coaching & education Bridging interventions	Coaching nurse self-presentation Delivery of a personalized patient booklet Care according best practice guidelines: - Confirm and document patient goals and treatment preferences, including advance directives. - Confirm and document patient's health care proxy or surrogate decision-maker. - In patients with existing advance directives, discuss new risks associated with the surgical procedure and an approach for potentially life-threatening problems consistent with the patient's values and preferences ("required reconsideration"). Weekly phone calls	Coaching nurse visits / phone calls Communication of patient's preference to the staff	Coaching nurse visit in the rehabilitation ward Communication of patient's preference and care difficulties to the staff (checklist): - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - pressure ulcers prevention	Coaching nurse bi-weekly phone call Communication of patient's care difficulties to the staff
Nutrition	W-4 : nutritional evaluation Nutritional plan based on measured intake W-3 : nutritional follow up - weight W-2 : nutritional follow up-weight W-1 : nutritional follow up-weight + pre-operative immunonutrition	If surgery: Care according best practice guidelines: - Consider shortened fluid fast (clear liquids up to 2 hours before anaesthesia).(29) - Normal food intake or enteral feeding should start as early as possible	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain
Physical activity	W-4 : physical performances evaluation Physical activity plan W-3 : group physical activity W-2 : + W-1 : functional follow-up	If surgery: care according best practice guidelines: - Early physical and/or occupational therapy. - Check for orthostatic hypotension. - Review physical environment to reduce injury risk. - Assistive walking devices (eg walkers) at bedside if used as outpatient	(to the discretion of the rehabilitation unit)	Pursuing of the pre-operative physical activity plan
Medication conciliation	Centralized medication conciliation and treatment optimization (STOPP/START guidelines)	Centralized medication conciliation Advices for care according best practice guidelines (16): - Adhere to existing best practices regarding antibiotic and venous thromboembolism prophylaxis. - Ensure nonessential medications have been stopped and essential medications have been taken.	Centralized medication conciliation	Centralized medication conciliation
Standardization of surgical procedures		If surgery: consider antiseptic toothpaste If surgery: care according best practice Guidelines (16): - Consideration of regional techniques to avoid postoperative complications and improve pain control. - Directed pain history. - Multi-modal or opioid-sparing techniques. - Postoperative nausea risk stratification and prevention strategies. - Strategies to avoid pressure ulcers and nerve damage. - Prevention of postoperative pulmonary complications and hypothermia. - Judicious use of intravenous fluids. - Appropriate hemodynamic management. - Continuation of indicated cardiac medications. - Daily post-operative rounding checklist: - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - Pressure ulcers prevention If surgery: consider IV iron supplementation		

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716 Table 2: PROADAPT pilot trial: questionnaires and screening tests

Domain	
Autonomy	Activity of Daily Living Scale (ADL)
	Instrumental Activities of Daily Living scale (IADL)
Geriatric screening	G8
Physical activity	RAPA (Rapid Assessment of Physical Activity), AIPVQ
Quality of life	QLQ-C30, QLQ-ED14, EQ-5D-3L, SF-36
Locomotion and balance	Time Up and Go, SPPB (Short Physical Performance Battery)
Pain	Pain scale evaluation
Nutrition	Nutrition scale evaluation
Tiredness severity	FSS
Depression/anxiety	MNA, GDS4/GDS15
Cognitive assessment	MINI-COG
Fall risk assessment	Tinetti test
Breathlessness	Borg scale

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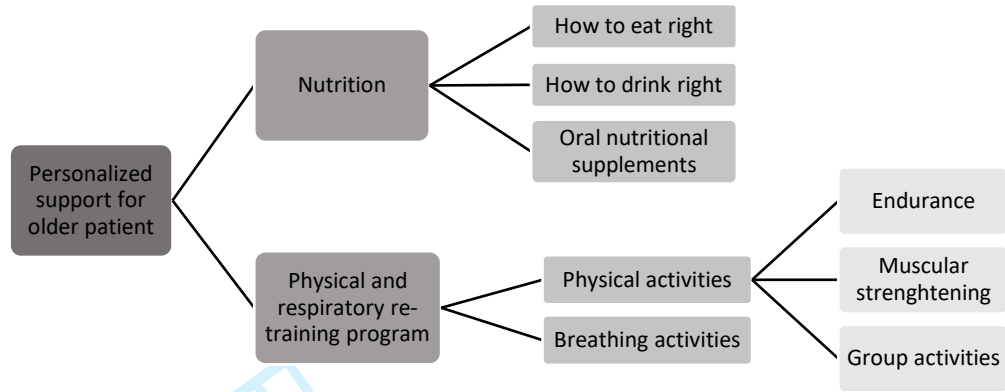
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719 Table 3: PROADAPT pilot trial: flow diagram

	Baseline	Pre-therapeutic visit (0-5 days before intervention)	M1, M3, M6	M12	End of study visit
<i>Complex geriatric assessment</i>					
G8	X			X	X
ADL/IADL	X			X	X
GDS4/GDS15	X			X	X
MINI COG	X			X	X
MNA	X			X	X
QLQ-C30	X		X	X	X
QLQ-ELD14	X		X	X	X
EQ-5D-3L	X		X	X	X
Pain scale evaluation	X	X	X	X	X
Nutrition scale evaluation	X	X	X	X	X
Socio-economic evaluation	X				
<i>Physical and respiratory assessments</i>					
FSS	X		X	X	X
SF-36	X		X	X	X
Time and Go	X			X	X
SPPB	X		X	X	X
Borg scale	X			X	X
RAPA questionnaire	X		X	X	X
AIPVQ scale	X		X	X	X
Tinetti test	X			X	X
Equimog evaluation	X			X	X
Triflo	X	X			
Voldyne	X	X			
Physical activity data collection		X	X	X	X
<i>Patients' satisfaction</i>					
Standardized questionnaire					X

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Figure 1 : PROADAPT program : interventions at the patient’s level



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Supplementary table 1 : Satisfaction questionnaire

 Hospices Civils de Lyon Direction de la Recherche Clinique et de l'Innovation	PATIENT ASSESSMENT OF THE PROADAPT PILOT PHASE PROGRAM
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Mrs, Mr,

You have been part of the PROADAPT - pilot phase study and we thank you for your involvement. In order to assess and improve this study, we would like to collect your opinion. This opinion is anonymous and does not affect your healthcare.

The following questions concern the patient booklet that was given to you as part of the study

If you consider the booklet globally

- The explanations seem appropriate to you ? Not at all A little Absolutely
- The information seem clear to you ? Not at all A little Absolutely
- The pages seem readable enough ? Not at all A little Absolutely
- The illustrations seem clear to you ? Not at all A little Absolutely

How would you rate the booklet ? 0 1 2 3 4 5 6 7 8 9 10
(useless = 0 ; very useful = 10)

The following questions concern the PROADAPT pilot phase program globally (breathing and physical exercises, booklet, calls and follow-up visits)

Did you have difficulty to understand the explanations given by the medical staff and the physician

- for breathing exercises ? Not at all A little A lot
- for physical exercises ? Not at all A little A lot
- for nutritional advices ? Not at all A little A lot
- during the assessment with the physician on the different drugs you are taking ? Not at all A little A lot

Did you encounter any difficulties

- for the realization of breathing exercises ? Not at all A little A lot
- for the realization of physical exercises ? Not at all A little A lot

- for the setting up of nutritional advice ? Not at all A little A lot
- for the filling of activities ? Not at all A little A lot

How do you estimate nursing phone calls

- at the beginning of your healthcare before your surgery / radiotherapy Useless Little important Needed
- after your surgery/radiotherapy Useless Little important Needed

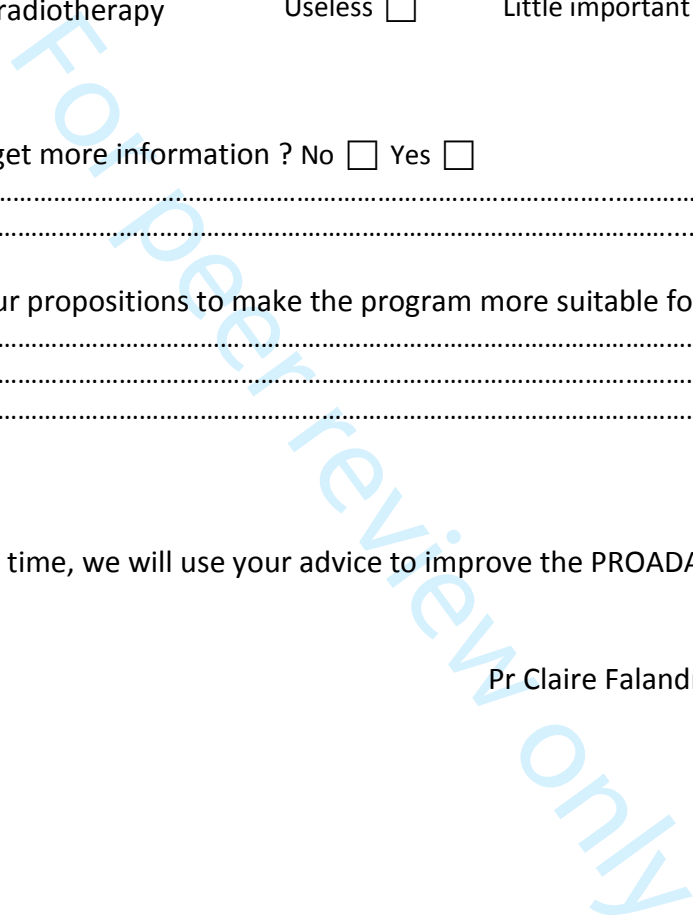
Would you like to get more information ? No Yes

If yes, which ones,.....
.....

What would be your propositions to make the program more suitable for patients?
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Thank you for your time, we will use your advice to improve the PROADAPT program and the patient booklet.

Pr Claire Falandry, study coordinator



Supplementary table 2: All items from the World Health Organization Trial Registration Data Set (SPIRIT item 2b)

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT03659123
Date of registration in primary registry	September 6, 2018
Secondary identifying numbers	69HCL16_0701 ID RCB N° 2018-A001026-49
Source(s) of monetary or material support	Agence Régionale de Santé Auvergne Rhône Alpes
Primary sponsor	Hospices Civils de Lyon
Secondary sponsor(s)	
Contact for public queries	David Dayde, +33.4.78.86.37.74, david.dayde@chu-lyon.fr
Contact for scientific queries	Claire Falandry, +33.4.78.86.66.34, claire.falandry@chu-lyon.fr
Public title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer
Scientific title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer, a Multicenter Pilot Study
Countries of recruitment	France
Health condition(s) or problem(s) studied	Old Injury
Intervention(s)	Behavioral: standardized geriatric intervention Nutritional care is based on: <ul style="list-style-type: none"> • A personalized evaluation of nutritional balance and nutritional needs of the patient • A weekly follow-up of weight and nutritional intake Total-body rehabilitation is based on: <ul style="list-style-type: none"> • 2 to 3 times a week: strength exercise • 2 to 3 times a week: endurance exercise, 20 to 45 min each sequence • 2 times a week: respiratory physiotherapy Pharmaceutical conciliation and optimization according STOPP/START criteria During peri-operative time, the nurse contacts the surgical team for transmission of patient's personal data, physical medication conciliation results During rehabilitation time and hospital-home transition time, the nurse contacts

Data category	Information
	the rehabilitation team for transmission of patient's personal data and care course, physical (nutritional, functional and/or comorbidities), medication conciliation results.
Key inclusion and exclusion criteria	<p>Inclusion Criteria:</p> <p>Patient ≥ 70 year old OR patient ≥ 60 years with significant comorbid condition (modified Charlson index ≥ 3) or disability (ADL score $< 6/6$);</p> <p>Histologically or cytologically proven cancer.</p> <p>Life expectancy > 3 months.</p> <p>Written informed consent obtained</p> <p>Covered by a Health System where applicable.</p> <p>Exclusion Criteria:</p> <p>Other malignancy within the last 5 years, except for adequately treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled limited basal cell skin cancer.</p> <p>Patient unable to be regularly followed for any reason (geographic, familial, social, psychological).</p> <p>Any mental or physical handicap at risk of interfering with the appropriate treatment.</p> <p>Any administrative or legal supervision where applicable</p>
Study type	<p>Interventional</p> <p>Allocation: N/A</p> <p>Intervention model: Single Group Assignment</p> <p>Masking: None (Open Label)</p> <p>Primary purpose: Health Services Research</p> <p>Phase II</p>
Date of first enrolment	July 3rd, 2018
Target sample size	122
Recruitment status	Recruiting
Primary outcome(s)	<p>Implementation of at least one item of PROADAPT standardized geriatric intervention of the program PROADAPT pilot study [Time Frame: 12 months]:</p> <ul style="list-style-type: none"> • Preoperative physical activity including strength and endurance exercise assessed by physical exercises accomplished under the supervision of a physiotherapist. Number of patients with at least 1 intervention achieved in the domain. • Nutrition guidelines before and after physical activity assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain.

Data category	Information
	<ul style="list-style-type: none"> • Patient education and coaching assessed by questionnaires and visits. Number of patients with at least 1 intervention achieved in the domain • Achievement of standardized intervention procedures, according to the checklist established in consensus with surgeons. Number of patients with at least 1 intervention achieved in the domain • Rehabilitation assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain • Accomplishment of pharmaceutical medication conciliation and treatment optimization. Number of patients with at least 1 intervention achieved in the domain • Bridging interventions for hospital-to-home transition. Number of patients with at least 1 intervention achieved in the domain
Key secondary outcomes	<ul style="list-style-type: none"> • Post operative morbidity [Time Frame: 30 and 90 days] according Clavien-Dindo classification • Post-operative morbidity [Time Frame: 90 days] according to NCI CTC v4.4 • Therapeutic strategy [Time Frame: 12 months]: Treatment plan completion rate: Number of patients for whom the treatment plan was completed. • Progression-free Survival [Time Frame: 12 months] • Post-treatment complication [Time Frame: 12 months]: Post-treatment complication grade\geq3 according the National Cancer Institute Common Toxicity Criteria version 4 (NCI-CTC-v4)



Supplementary table 1: SPIRIT 2013 checklist of the trial

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Reported on page #
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary table 2 Ref 24
Protocol version	3	Date and version identifier	17 (Ethics and Consent to participate)
Funding	4	Sources and types of financial, material, and other support	17-18 (Funding)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1 (Authors' list) 18 (Authors' contributions)
	5b	Name and contact information for the trial sponsor	Supplementary table 2 Ref 24

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	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	10 (Ethical and legal considerations) 17 (Funding)
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13 (Data management and statistical analyses) 14 (Data monitoring)
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5

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4	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
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8	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
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11		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14 (End of protocol) And N/4 (no dose modifications)
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15		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	6 (two turns of validations of the PROADAPT booklet by candidate patients)
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21		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
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24	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
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31	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8-9
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36	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12-13 (Sample size calculation)
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Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A (no problem for accrual)
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Methods: Assignment of interventions (for controlled trials) **N/A**

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	-
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial	-

Methods: Data collection, management, and analysis

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4	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 3
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12		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
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16	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13 (Data management and statistical analyses)
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22	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13-14 (Data management and statistical analyses)
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26		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
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28		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
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Methods: Monitoring

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Data monitoring

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Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

14 (Data Monitoring)

21b

Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial

N/A

Harms

22

Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

11 (Secondary outcomes: NCI CTCAE, QOL)

Auditing

23

Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

N/A

Ethics and dissemination

Research ethics approval

24

Plans for seeking research ethics committee/institutional review board (REC/IRB) approval

10 (Ethical and legal considerations)

Protocol amendments

25

Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)

10 (Ethical and legal considerations)
14 (Protocol amendments)

Consent or assent

26a

Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)

10-11 (Ethical and legal considerations)

26b

Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable

N/A

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4	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14 (Confidentiality)
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8	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17 (Competing interests)
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10				
11	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17 (Availability of data and materials)
12				
13				
14	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
15				
16				
17				
18	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15 (Dissemination policy)
19				
20				
21				
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23				
24		31b	Authorship eligibility guidelines and any intended use of professional writers	15 (Dissemination policy), N/A
25				
26				
27		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
28				
29				
30	Appendices			
31				
32	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Annex 1 (in French)
33				
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35	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

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BMJ Open

Feasibility of a prehabilitation program dedicated to older cancer patients before complex medico-surgical procedures: the PROADAPT pilot study protocol

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	microenvironnement Dayde, David; Hospices Civils de Lyon, Plateforme Transversale de Recherche de l'ICHCL Falandry, Claire; Hospices Civils de Lyon, Geriatrics unit; University of Lyon, CarMeN Laboratory, Inserm U1060, INRA U1397, Université Claude Bernard Lyon 1, INSA Lyon, Charles Mérieux Medical School
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Secondary Subject Heading:	Geriatric medicine, Surgery
Keywords:	Adult oncology < ONCOLOGY, GERIATRIC MEDICINE, REHABILITATION MEDICINE, Adult surgery < SURGERY

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4 1 **Feasibility of a prehabilitation program dedicated to older cancer**
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6 2 **patients before complex medico-surgical procedures: the PROADAPT**
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8 3 **pilot study protocol**
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26 Abstract

27 **Background:** Aging is associated with an increased prevalence of co-morbidities and sarcopenia and
28 with a decline of functional reserve of multiple organ systems, eventually leading in the context of the
29 disease and/or treatment-related stress to functional deconditioning or organ failure. The
30 multicomponent intervention “PROADAPT” was built multi-professionally to implement
31 prehabilitation in older cancer patients.

32 **Methods:** PROADAPT-pilot study is an interventional, non-randomized, prospective, multicenter
33 study. It will include 122 patients oriented to complex medico-surgical curative procedures (major
34 surgery or radiation therapy +/- chemotherapy). After informed consent, patients will undergo a
35 comprehensive geriatric assessment and will be offered a prehabilitation kit “PROADAPT” including an
36 advices booklet with personalized objectives and respiratory rehabilitation devices. Patients will then
37 be called weekly and monitored for physical and respiratory rehabilitation, pre-operative re-nutrition,
38 motivational counseling, and iatrogenic prevention. Six outpatient consultations will be planned at
39 inclusion, few days before the procedure, at 1, 3, 6 and 12 months after the end of the procedure. The
40 main outcome of the study is the feasibility of the intervention, defined as the ability to perform at
41 least one of the components of the program. Clinical data collection will include patient-specific and
42 cancer-specific characteristics.

43 **Ethics and dissemination:** Study protocol and several amendments were ethically approved by Ile de
44 France 8 Ethics Committee on May 3, 2018. The results of the primary and secondary objectives will
45 be published in peer-reviewed journals. ClinicalTrials registration: NCT03659123.

46 **Keywords:** oncogeriatrics, prehabilitation, motivation, sarcopenia, older cancer patients, care
47 pathway.

49 Article summary

50 Strengths and limitations of this study

- 51 - PROADAPT program is a prehabilitation intervention specifically tailored for older cancer
52 patients
- 53 - PROADAPT pilot trial is a prospective and multicentre trial designed to evaluate the feasibility
54 of the intervention
- 55 - Different secondary outcomes including quality of life will be collected to better adapt the
56 program to patients' specificities

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3 57 - The main limitation of such an intervention is the risk of poor adherence of the patients to the
4 program
5 58
6 59 - This non comparative study will appeal, if satisfactory, to randomized studies in the future.
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60 Introduction

61 Many oncological situations involve complex medical-surgical procedures at risk of patient's
62 deconditioning. Surgery or complex medico-surgical procedures can be considered as one proof-of
63 principle of such risks, since major cancer surgery exposes the older population to a higher risk of
64 morbi-mortality and unplanned hospitalization for geriatric events (1). Outpatient treatments and
65 rapid post-operative rehabilitation strategies are used to decrease post-operative deconditioning but
66 do not take geriatric risk factors into account. The deconditioning of older patients, not anticipated,
67 can thus lead to prolonged and iatrogenic hospitalizations such as immobilization syndrome, acute
68 confusion, undernutrition, falls, de novo urinary incontinence and adverse drug events, generating
69 frustration, appeals by patients and their families and additional hospital costs.

70 In order to reduce complications after surgery, prehabilitation has often been considered, and it can
71 be estimated that a majority of surgeons would accept a 4 weeks delay before surgery to improve
72 older patients' outcomes if shown to be beneficial (2–9). However, the actual level of evidence
73 depends on the interventions: high for pre-operative nutrition (10), but low for physical exercise, due
74 to heterogeneous programs with often bad adherence (11). In addition, geriatric validated
75 interventions, in order to prevent iatrogenic event, may be added in a multi-interventional model of
76 intervention.

77 To date, the interventions likely to prevent geriatric deconditioning include nutritional care, pre-
78 therapeutic (prehabilitation) and post-therapeutic (rehabilitation) physical reconditioning, iatrogenic
79 prevention (drug and care system-related) and hospital-to-home transition to limit the risk of early
80 readmission of patients. Nevertheless, the level of evidence for each of these care segments remains
81 limited, and not specific to the oncogeriatric population. Indeed, studies about more specific care have
82 already been carried out but do not consider all of the above interventions (12). Moreover, cancer in
83 the older patient is often associated with comorbidities, particularly cardiovascular disease (13,14).
84 The older population also has a higher risk of loss of autonomy and cognitive impairment, which can
85 be increased with surgery (15–17). In response to the growing population of older cancer patients, a
86 modification of oncological care and the implementation of specific geriatric interventions have been
87 developed (18–20).

88 PROADAPT (Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning risk and
89 Accompaniment of Patients' Trajectories) is a geriatric intervention program constructed on a multi-
90 professional and multi-disciplinary basis after a systematic analysis of published data. It includes: 1)
91 before surgery: prehabilitation of patients, including nutritional, physical, respiratory and motivational
92 counselling; 2) during hospitalisation for surgery (if performed): optimization of their treatment by
93 pharmaceutical reconciliation, educational interventions, standardization of surgical interventions and

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2
3 94 improved rehabilitation after surgery; 3) bridging and post-discharge interventions for hospital-to-
4 home transition (table 1).
5 95
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7

8 97 **Methods and analysis**

10 98 **Objectives**

11 99 *Primary objective*

12
13 100 The primary objective of the PROADAPT pilot study is to assess the feasibility of the program, defined
14 as the achievement of at least one item of the program during patient's follow up.
15 101
16 102

17 103 *Secondary objectives*

18 104 The secondary objectives of the study are:

- 19 105 1) To assess the achievement of each item of the program independently of each other (rate of
20 achievement of all or part of the instructions);
- 21 106 2) To assess patients' satisfaction with the program;
- 22 107 3) To estimate the rate of adherence to each item of the program during the various visits;
- 23 108 4) To appreciate the longitudinal evolution of health-related quality of life over 1 year.
- 24 109 5) To assess patients' post treatment complications according Clavien Dindo and NCI-CTC version
25 4 scoring systems (21);
- 26 110 6) To estimate the rate and the nature of post-operative complications at 30 and 90 days;
- 27 111 7) To estimate the post-operative mortality at 30 and 90 days;
- 28 112 8) To estimate the costs of treatments (health system, patients);
- 29 113 9) To study the therapeutic strategies (treatment completion rate);
- 30 114 10) To estimate the progression-free survival rate at one year (PFS);
- 31 115 11) To estimate the overall survival rate at one year (OS);
- 32 116 12) To study the physical performance tests and the evolution of these performances through the
33 proposed exercises;
- 34 117 13) To study the other dimensions of quality of life relating to health at 3 months;
- 35 118 14) To estimate the longitudinal evolution of QoL;
- 36 119 15) To estimate the tolerance of treatments;
- 37 120 16) To estimate the evolution of geriatric covariates.

38 121 **Study design**

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3 125 PROADAPT - pilot phase is a second category interventional study involving the Human Person with
4 126 minimal risks and constraints excluding health products. It is a prospective, non-randomized
5 127 multicenter opened in different centers of Auvergne-Rhône-Alpes region, France (n=7).

8 9 128 **Study sites and participants**

10
11 129 The study population will include older patients identified during multidisciplinary consultation
12 130 meetings and oriented to complex medico-surgical curative procedures in the including centers (Lyon
13 131 Sud Hospital, Croix Rousse Hospital and Edouard Herriot Hospital from the Hospices Civils de Lyon,
14 132 Nord-Ouest Villefranche-sur-Saône Hospital, Annecy-Genevois Hospital, Chambéry Hospital, Lyon-
15 133 Villeurbanne Médipôle).

16 134 Inclusion criteria are: patient aged 70 and over or 60 and over with significant comorbid condition
17 135 (Cumulative Illness Rating Scale (CIRS-G) ≥ 3 (22)) or disability (ADL score $< 6/6$ (23)), histologically or
18 136 cytologically proven cancer, life expectancy > 3 months planned for a complex medico-surgical
19 137 procedure in a curative intent. Complex medico-surgical procedures are defined as major abdominal
20 138 surgery (breast excluded) either minimally invasive or open.

21 139 Exclusion criteria are: patient with other malignancy within the last 5 years (except for adequately
22 140 treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled
23 141 limited basal cell skin cancer), unable to be regularly followed for any reason (geographic, familial,
24 142 social, psychologic) or with any mental or physical handicap at risk of interfering with the appropriate
25 143 treatment.

26 144 A screening of older patients will be systematically performed during multidisciplinary meetings and
27 145 described in the CONSORT diagram of the study.

28 146 **Intervention**

29 147 PROADAPT intervention program was built according to a multi-dimensional and multidisciplinary
30 148 basis. From January 2016 to April 2018, nine regional meetings were organized, gathering 40
31 149 representatives of the following medical and paramedical specialties: geriatricians, nutritionists,
32 150 surgeons (subspecialties: gynaecology, digestive surgery, urology), oncologists, anaesthesiologists,
33 151 nurses, physiotherapists, occupational therapists, adapted physical activity monitors. A systematic
34 152 review of published data was done in the following axes, to provide a graded state-of-the-art: nutrition,
35 153 physical activity, patient education, medication rationalization, cardiovascular optimization, transition
36 154 and standardization of surgical procedures. Based on the qualitative grading of existing data, a
37 155 modified DELPHI method was performed, to co-validate the content of the standardized intervention
38 156 checklist, and the feasibility of the implementation of each point of this checklist (Table 1).

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2
3 157 A PROADAPT booklet was built, to propose a standardized, adapted and evolutive tool designed to
4
5 158 explain physical exercise and nutrition counselling and to insure a follow-up of patients' day-to-day
6
7 159 achievements. This first version was tested by candidate patients during two turns of validation before
8
9 160 the validation of the current version 3 of the booklet.

10
11 161 *PROADAPT standardized geriatric intervention program includes:*

12
13 162 - Pre-operative physical activity including strength and endurance exercise +/- group activities
14
15 163 during 4 +/-2 weeks. Interventions with high level of evidence were retained, according to an ongoing
16
17 164 systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42020100110; (24,25)). Since the
18
19 165 intervention is expected to be performed in any health system context, with a vast majority of the
20
21 166 intervention to be performed at home, the content of the intervention was standardized and
22
23 167 presented in the booklet, but the conditions of the implementation were left to the investigator's
24
25 168 decision (physiotherapist intervention at home, group activities when available, etc...).

26
27 169 - Nutrition: nutrition before and after physical activity, pre-postoperative immuno-nutrition +/-
28
29 170 artificial nutrition (ie enteral or parenteral nutrition) according international guidelines (10);

30
31 171 - Patient (and caregiver) education and coaching (on nutrition, physical exercise) according to a
32
33 172 weekly schedule with the activation of integrated supports by hetero- and self-management (26);

34
35 173 - Standardized intervention procedures, according to a checklist established in consensus with
36
37 174 surgeons' representatives;

38
39 175 - Enhanced rehabilitation will be promoted according to international guidelines (27);

40
41 176 - Pharmaceutical medication conciliation, treatment optimization, according to a centralized
42
43 177 process with pharmaceutical expertise.

44
45 178 - Bridging interventions for hospital-to-home transition, according to a proposed standardized
46
47 179 procedure including training of dedicated nurses, and post-discharge phone-calls follow-up during 12
48
49 180 weeks after surgery. In practice, only 2 or 3 people from the coordination team are in charge of
50
51 181 coaching for all patients. In the future, a "special nurse coach" will be trained in each center and
52
53 182 responsible for patients' coaching. Interventions with high level of evidence were retained, according
54
55 183 to an ongoing systematic analysis (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42017055698).

56
57 184 The intervention is designed to be implemented at different times of patients' care (table 1).

58
59 185

60
61 186 *During the prehabilitation time:*

62
63 187 • A dedicated nurse, trained in patient education by the coordination team ("coaching nurse")
64
65 188 presents him/herself to the patient for:

66
67 189 - Presentation of the program to the patient and his/her caregiver(s)

68
69 190 - Personalization of the PROADAPT booklet (see after) to the patient's characteristics

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- 191 - Collection of personal data, nutritional and functional habits
- 192 - Evaluation of psycho-cognitive context using questionnaires (GDS4/GDS15, MNA,
- 193 MINI-COG)
- 194 - Gathering of the information needed: comorbidities, comedications (for transmission
- 195 to the centralized pharmaceutical expertise)
- 196 - Anticipation and organization of the future appointments (anesthesiologist,
- 197 stomatherapist, ...)
- 198 - A weekly visit or phone call according to a structured interview for health education
- 199 and transmission of nutritional and functional advices (see after)
- 200 • Nutritional care is based on:
 - 201 - A personalized evaluation of nutritional balance and nutritional needs of the patient
 - 202 according to dietician diagnosis based on measured intake and international
 - 203 recommendations
 - 204 - A weekly follow-up of weight and nutritional intake. If the coaching nurse identifies an
 - 205 unfavorable nutritional trend, she reports it to the referring physician and nutritionist.
 - 206 - Artificial nutrition if needed according ESPEN recommendations (10,28,29)
 - 207 - Pre-operative immune-nutrition during 7 days before surgery (29)
- 208 • Total-body rehabilitation:
 - 209 - 2 to 3 times a week: strength exercise (each time with dedicated exercises for upper
 - 210 members, legs and abs, 20 to 45 minutes each sequence)
 - 211 - 2 to 3 times a week: endurance exercise (walk or cycle ergometer), 20 to 45 min each
 - 212 sequence
 - 213 - 3 times a day: respiratory physiotherapy
 - 214 - Once a week (if possible): group activities (according to the center organization and
 - 215 home-hospital distance)
- 216 • Pharmaceutical conciliation and optimization according to STOPP/START criteria and
- 217 international recommendations about peri-operative care (30): to be transmitted to the surgical and
- 218 anesthesia team without any obligation.
- 219
- 220 *During peri-operative time*
- 221 • The coaching nurse contacts the surgical team for transmission of:
 - 222 o patient's personal data
 - 223 o physical (nutritional, functional and/or comorbidities) as well as psychological
 - 224 difficulties
 - 225 o medication conciliation results

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4
5 227 *During rehabilitation time*

- 6 228 • The coaching nurse contacts the rehabilitation team for transmission of:
- 7
8 229 o patient's personal data and care course
- 9
10 230 o physical (nutritional, functional and/or comorbidities) as well as psychological
- 11 231 difficulties
- 12
13 232 o medication conciliation results
- 14
15 233 • The rehabilitation program is left at the discretion of the rehabilitation team (standard care
- 16 234 and local habits).
- 17
18 235 • A weekly phone call of the coaching nurse to the rehabilitation team for nutritional and
- 19
20 236 functional follow-up as well as medication conciliation

21 237

22
23 238 *During hospital-home transition time*

- 24
25 239 • The coaching nurse contacts the patient's general practitioner for transmission of:
- 26 240 o patient's personal data and care course
- 27
28 241 o physical (nutritional, functional and/or comorbidities) as well as psychological
- 29 242 difficulties
- 30
31 243 o medication conciliation results
- 32
33 244 • Bi-weekly phone call of the coaching nurse to the patient for nutritional and functional follow-
- 34
35 245 up
- 36
37 246 • Advices for optimization of symptoms management: abdominal pain, nausea, vomiting...

38 247

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41 248 **Participant timeline**

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43 249 Six successive evaluations are planned for the participants.

44
45 250 *The inclusion visit* is planned during a geriatric consultation planned before the start day of the complex

46 251 medico-surgical procedure, at least 7 days before start date. If the start date is delayed for any reason

47
48 252 or the patient is included into a neo-adjuvant treatment, the prehabilitation time may be prolonged

49
50 253 until 9 months. In that case, the frequency of the phone calls is decreased (from 1/week to 1/month)

51
52 254 after 4 weeks. During the inclusion visit, lasting about 1 hour, the following steps are planned:

- 53
54 255 - Clinic (blood pressure, heart rate, ECOG scale(31), patient's comorbidities), biologic (albumin,
- 55 256 prealbumin, C-reactive protein) and paraclinic (year of birth, gender, weight, height, body
- 56
57 257 mass index, weight evolution over the last 3 and 6 months) data collection
- 58
59 258 - All concomitant treatments and drug conciliation
- 60

- 1
2
3 259 - The history of the disease (primitive site, metastasis, histology of the initial tumor, presence
4 of tumor markers)
5 260
6 261 - Radiological disease assessments (date and nature)
7
8 262 - A standardized geriatric assessment using validated questionnaires with a particular attention
9 on physical activity and nutrition (ADL(23)/IADL(32), G8 (33), Rapid Assessment of Physical
10 263 Activity (RAPA) (34), AIPVQ (35), EORTC QLQ-C30 (36), EORTC QLQ-ED14 (37), EQ-5D-3L (38),
11 264 Short Form Health Survey in 36-items (SF-36) (39), Short Physical Performance Battery (SPPB)
12 265 (40), Fatigue Severity Scale (FSS) (41), Mini-Nutritional Assessment (MNA) (42), Geriatric
13 266 Depression Scale (GDS4/GDS15) (43), MINI-COG (44), Tinetti test (45), Borg scale (46), Pain
14 267 scale (47), Nutrition scale (48)) (**Error! Reference source not found.**tables 2 and 3).
15
16 268
17
18 269 - Delivery of the “PROADAPT kit” device during a meeting with a dedicated paramedic (nurse,
19 270 physiotherapist, ergotherapist...) in order to:
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- Provide to the patient VOLDYNE® and TRIFLO® devices for inspiratory training
 - Present the PROADAPT booklet that includes a battery of exercises and nutritional counselling specifically designed for this older population:
 - muscle strengthening of upper limbs (6 exercises, 3 difficulty levels), lower limbs (6 exercises, 3 difficulty levels), abdominal wall (4 exercises, 3 difficulty levels) (objective: 2 to 3 sessions per day for a total time between 20 and 45 minutes)
 - endurance/aerobic activities (7 exercises, 3 difficulty levels with 3 duration objectives, objective: every day)
 - inspiratory training with VOLDYNE® and TRIFLO® devices (objective: 3 sessions per day for a total time of 30 minutes)
 - general nutritional counselling adapted to the older population: food enrichment, inter-meals collations, oral nutritional supplements.
 - A fulfilling of 3-day food statement allows, in the 7 days after inclusion, to deliver a dietician-driven personalized nutritional counseling. If needed, in case of unfavorable nutritional parameters, artificial nutrition is introduced.
 - Delivery, if needed, of medical prescription:
 - o for home physiotherapy according PROADAPT program for respiratory training sessions and physical activity training sessions
 - o For oral nutritional supplements
 - o For usual medicines, including pharmaceutical review
 - For patients requiring inpatient follow-up, hospital admission for a few days in a rehabilitation unit for a physiotherapeutic program and/or artificial nutrition (enteral preferred).

294 During pre-intervention time, phone calls are planned by a dedicated paramedic (once a week for the
295 first 4 weeks and then once a month until the intervention). Calls are semi-directed interviews focused
296 on the patient's autonomy, physical activity, appetite and sleep over the last period (week/month). A
297 special attention is paid on encouraging patient's motivation and adherence to the program.

298 *The pre-therapeutic visit* is scheduled when possible between 5 days and the day of the intervention.
299 This visit is performed in the surgery or radiotherapy unit only if the visit is necessary before the
300 intervention still without modifying the standard therapeutic care for:

- 301 - Clinic, biologic and paraclinic data collection
- 302 - All concomitant treatments and drug conciliation
- 303 - Questionnaires about pain, nutrition, fitness and physical tests (table 2 and 3)
- 304 - Therapeutic care data collection (date, nature, entitled, reason)

305 During post-intervention time, paramedics trained in clinical research will resume follow-up calls as
306 before the intervention once a week during 12 weeks after D0 and once a month up to 12 months after
307 D0. The D0 date is determined as the last day of surgery (day of the last resumption of surgery in the
308 limit of 30 days after the first intervention) or the last day of the radiotherapy. For weekly calls, a
309 margin of +/- 2 days is allowed and for monthly calls, a margin of +/- 7 days is allowed.

310 *Visits at 1, 3 and 6 months after the intervention (+/- 7 days):* The patient may have started an
311 antineoplastic treatment according to standard of care. The visit could be performed with the surgeon,
312 the radiotherapist or the oncologist according local habits:

- 313 - Clinic (blood pressure, heart rate, ECOG scale(31)), biologic (albumin, prealbumin, C-reactive
314 protein) and paraclinic (weight, body mass index) data collection
- 315 - All concomitant treatments and drug conciliation
- 316 - Patient care data (surgery and complications, treatment for the cancer)
- 317 - Radiological disease assessments (date and nature)
- 318 - Questionnaires about quality of life, pain, nutrition, fitness and physical tests (table 2 and 3)
- 319 - Socio-economic assessment with patient's care data (date, nature of acts, designation, reason)

320 *The end of study visit* is planned at 12 months (per-protocol) or at the date of trial premature
321 discontinuation (+/- 7 days) for a final assessment of the same outcomes as previously listed. When
322 requested, if previous visits were omitted, a final assessment of all the complications during the post-
323 therapeutic period is performed.

324 **Outcomes and measurements**

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3 325 **Primary outcome**
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5 326 The main outcome measure will be the percentage of patients who have completed at least one item
6
7 327 in the PROADAPT program after 12 months after the start of therapeutic treatment. The start of
8
9 328 treatment is defined in this study by the last day of surgery (date of the last recovery within the limit
10
11 329 of 30 days after the date of the initial intervention) or the last day of radiotherapy. The workshops of
12
13 330 the program are:

14 331 - Physical and respiratory rehabilitation

15 332 - Re-nutrition session

16 333 - Telephone nurse follow-up
17
18
19 334

20
21 335 **Secondary outcomes**
22

23 336 The secondary outcomes of the study are:

24
25 337 - To evaluate the feasibility of each stage of the program independently of each other (rate of
26
27 338 achievement of all or part of the instructions)

28
29 339 ○ Pre-operative physical rehabilitation including (figure 1):

30 340 ● Muscle strengthening

31
32 341 ● Respiratory rehabilitation

33
34 342 ● Endurance work

35 343 ○ Pre-operative nutrition counselling (figure 1)

36
37 344 ○ Drug reconciliation / iatrogenic prevention

38
39 345 ○ Pre-therapeutic follow-up calls

40
41 346 ○ Post-surgery or post-radiotherapy follow-up calls
42
43 347

44 348 - To estimate patients' satisfaction with the overall program, at the end of the study (end of follow-up
45
46 349 or study discontinuation) using a questionnaire (Supplemental material).

47
48 350 - To estimate the rate of adherence to the items (physical activity, nutrition and nursing follow-up)
49
50 351 during follow-up time. To evaluate this criterion, various parameters will be recorded: physical activity
51
52 352 duration (in h/week), kinetics (duration (% increase), level of difficulty), respiratory activity, food intake
53
54 353 during phone calls.

55 354 - To assess the longitudinal evolution over 1 year of:

56
57 355 ○ patient's physical performance (SPPB, gait speed, TUG test) and functional independence on
58
59 356 ADL (23), IADL (32), AIPVQ (49)

60 357 ○ nutritional parameters of the patient (weight, albuminemia, appetite)

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3 358 ○ health-related quality of life for patients based on QLQ-C30 and ELD14 (5 dimensions: mobility,
4 359 disease burden, emotional and physical functioning, tiredness) (50,51)
5
6 360 ○ pharmaceutical conciliation
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8 361

9
10 362 In parallel to these secondary objectives, a series of parameters will be measured and monitored in
11 363 order to:

- 12
13 364 - Estimate the rate and nature of post-operative complications at 30 days (NCI-CTCAE)
14
15 365 - Estimate the rate and nature of post-operative complications according to the CCI at 30 and 90 days
16
17 366 - Estimate post-operative mortality at 30 and 90 days
18
19 367 - Estimate the overall one-year survival rate (OS)
20
21 368 - Estimate the one-year progression-free survival rate (PFS)
22
23 369 - Estimate the longitudinal evolution of QoL according to QLQ C30, ELD14, EQ-5D
24
25 370 - Estimate treatment costs (health system, patients)
26
27 371 - Study therapeutic strategies (treatment completion rate)
28
29 372 - Estimate the evolution of geriatric covariates.
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31

374 **Sample size calculation**

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33 375 The program will be considered feasible, at the patient level, if all or part of the program is
34 376 implemented in at least 50 % of the included patients (= alternative hypothesis). This threshold was
35 377 defined in line with previous studies on prehabilitation for older cancer patients, that showed
36 378 compliance rates between 16 and 95% (52,53). Considering that PROADAPT program is highly complex
37 379 even if tailored for older patients, we anticipate modest compliance rates.

40
41
42 380 The calculation of the required sample size was done as follows: to reject the null hypothesis of the
43 381 program feasibility rate lower than 35 %, with a bilateral alpha error risk of 5 % and a statistical power
44 382 of 90 % (beta=10 %), the number of required patients to be analyzed is 111. Including 10 % non-
45 383 treatable patients, a total of 122 patients should be included.

49 384 **Data management and statistical analyses**

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51 385 Data are monitored by a clinical research associate (CRA). Inconsistencies will be reported to the study
52 386 investigators in order to decide whether the data should be corrected or considered as missing data.

53
54 387 Any changes in the data will be reported.

55
56 388 Data analyses will be performed by the data management and analysis centre. The analyses will be
57 389 carried out by an independent statistician with the latest version of the R software environment and
58
59 390 SAS software version 9.4.
60

1
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3 391 All of the characteristics collected will be subjected to a descriptive analysis.
4
5 392

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7 393 ***Descriptive analyses***
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9 394 A flow-chart diagram will describe the data available for the patient population at baseline, and during
10
11 395 each follow-up visit. Eligibility criteria for treated patients will be verified, as well as follow-up and end
12
13 396 of study visits. Reasons for premature end of study will be provided.
14

15 397 Characteristics of the study population and proportions of missing values will be reported. Patient
16
17 398 characteristics will be described using mean and standard deviation or median and interquartile range
18
19 399 for quantitative variables, and frequencies and distribution for categorical variables. A comparison of
20
21 400 baseline characteristics between patients with complete follow-up and those with attrition will be
22
23 401 performed. If needed, methods for handling missing data (multiple imputation, mixed model or
24
25 402 auxiliary variable) will be used when appropriate.
26

27 403
28 404 ***Primary analysis***

29
30 405 The number and percentage of patients who have completed at least one PROADAPT program activity
31
32 406 at the end of 12 months after the start of treatment will be reported. All included patients will be
33
34 407 analysed in the primary analysis as intention to treat, defined as all included patients with or without
35
36 408 the respect of the eligibility criteria and whatever the respect or not of the intervention.
37

38 409 ***Secondary analyses***

39 410 **Time-to-event variables: follow-up, overall survival, progression free survival**

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41
42 411 The proportion of events at specific measurement times will be estimated according to the Kaplan-
43
44 412 Meier curve. Medians of event-free survival will be reported by treatment arm with its 95 % confidence
45
46 413 interval (95 % CI), if the number of events allows estimation of the median.
47

48 414 Overall survival rate and progression free survival rate at 12 months (after the day of the last revision
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50 415 of surgery or the last day of radiotherapy) will be provided with 95 % CI.

51 416 **Quality of life**

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53
54 417 Analyses of the QoL data will be performed with modified intention to treat (mITT) population, i.e.
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56 418 including all included patients with at least a QoL score available at baseline. Patients' quality of life,
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58 419 linked to health, will be analysed after 3 months through 4 targeted dimensions: mobility, disease
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60 420 burden, emotional and physical functioning. All other dimensions will be analysed as exploratory

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3 421 purpose only. QoL scores will be described at baseline and at 3 months using the mean and standard
4 422 deviation or median and range. Mean difference between baseline and 3 months will be reported with
5 423 its 95% confidence interval. A 10-point difference will be considered as the minimal important
6 424 difference for each score of the EORTC questionnaires.
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9

10 425 **Longitudinal follow-up**

11
12 426 Covariates planned to be repeatedly tested during entire 1-year follow up will help analysing the
13 427 resilience concept ie the ability and the celerity with which one individual will recover to his baseline
14 428 level (54). Will be included in such analyses the covariates evaluating functional and physical
15 429 performance levels (SPPB, gait speed, TUG test, ADL, IADL, AIPVQ), nutritional parameters (weight,
16 430 albuminemia, appetite), and health-related quality of life. The longitudinal changes of these variables
17 431 will be analysed using linear mixed models (55). A “time-to-recovery” composite endpoint will be also
18 432 proposed as exploratory, defined as the time to complete functional and nutritional recovery of the
19 433 patients, a construction similar to the “Time to deterioration” composite endpoint proposed in the
20 434 oncologic field (56).”
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29 435 **Data monitoring**

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31 437 The successful completion of the database is ensured by the hospital CRA. The hospital CRA also
32 438 ensures compliance with the study protocol. The sponsor CRA verifies that the rights of the participants
33 439 are respected.
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38 440 **End of protocol**

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40 442 Patients leave the study either on a per-protocol basis during the “end of study visit” on month 12
41 443 after the intervention or at any time during the conduct of the study if they no longer wish to
42 444 participate. However, as indicated in the information letter to the patients/caregivers, the data
43 445 collected before exclusion may be used as part of the study.
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48 446 **Confidentiality**

49 447
50 448 Correspondence tables will be kept in a separate file that does not contain clinical data. The access to
51 449 the nominative information is protected by a password and confidentiality is guaranteed by the study.
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56 450 **Protocol amendments**

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3 452 Any important modifications requiring a new ethics committee approval will be communicated in
4 453 future publications. Any potential impact of protocol modifications on the results will be discussed as
5 454 appropriate.
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10 456 ***Trial status***

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12 457 Patient enrolment began on July 3, 2018. Data are collecting.
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14 458

15 459 ***Patients' and public involvement***

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18 460 Patients were involved at different steps of the trial: (i) during PROADAPT booklet conception, several
19 461 (30) patients were asked to answer an anonymous questionnaire in order to improve its ergonomics;
20 462 (ii) the information note and consent form of the protocol have been re-read by the patients' review
21 463 committee of the Ligue Nationale de Lutte contre le Cancer (a French association of cancer patients).
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26 465 **Discussion**

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29 466 **Discussion of the intervention**

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31 467 Prehabilitation has long been conceptualized as an effective means of improving the functional
32 468 capacity of the individual to enable him to resist various stressors. Originally developed in the military
33 469 as the association of physical training to improve strength and endurance, improving nutritional intake
34 470 and general education (57), it has been transposed into medicine and major surgery – initially when
35 471 an ICU admission is planned - at the beginning of this century (58).
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40 472 Despite a growing interest in the medical community for prehabilitation and particularly cancer
41 473 prehabilitation, the level of evidence for specific interventions stays too low to be implemented in
42 474 common care. Among the main disadvantages of published data include the heterogeneity of
43 475 programs, sometimes poor patient adherence and the fact that most studies were small pilot studies
44 476 developed for patients more fit and younger than those who should make the best part of
45 477 prehabilitation. Another point to emphasize is that most programs include only one intervention -
46 478 physical, nutritional, or psychological rehabilitation - when multimodal interventions are often
47 479 considered to be more effective in older populations.
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54 480 Considering these points, the PROADAPT intervention was developed according to an innovative
55 481 management strategy since it started in 2016 by multi-professional meetings conceived as
56 482 brainstorming sessions in order to develop a multidisciplinary program dedicated to prehabilitation
57 483 and follow-up of older patients. The multidisciplinary conception of the intervention, the particular
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3 484 attention paid to older patients' specificities and the previous experience of the participants in as
4
5 485 various fields as patients' education, cognition, physiotherapy were hopefully the warrants of the most
6
7 486 tailored approach to the target population. For example, the booklet typography was of big character
8
9 487 font and the illustrations highly schematic with high contrast. Each sentence was verified by a panel of
10
11 488 patients in order to insure proper understanding. Finally, the booklet was evaluated by 30 patients,
12
13 489 with a high rate of satisfaction (Ravot et al, PROADAPT Pilot trial: A survey on patients' expectations
14
15 490 and satisfaction, unpublished data).

16 491 The fact that the PROADAPT intervention was constructed as an outpatient program may be
17
18 492 considered as at risk of poor and heterogeneous supervision of the physical exercises. However, this
19
20 493 limitation is balanced by a weekly phone calls to the patients, able to evaluate partially patients' skills
21
22 494 and motivation for the program. In addition, such design allows to neutralize somehow the
23
24 495 consequences of any inequalities or heterogeneity arising from the health system. As an example,
25
26 496 PROADAPT pilot study was able, during the last months, to maintain accrual and patients' coaching
27
28 497 and follow up, despite sudden closing of geriatric wards and surgical rooms during COVID pandemic.

29 498 This pilot study is the first step towards an ambitious program, since PROADAPT program will be
30
31 499 declined in the future into two randomized studies, PROADAPT-ovary/EWOC-2 (NCT04284969) and
32
33 500 PROADAPT sus-mesocolic, designed to evaluate the impact of PROADAPT program on post-treatment
34
35 501 complications versus common care. In order to favor patients' compliance and follow-up, an eHealth
36
37 502 tool has been developed that will help supervising patients' care courses.

37 503 **Discussion of the study design**

38
39 504 In line with the previous points, this pilot study was designed in order to answer to this critical
40
41 505 question: is a multidomain prehabilitation program feasible in an older cancer population? This
42
43 506 question encompasses several points: (i) Is the program physically adapted to an older population? (ii)
44
45 507 Is such a program applicable in ambulatory care? (iii) How to build pedagogic tools adapted for such
46
47 508 ambulatory use? (iv) Are such pedagogic tools understandable? (v) What is the compliance of the
48
49 509 patients for each domain of the intervention program?... Another point is to know whether the
50
51 510 patient's care team is expected to accept such intervention, but this point was previously evaluated by
52
53 511 Ghignone et al. They demonstrated through an international survey that surgeons are generally in
54
55 512 favor for such programs since 71 % of them would accept to prehabilitate their elderly patients 4 weeks
56
57 513 before surgery, if such intervention is proven to be effective (2). Nevertheless, the participation of
58
59 514 surgeons and anesthesiologists during initial brainstorming sessions was of major interest since they
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515 enriched a lot the structure of the program.

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3 516 Thus, the construct of this trial may appear as highly complex with overabundant secondary endpoints,
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5 517 but this design encompasses as much as possible the complexity of prevention care in an older
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7 518 population, which has to mix the adaptation to the target population and the ability to maintain
8
9 519 compliance over time.

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11 520

12 13 521 **Ethics and dissemination**

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15 522 The study sponsor is the Hospices Civils de Lyon, responsible for study insurance and
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17 523 pharmacovigilance. The study protocol was approved by the Ile de France 8 Ethics Committee on May
18
19 524 3, 2018 and cover all sites involved in this study. Several amendments have been added to the first
20
21 525 version of the protocol. The initial approved version was V2 of May 28, 2018, then the amended
22
23 526 versions were as follows: V3 of October 23, 2018 (change in the recruitment period, addition of new
24
25 527 investigation centers), V4 of May 17, 2019 (request for an additional 12 months extension, update with
26
27 528 the GDPR and update of the patient booklet), V5 of July 17, 2020 (addition of a cohort of 30 patients
28
29 529 to test the follow-up program with an e-health interface, request for an additional 8 months
30
31 530 extension). Current version is the V5 of July 17, 2020, authorized on September 10, 2020. The research
32
33 531 will be carried out in accordance with the Helsinki Declaration and ICH GCP Guidelines. Trial protocol
34
35 532 fulfills SPIRIT 2013 checklist (Supplementary table 1) and World Health Organization Trial Registration
36
37 533 Data Set (Supplementary table 2). The study complies with the principles of the data protection act in
38
39 534 France and with the General Data Protection Regulations in force in Europe. Each investigator must
40
41 535 collect a written consent at the beginning of the procedure. This consent is retained in the patient's
42
43 536 medical chart. The patient can stop the study at any time with an oral information at his investigator
44
45 537 or clinical research assistant. Patients will be informed on additional amendments according the law
46
47 538 in force.

48
49 539 The results of the primary and secondary objectives will be published in peer-reviewed journals. All
50
51 540 authors of future publications will have to meet the criteria for authorship stated in the Uniform
52
53 541 Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of
54
55 542 Medical Journal Editors.

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57 543

58 544 Total words count : 5161

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60 545

61 546 **Abbreviations**

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3 547 ADL: Activities of Daily Living; AIPVQ: Physical Instrumental activities of daily living (in French: Activités
4 Instrumentales Physiques de la Vie Quotidienne); CRA: Clinical Research Assistant; ESPEN: European
5 548 Society for Clinical Nutrition and Metabolism; FSS: Fatigue Severity Scale; GDS: Geriatric Depression
6 549 Scale; IADL: Instrumental Activities of Daily Living; ICU: Intensive Care Unit; mITT:Modified Intention
7 550 To Treat; MNA: Mini Nutritional Assessment; QLQ: Quality of Life Questionnaire; QoL: Quality of Life;
8 551 RAPA: Rapid Assessment of Physical Activity; SF: Short Form Health Survey in 36 items; SPPB: Short
9 552 Physical Performance Battery
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18 555 **Declarations**

19
20 556

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23
24
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44
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55 576 dieticians, physiotherapists, and clinical research assistants.

56 57 58 59 60 577 **Availability of data and materials**

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2
3 578 The final dataset of the PROADAPT pilot study will be available on reasonable request after publication
4 of the primary objective. Data requests can be submitted to the corresponding author.
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6
7 580 **Competing interest**
8

9 581 The authors declare that they have no competing interests.
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11
12 582 **Consent for publication**
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14 583 Not applicable
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16 584 **Author contributions**
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18
19 585 All authors participated to the PROADAPT intervention conception. Study protocol was conceived by
20 586 DD, CF, CG, SPB, OLS, AM, VP and CR. DD and CF assumed fundraising and grant follow-up. MR led the
21 587 drafting of the manuscript. All authors (MR, CR, AM, SPB, CG, VP, MT, BR, BG, MG, Cba, CBo, EG, LS,
22 588 MH, ECK, IMS, VC, OLS, DD and CF) critically reviewed and approved the final version of the protocol.
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747 **Illustrations' legends**

748 Figure 1: PROADAPT program: interventions at the patient's level

749 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
750 steps (before, during and after complex medico-surgical procedure)

751 Table 2: PROADAPT pilot trial: questionnaires and screening tests

752 Table 3: PROADAPT pilot trial: flow diagram

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755 Table 1: PROADAPT program: tasks according the different domains and the successive chronological
756 steps (before, during and after complex medico-surgical procedure)

Nurse coaching & education Bridging interventions	Coaching nurse self-presentation Delivery of a personalized patient booklet Care according best practice guidelines: - Confirm and document patient goals and treatment preferences, including advance directives. - Confirm and document patient's health care proxy or surrogate decision-maker. - In patients with existing advance directives, discuss new risks associated with the surgical procedure and an approach for potentially life-threatening problems consistent with the patient's values and preferences ("required reconsideration"). Weekly phone calls	Coaching nurse visits / phone calls Communication of patient's preference to the staff	Coaching nurse visit in the rehabilitation ward Communication of patient's preference and care difficulties to the staff (checklist): - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - pressure ulcers prevention	Coaching nurse bi-weekly phone call Communication of patient's care difficulties to the staff
Nutrition	W-4 : nutritional evaluation Nutritional plan based on measured intake W-3 : nutritional follow up - weight W-2 : nutritional follow up-weight W-1 : nutritional follow up-weight + pre-operative immunonutrition	If surgery: Care according best practice guidelines: - Consider shortened fluid fast (clear liquids up to 2 hours before anaesthesia).(29) - Normal food intake or enteral feeding should start as early as possible	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain
Physical activity	W-4 : physical performances evaluation Physical activity plan W-3 : group physical activity W-2 : + W-1 : functional follow-up	If surgery: care according best practice guidelines: - Early physical and/or occupational therapy. - Check for orthostatic hypotension. - Review physical environment to reduce injury risk. - Assistive walking devices (eg walkers) at bedside if used as outpatient	(to the discretion of the rehabilitation unit)	Pursuing of the pre-operative physical activity plan
Medication conciliation	Centralized medication conciliation and treatment optimization (STOPP/START guidelines)	Centralized medication conciliation Advices for care according best practice guidelines (16): - Adhere to existing best practices regarding antibiotic and venous thromboembolism prophylaxis. - Ensure nonessential medications have been stopped and essential medications have been taken.	Centralized medication conciliation	Centralized medication conciliation
Standardization of surgical procedures		If surgery: consider antiseptic toothpaste If surgery: care according best practice Guidelines (16): - Consideration of regional techniques to avoid postoperative complications and improve pain control. - Directed pain history. - Multi-modal or opioid-sparing techniques. - Postoperative nausea risk stratification and prevention strategies. - Strategies to avoid pressure ulcers and nerve damage. - Prevention of postoperative pulmonary complications and hypothermia. - Judicious use of intravenous fluids. - Appropriate hemodynamic management. - Continuation of indicated cardiac medications. - Daily post-operative rounding checklist: - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - Pressure ulcers prevention If surgery: consider IV iron supplementation		

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759 Table 2: PROADAPT pilot trial: questionnaires and screening tests

Domain	
Autonomy	Activity of Daily Living Scale (ADL)
	Instrumental Activities of Daily Living scale (IADL)
Geriatric screening	G8
Physical activity	RAPA (Rapid Assessment of Physical Activity), AIPVQ
Quality of life	QLQ-C30 cancer specific QoL questionnaire, QLQ-
	ED14 older cancer patients questionnaire, EQ-5D-3L
	utility questionnaire, SF-36 general QoL
	questionnaire
Locomotion and balance	Timed Up and Go test, SPPB (Short Physical
	Performance Battery)
Pain	Pain scale evaluation
Nutrition	Nutrition scale evaluation
Tiredness severity	FSS
Depression/anxiety	MNA, GDS4/GDS15
Cognitive assessment	MINI-COG
Fall risk assessment	Tinetti test
Breathlessness	Borg scale

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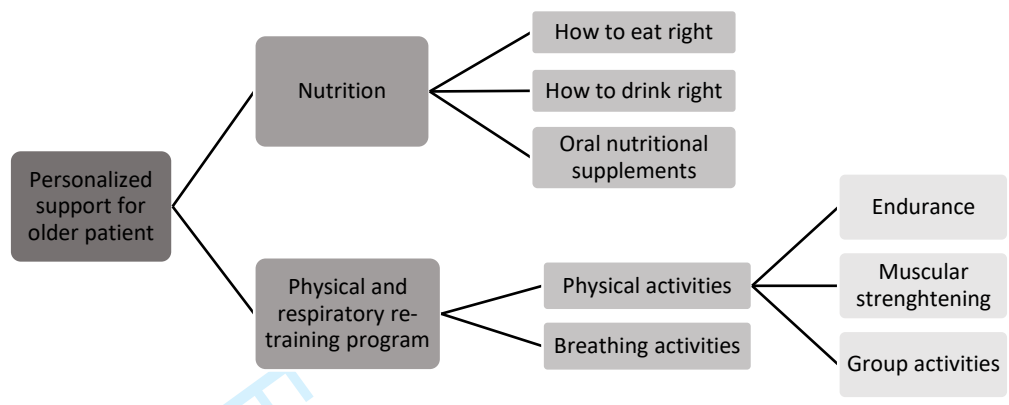
762 Table 3: PROADAPT pilot trial: flow diagram

	Baseline	Pre-therapeutic visit (0-5 days before intervention)	M1, M3, M6	M12	End of study visit
<i>Complex geriatric assessment</i>					
G8	X			X	X
ADL/IADL	X			X	X
GDS4/GDS15	X			X	X
MINI COG	X			X	X
MNA	X			X	X
QLQ-C30	X		X	X	X
QLQ-ELD14	X		X	X	X
EQ-5D-3L	X		X	X	X
Pain scale evaluation	X	X	X	X	X
Nutrition scale evaluation	X	X	X	X	X
Socio-economic evaluation	X				
<i>Physical and respiratory assessments</i>					
FSS	X		X	X	X
SF-36	X		X	X	X
Timed Up and Go test	X			X	X
SPPB	X		X	X	X
Borg scale	X			X	X
RAPA questionnaire	X		X	X	X
AIPVQ scale	X		X	X	X
Tinetti test	X			X	X
Equimog evaluation	X			X	X
Triflo	X	X			
Voldyne	X	X			
Physical activity data collection		X	X	X	X
<i>Patients' satisfaction</i>					
Standardized questionnaire					X


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Figure 1 : PROADAPT program : interventions at the patient’s level



Supplementary table 1 : Satisfaction questionnaire

 Hospices Civils de Lyon Direction de la Recherche Clinique et de l'Innovation	<h2 style="margin: 0;">PATIENT ASSESSMENT OF THE PROADAPT PILOT PHASE PROGRAM</h2>
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Mrs, Mr,

You have been part of the PROADAPT - pilot phase study and we thank you for your involvement. In order to assess and improve this study, we would like to collect your opinion. This opinion is anonymous and does not affect your healthcare.

The following questions concern the patient booklet that was given to you as part of the study

If you consider the booklet globally

- The explanations seem appropriate to you ? Not at all A little Absolutely
- The information seem clear to you ? Not at all A little Absolutely
- The pages seem readable enough ? Not at all A little Absolutely
- The illustrations seem clear to you ? Not at all A little Absolutely

How would you rate the booklet ? 0 1 2 3 4 5 6 7 8 9 10
 (useless = 0 ; very useful = 10)

The following questions concern the PROADAPT pilot phase program globally (breathing and physical exercises, booklet, calls and follow-up visits)

Did you have difficulty to understand the explanations given by the medical staff and the physician

- for breathing exercises ? Not at all A little A lot
- for physical exercises ? Not at all A little A lot
- for nutritional advices ? Not at all A little A lot
- during the assessment with the physician on the different drugs you are taking ? Not at all A little A lot

Did you encounter any difficulties

- for the realization of breathing exercises ? Not at all A little A lot
- for the realization of physical exercises ? Not at all A little A lot

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- for the setting up of nutritional advice ? Not at all A little A lot
- for the filling of activities ? Not at all A little A lot

How do you estimate nursing phone calls

- at the beginning of your healthcare before your surgery / radiotherapy Useless Little important Needed
- after your surgery/radiotherapy Useless Little important Needed

Would you like to get more information ? No Yes

If yes, which ones,.....
.....

What would be your propositions to make the program more suitable for patients?
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Thank you for your time, we will use your advice to improve the PROADAPT program and the patient booklet.

Pr Claire Falandry, study coordinator

Supplementary table 2: All items from the World Health Organization Trial Registration Data Set (SPIRIT item 2b)

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT03659123
Date of registration in primary registry	September 6, 2018
Secondary identifying numbers	69HCL16_0701 ID RCB N° 2018-A001026-49
Source(s) of monetary or material support	Agence Régionale de Santé Auvergne Rhône Alpes
Primary sponsor	Hospices Civils de Lyon
Secondary sponsor(s)	
Contact for public queries	David Dayde, +33.4.78.86.37.74, david.dayde@chu-lyon.fr
Contact for scientific queries	Claire Falandry, +33.4.78.86.66.34, claire.falandry@chu-lyon.fr
Public title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer
Scientific title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer, a Multicenter Pilot Study
Countries of recruitment	France
Health condition(s) or problem(s) studied	Old Injury
Intervention(s)	Behavioral: standardized geriatric intervention Nutritional care is based on: <ul style="list-style-type: none"> • A personalized evaluation of nutritional balance and nutritional needs of the patient • A weekly follow-up of weight and nutritional intake Total-body rehabilitation is based on: <ul style="list-style-type: none"> • 2 to 3 times a week: strength exercise • 2 to 3 times a week: endurance exercise, 20 to 45 min each sequence • 2 times a week: respiratory physiotherapy Pharmaceutical conciliation and optimization according STOPP/START criteria During peri-operative time, the nurse contacts the surgical team for transmission of patient's personal data, physical medication conciliation results During rehabilitation time and hospital-home transition time, the nurse contacts

Data category	Information
	the rehabilitation team for transmission of patient's personal data and care course, physical (nutritional, functional and/or comorbidities), medication conciliation results.
Key inclusion and exclusion criteria	<p>Inclusion Criteria:</p> <p>Patient ≥ 70 year old OR patient ≥ 60 years with significant comorbid condition (modified Charlson index ≥ 3) or disability (ADL score $< 6/6$);</p> <p>Histologically or cytologically proven cancer.</p> <p>Life expectancy > 3 months.</p> <p>Written informed consent obtained</p> <p>Covered by a Health System where applicable.</p> <p>Exclusion Criteria:</p> <p>Other malignancy within the last 5 years, except for adequately treated carcinoma in situ of the cervix or squamous carcinoma of the skin, or adequately controlled limited basal cell skin cancer.</p> <p>Patient unable to be regularly followed for any reason (geographic, familial, social, psychological).</p> <p>Any mental or physical handicap at risk of interfering with the appropriate treatment.</p> <p>Any administrative or legal supervision where applicable</p>
Study type	<p>Interventional</p> <p>Allocation: N/A</p> <p>Intervention model: Single Group Assignment</p> <p>Masking: None (Open Label)</p> <p>Primary purpose: Health Services Research</p> <p>Phase II</p>
Date of first enrolment	July 3rd, 2018
Target sample size	122
Recruitment status	Recruiting
Primary outcome(s)	<p>Implementation of at least one item of PROADAPT standardized geriatric intervention of the program PROADAPT pilot study [Time Frame: 12 months]:</p> <ul style="list-style-type: none"> • Preoperative physical activity including strength and endurance exercise assessed by physical exercises accomplished under the supervision of a physiotherapist. Number of patients with at least 1 intervention achieved in the domain. • Nutrition guidelines before and after physical activity assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain.

Data category	Information
	<ul style="list-style-type: none"> • Patient education and coaching assessed by questionnaires and visits. Number of patients with at least 1 intervention achieved in the domain • Achievement of standardized intervention procedures, according to the checklist established in consensus with surgeons. Number of patients with at least 1 intervention achieved in the domain • Rehabilitation assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain • Accomplishment of pharmaceutical medication conciliation and treatment optimization. Number of patients with at least 1 intervention achieved in the domain • Bridging interventions for hospital-to-home transition. Number of patients with at least 1 intervention achieved in the domain
Key secondary outcomes	<ul style="list-style-type: none"> • Post operative morbidity [Time Frame: 30 and 90 days] according Clavien-Dindo classification • Post-operative morbidity [Time Frame: 90 days] according to NCI CTC v4.4 • Therapeutic strategy [Time Frame: 12 months]: Treatment plan completion rate: Number of patients for whom the treatment plan was completed. • Progression-free Survival [Time Frame: 12 months] • Post-treatment complication [Time Frame: 12 months]: Post-treatment complication grade\geq3 according the National Cancer Institute Common Toxicity Criteria version 4 (NCI-CTC-v4)



Supplementary table 1: SPIRIT 2013 checklist of the trial

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Reported on page #
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary table 2 Ref 24
Protocol version	3	Date and version identifier	17 (Ethics and Consent to participate)
Funding	4	Sources and types of financial, material, and other support	17-18 (Funding)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1 (Authors' list) 18 (Authors' contributions)
	5b	Name and contact information for the trial sponsor	Supplementary table 2 Ref 24

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4		5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities
5			10 (Ethical and legal considerations)
6			17 (Funding)
7			
8			
9		5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)
10			13 (Data management and statistical analyses)
11			14 (Data monitoring)
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15	Introduction		
16			
17	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention
18			3
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22		6b	Explanation for choice of comparators
23			N/A
24	Objectives	7	Specific objectives or hypotheses
25			4
26	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
27			5
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32	Methods: Participants, interventions, and outcomes		
33			
34	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained
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Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14 (End of protocol) And N/4 (no dose modifications)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	6 (two turns of validations of the PROADAPT booklet by candidate patients)
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-12
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8-9
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12-13 (Sample size calculation)

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4 Recruitment 15 Strategies for achieving adequate participant enrolment to reach target sample size N/A (no problem for accrual)
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7 **Methods: Assignment of interventions (for controlled trials)**

N/A

8 Allocation:

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10 Sequence generation 16a Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions -
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17 Allocation concealment 16b Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned -
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22 Implementation 16c Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions -
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25 Blinding (masking) 17a Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how -
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28 17b If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial -
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32 **Methods: Data collection, management, and analysis**

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Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 3
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13 (Data management and statistical analyses)
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13-14 (Data management and statistical analyses)
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A

Methods: Monitoring

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4	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	14 (Data Monitoring)
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11		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
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15	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11 (Secondary outcomes: NCI CTCAE, QOL)
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19	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
20				
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23	Ethics and dissemination			
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25	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	10 (Ethical and legal considerations)
26				
27				
28	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	10 (Ethical and legal considerations) 14 (Protocol amendments)
29				
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34	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11 (Ethical and legal considerations)
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38		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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4	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14 (Confidentiality)
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8	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17 (Competing interests)
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11	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17 (Availability of data and materials)
12				
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14	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
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18	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15 (Dissemination policy)
19				
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24		31b	Authorship eligibility guidelines and any intended use of professional writers	15 (Dissemination policy), N/A
25				
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27		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
28				
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30	Appendices			
31				
32	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Annex 1 (in French)
33				
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35	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
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3 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on
4 the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative
5 Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.
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BMJ Open

Feasibility of a prehabilitation programme dedicated to older cancer patients before complex medical-surgical procedures: the PROADAPT pilot study protocol

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Primary Subject Heading :	Oncology
Secondary Subject Heading :	Geriatric medicine, Surgery
Keywords :	Adult oncology < ONCOLOGY, GERIATRIC MEDICINE, REHABILITATION MEDICINE, Adult surgery < SURGERY

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3 **1 Feasibility of a prehabilitation programme dedicated to older**
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6 **2 cancer patients before complex medical-surgical procedures: the**
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9 **3 PROADAPT pilot study protocol**

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3 75 **Abstract**
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5 76 **Background:** Aging is associated with an increased prevalence of co-morbidities and
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7 77 sarcopenia as well as a decline of functional reserve of multiple organ systems, which may lead,
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9 78 in the context of the disease- and/or treatment-related stress, to functional deconditioning. The
10
11 79 multicomponent “PROADAPT” intervention was developed multi-professionally to implement
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13 80 prehabilitation in older cancer patients.
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17 81 **Methods:** The PROADAPT pilot study is an interventional, non-comparative, prospective,
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19 82 multicentre study. It will include 122 patients oriented to complex medical-surgical curative
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21 83 procedures (major surgery or radiation therapy with or without chemotherapy). After informed
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23 84 consent, patients will undergo a comprehensive geriatric assessment and will be offered a
24
25 85 prehabilitation kit that includes an advice booklet with personalised objectives and respiratory
26
27 86 rehabilitation devices. Patients will then be called weekly and monitored for physical and
28
29 87 respiratory rehabilitation, pre-operative re-nutrition, motivational counselling, and iatrogenic
30
31 88 prevention. Six outpatient visits will be planned: at inclusion, a few days before the procedure,
32
33 89 and at 1, 3, 6 and 12 months after the end of the procedure. The main outcome of the study is
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35 90 the feasibility of the intervention, defined as the ability to perform at least one of the
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37 91 components of the programme. Clinical data collected will include patient- and cancer-specific
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39 92 characteristics.
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44 93 **Ethics and dissemination:** The study protocol was approved by the Ile de France 8 ethics
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46 94 committee on 5 June 2018. The results of the primary and secondary objectives will be
47
48 95 published in peer-reviewed journals. ClinicalTrials registration: NCT03659123.
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51 96 **Keywords:** oncogeriatrics; prehabilitation; motivation; sarcopenia; older cancer patients; care
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53 97 pathway.
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3 100 **Article summary**
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5 101 Strengths and limitations of this study
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8 102 - The PROADAPT programme is a prehabilitation programme specifically tailored for
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10 103 older cancer patients

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12 104 - The programme was designed according to a multidisciplinary analysis of available
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14 105 evidence and according to a multistep validation process involving patients

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17 106 - The PROADAPT pilot study is a prospective and multicentre trial designed to evaluate
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19 107 the feasibility of the intervention

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22 108 - Different secondary outcomes, including quality of life, will be evaluated to better adapt
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24 109 the programme to patient specificities

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26 110 A specific attention will be paid to programme safety and patient compliance to the
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28 111 programme.
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114 **Introduction**

115 Many oncological situations involve complex medical-surgical procedures that increase the risk
116 of patient deconditioning in older and/or sarcopenic patients (1). This may lead to a disabling
117 cascade, a “domino effect”, defined as the succession of adverse events in response to a primary
118 stress (2). This is illustrated by increased morbidity and mortality (3), but also a higher risk of
119 unplanned hospitalisations for geriatric events, defined as immobilisation syndrome, acute
120 confusion, undernutrition, falls, *de novo* urinary incontinence, and adverse drug events (4).
121 These generate frustration, appeals by patients and their families, additional hospital costs (5),
122 and more importantly, a reduced duration of life without disability (6). One of the responses to
123 this situation is enhanced rehabilitation after surgery (7).

124 In order to reduce complications after surgery, pre-operative rehabilitation (or prehabilitation)
125 has often been considered for the general population (8). The majority of the programmes
126 include nutrition, physical activity, motivational coaching, and, for some tobacco cessation (8);
127 the level of evidence is high for pre-operative nutrition (9), but it is low for physical exercise,
128 due to heterogeneous programmes with often poor compliance (10), and is deemed insufficient
129 considering psychological preparation (11). Some programmes adapted interventions on
130 nutrition, physical activity, and motivational coaching to geriatric patients but conclusions as
131 to the effectiveness of these are difficult to draw (12). It is also of note that Carli et al. did not
132 report any significant difference in the efficacy of prehabilitation versus post-operative
133 rehabilitation only in 110 frail patients aged 65 years or above operated on for colon cancer
134 (13), questioning the ability of standard prehabilitation to improve outcomes for frail older
135 patients.

136 It would, therefore, potentially be of interest to widen the spectrum of interventions included in
137 prehabilitation of older patients. To date, the other interventions known to prevent hospital-
138 related geriatric deconditioning include comprehensive geriatric assessment (14,15), iatrogenic

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2
3 139 prevention (drug and care system-related) (16,17), and hospital-to-home transition to limit the
4
5 140 risk of early readmission of patients (18). In addition, some degree of individualization is also
6
7 141 needed since cancer in the older patient is often associated with comorbidities, particularly
8
9 142 cardiovascular disease (19,20), and the older population also has a higher risk of loss of
10
11 143 autonomy and cognitive impairment, which can be increased with surgery (21–23).
12
13
14 144 In this context, and after a systematic analysis of published data, we developed the
15
16 145 Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning risk and
17
18 146 Accompaniment of Patients' Trajectories (PROADAPT), a geriatric multi-professional
19
20 147 intervention programme. Such a multi-domain intervention should be evaluated according the
21
22 148 methodology of complex interventions evaluation (24). Hence, we designed the PROADAPT
23
24 149 pilot study to evaluate the feasibility of such a complex intervention. This manuscript describes
25
26 150 both PROADAPT multi-domain intervention and PROADAPT pilot study.
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35 153 **Methods and analysis**

36 154 **Objectives**

37 155 *Primary objective*

38 156 The primary objective of the PROADAPT pilot study is to assess the feasibility of the
39
40 157 programme, defined as the achievement of at least one item of the programme during patient
41
42 158 follow-up.
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49 159 50 51 160 *Secondary objectives*

52 161 The secondary objectives of the study are:

- 53 162 1) To assess the achievement of each item of the programme independently of each other
54
55 163 (rate of achievement of all or part of the instructions);
56
57
58
59
60

- 164 2) To assess patient satisfaction with the programme (Supplementary file 1);
- 165 3) To estimate the rate of compliance to items during the various visits;
- 166 4) To evaluate the functional status and quality of life (QoL) over one year following
167 surgery (health-related QoL, other dimensions)
- 168 5) To assess post-treatment complications, their rates, and their severity at 30 and 90 days
169 according to the Clavien-Dindo and National Cancer Institute Common Terminology
170 Criteria for Adverse Events (NCI-CTCAE) version 4 classification systems (25);
- 171 6) To estimate the post-operative mortality at 30 and 90 days;
- 172 7) To estimate the costs of treatments (health system);
- 173 8) To study the therapeutic strategies (treatment completion rate);
- 174 9) To estimate the progression-free survival (PFS) rate at one year;
- 175 10) To estimate the overall survival (OS) at one year;
- 176 11) To estimate the tolerance of treatments;
- 177 12) To assess the change in geriatric covariates over one year.

178

179 **Study design**

180 PROADAPT - pilot study is a prospective, non-comparative multicentre conducted in seven
181 centres of the Auvergne-Rhône-Alpes region of France.

182

183 **Study sites and participants**

184 The study population will include older patients identified during multidisciplinary consultation
185 meetings and oriented to complex medical-surgical curative procedures in the study centres
186 (Lyon Sud hospital, Croix Rousse hospital and Edouard Herriot hospital from the Hospices
187 Civils de Lyon, Nord-Ouest Villefranche-sur-Saône hospital, Annecy-Genevois hospital,
188 Chambéry hospital, Lyon-Villeurbanne Médipôle).

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2
3 189 Inclusion criteria are: age ≥ 70 years, or ≥ 60 years with significant comorbidity (Cumulative
4
5 190 Illness Rating Scale for Geriatrics (CIRS-G) ≥ 3 (26)) or disability (Activities of Daily Living
6
7 191 (ADL) score $< 6/6$ (27)), histologically or cytologically proven cancer, life expectancy > 3
8
9 192 months, planned complex medical-surgical procedure with curative intent. Complex medical-
10
11 193 surgical procedures are defined as major abdominal surgery (breast excluded), either minimally
12
13 194 invasive or open.

14
15
16 195 Exclusion criteria are: other malignancy within the previous 5 years (except for adequately
17
18 196 treated carcinoma *in situ* of the cervix or squamous carcinoma of the skin, or adequately
19
20 197 controlled limited basal cell skin cancer), unable to be regularly followed for any reason
21
22 198 (geographic, familial, social, psychological), or with any mental or physical handicap at risk of
23
24 199 interfering with the appropriate treatment.

25
26
27 200 A screening of older patients will be systematically performed during multidisciplinary
28
29 201 meetings and described in the CONSORT flow diagram of the article reporting the study.
30
31
32

33 202

34 35 203 **Intervention**

36
37 204 The PROADAPT intervention programme was developed on a multi-dimensional and
38
39 205 multidisciplinary basis. From January 2016 to April 2018, nine regional meetings were
40
41 206 organised, gathering 40 representatives of the following medical and paramedical specialties:
42
43 207 geriatricians, nutritionists, surgeons (subspecialties: gynaecology, digestive surgery, urology),
44
45 208 oncologists, anaesthesiologists, nurses, physiotherapists, occupational therapists, adapted
46
47 209 physical activity monitors. A systematic review of published data was conducted in the
48
49 210 following axes, to provide a graded state-of-the-art: nutrition, physical activity, patient
50
51 211 education, medication rationalisation, cardiovascular optimisation, transition, and
52
53 212 standardisation of surgical procedures. Based on the qualitative grading of existing data, a
54
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2
3 213 modified Delphi method was used to co-validate the content of the standardised intervention
4
5 214 checklist, and the feasibility of the implementation of each point of this checklist (Table 1).
6
7
8 215 A PROADAPT booklet was developed; it is a standardised, adapted, and evolutive tool
9
10 216 designed to explain physical exercise and nutrition counselling, and to ensure the collection of
11
12 217 patients' day-to-day achievements. The first version was tested by candidate patients before the
13
14 218 validation of the current (version 3) of the booklet.
15
16

17 219

18
19 220 PROADAPT standardised geriatric intervention programme includes:

20
21 221 - Pre-operative physical activity, including strength and endurance exercise \pm group
22
23 222 activities over 4 \pm 2 weeks. Interventions with a high level of evidence were retained, according
24
25 223 to an ongoing umbrella review of systematic reviews (<http://www.crd.york.ac.uk/PROSPERO>
26
27 224 [Ref CRD42020100110](http://www.crd.york.ac.uk/PROSPERO); (28,29));

28
29
30 225 - Nutrition: nutrition before and after physical activity, pre-postoperative immuno-
31
32 226 nutrition \pm artificial nutrition (*i.e.* enteral or parenteral nutrition) according international
33
34 227 guidelines (9);

35
36
37 228 - Patient (and caregiver) education and coaching (on nutrition and physical exercise)
38
39 229 according to a weekly schedule with the activation of integrated supports (30);

40
41
42 230 - Standardised intervention procedures, according to a checklist established in consensus
43
44 231 with surgeons;

45
46 232 - Enhanced rehabilitation will be promoted according to international guidelines (31);

47
48
49 233 - Pharmaceutical medication conciliation and treatment optimisation, according to a
50
51 234 centralised process with pharmaceutical expertise;

52
53
54 235 - Bridging interventions for hospital-to-home transition, according to a proposed
55
56 236 standardised procedure including training of dedicated nurses, and post-discharge phone calls
57
58 237 follow-up over the 12 weeks after surgery. In practice, only 2 or 3 people from the coordination
59
60

1
2
3 238 centre team are in charge of coaching for all patients. In the future, a nurse coach will be trained
4
5 239 in each centre and will be responsible for patient coaching. Interventions with a high level of
6
7 240 evidence were retained, according to an ongoing umbrella review of systematic reviews
8
9 241 (<http://www.crd.york.ac.uk/PROSPERO> Ref CRD42017055698).

12 242 The intervention is designed to be implemented at different moments of patient care (Table 1).

14
15 243

17 244 *During the prehabilitation period:*

19 245 • A dedicated nurse, trained in patient education by the coordinating centre team
20
21 246 (“coaching nurse”) presents him/herself to the patient for:

24 247 - Presentation of the programme to the patient and his/her caregiver(s)

26 248 - Personalisation of the PROADAPT booklet (see below) to the patient’s
27
28 249 characteristics

30 250 - Collection of personal data, nutritional, and functional habits

33 251 - Geriatric assessment using standardised scores (cognition using the Mini-COG
34
35 252 screening tool (32), depression using the geriatric depression scale in 4 and 15 items
36
37 253 [GDS4/GDS15] (33), nutrition using the mini-nutritional assessment [MNA] (34))

40 254 - Collection of the information to be sent to the pharmacist: comorbidities,
41
42 255 comedications

44 256 - Anticipation and organisation of the future appointments (anaesthetists,
45
46 257 stomatherapist, ...)

49 258 - A weekly visit or phone call according to a structured interview for health
50
51 259 education and transmission of nutritional and functional advice (see below)

53
54 260 • Nutritional care is based on:

- 1
2
3 261 - A personalised evaluation of nutritional balance and nutritional needs of the
4
5 262 patient according to dietician diagnosis based on measured intake and international
6
7 263 recommendations
8
9
10 264 - A weekly follow-up of weight and nutritional intake. If the coaching nurse
11
12 265 identifies an unfavourable nutritional trend, s/he reports it to the referring physician and
13
14 266 nutritionist
15
16
17 267 - Artificial nutrition if needed according European Society for Clinical Nutrition
18
19 268 and Metabolism (ESPEN) recommendations (9,35,36)
20
21 269 - Pre-operative immunonutrition during 7 days before surgery (36)
22
23
24 270 • Total-body rehabilitation:
25
26 271 - 2 to 3 times a week: strength exercise (each time with dedicated exercises for
27
28 272 upper and lower limbs, as well as abdominal muscles; 20 to 45 minutes each sequence)
29
30 273 - 2 to 3 times a week: endurance exercise (walking or cycle ergometer), 20 to 45
31
32 274 minutes each sequence
33
34
35 275 - 3 times a day: respiratory physiotherapy
36
37 276 - Once a week (if possible): group activities (according to the centre organisation
38
39 277 and home-hospital distance)
40
41
42 278 • Pharmaceutical conciliation and optimisation according to Screening Tool of Older
43
44 279 Persons' Prescriptions and Screening Tool to Alert to Right Treatment (STOPP/START)
45
46 280 criteria version 2 (37) and international recommendations concerning peri-operative care (7):
47
48 281 to be transmitted to the surgical and anaesthesia team without any obligation to change patient
49
50 282 care.
51
52
53 283
54
55
56 284 *During peri-operative period*
57
58 285 • The coaching nurse contacts the surgical team for transmission of:
59
60

- 1
2
3 286 o patient's personal data
4
5 287 o physical (nutritional, functional, and/or comorbidities) as well as psychological
6
7 difficulties
8 288
9
10 289 o results of medication conciliation
11
12 290

13
14
15 291 *During rehabilitation period*

- 16
17 292 • The coaching nurse contacts the rehabilitation team for transmission of:
18
19 293 o patient's personal data and care course
20
21 294 o physical (nutritional, functional, and/or comorbidities) as well as psychological
22
23 difficulties
24 295
25
26 296 o results of medication conciliation
27
28 297 • The rehabilitation programme is left to the discretion of the rehabilitation team (standard
29
30 care and local habits).
31 298
32
33 299 • A weekly phone call from the coaching nurse to the rehabilitation team for nutritional
34
35 300 and functional follow-up, as well as medication conciliation
36
37
38 301

39
40 302 *During hospital-home transition period*

- 41
42 303 • The coaching nurse contacts the patient's general practitioner for transmission of:
43
44 304 o patient's personal data and care course
45
46 305 o physical (nutritional, functional, and/or comorbidities) as well as psychological
47
48 difficulties
49 306
50
51 307 o results of medication conciliation
52
53
54 308 • Bi-weekly phone call of the coaching nurse to the patient for nutritional and functional
55
56 309 follow-up
57
58 310 • Advice for optimisation of symptom management: abdominal pain, nausea, vomiting...
59
60

1
2
3 3114
5 312 **Participant timeline**6
7
8 313 Six successive evaluations are planned for the participants.9
10 314 *The inclusion visit* is planned during a geriatric consultation planned at least 7 days before the
11
12 315 start day of the complex medical-surgical procedure. If the complex medical-surgical procedure
13
14 316 is delayed for any reason or the patient receives a neo-adjuvant treatment, the prehabilitation
15
16 317 period may be prolonged up to 9 months. In such cases, the frequency of the phone calls is
17
18 318 decreased (from 1/week to 1/month) after 4 weeks. During the inclusion visit, lasting about 1
19
20 319 hour, the following data are collected:

- 21
-
- 22
-
- 23
-
- 24 320 - Clinical (blood pressure, heart rate, Eastern Cooperative Oncology Group (ECOG)
-
- 25
-
- 26 321 score (38), comorbidities), laboratory (albumin, prealbumin, C-reactive protein), and
-
- 27
-
- 28 322 paraclinic (year of birth, sex, weight, height, body mass index, change in weight over
-
- 29
-
- 30 323 the last 3 and 6 months)
-
- 31
-
- 32
-
- 33 324 - All concomitant treatments and drug conciliation
-
- 34
-
- 35 325 - The history of the disease (primitive site, metastases, histology of the initial tumour,
-
- 36
-
- 37 326 presence of tumour markers)
-
- 38
-
- 39
-
- 40 327 - Radiological disease assessments (date and nature)
-
- 41
-
- 42 328 - Results of a standardised geriatric assessment using validated questionnaires with a
-
- 43
-
- 44 329 particular attention on physical activity and nutrition (ADL(27)/instrumental ADL
-
- 45
-
- 46 330 (IADL) (39), G8 (40), Rapid Assessment of Physical Activity (RAPA) (41), daily
-
- 47
-
- 48 331 physical instrumental activities (AIPVQ) (42), European Organization for the Research
-
- 49
-
- 50 332 and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (43) and
-
- 51
-
- 52 333 Elderly specific questionnaire in 14 items, (QLQ-ELD14) (44), the EUROQOL EQ-5D-
-
- 53
-
- 54 334 3L evaluating five dimensions: mobility, self-care, usual activities, pain/discomfort and
-
- 55
-
- 56 335 anxiety/depression in three levels (45), fatigue short form inventory (SF-36) (46), Short
-
- 57
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- 58
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- 59
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- 60

1
2
3 336 physical performance battery (SPPB) (47), Timed up and go (TUG) test (48), 9-item
4
5 337 Fatigue Severity Scale (FSS) (49), MNA (34), GDS4/GDS15 (33), Mini-COG (32),
6
7 338 Tinetti test (50), Borg scale (51), Pain scale (52), Nutrition scale (53)) (**Error!**
9
10 339 **Reference source not found.**Tables 2 and 3).

11
12 340 - Delivery of the “PROADAPT kit” during a meeting with a dedicated paramedic (nurse,
13
14 341 physiotherapist, ergotherapist...) to:

15
16
17 342 ○ Provide to the patient Voldyne® (Hudson RCI, Temecula, CA, USA) and Triflo
18
19 343 II® (Tyco Healthcare, Mansfield, MA, USA) incentive spirometry devices for
20
21 344 inspiratory muscle training

22
23
24 345 ○ Present the PROADAPT booklet that includes a battery of exercises and
25
26 346 nutritional counselling specifically designed for this older population:

27
28 347 ■ muscle strengthening of the upper limbs (6 exercises, 3 difficulty levels),
29
30 348 lower limbs (6 exercises, 3 difficulty levels), abdominal wall (4
31
32 349 exercises, 3 difficulty levels); objective: 2 to 3 sessions per day for a total
33
34 350 duration of between 20 and 45 minutes

35
36
37 351 ■ endurance/aerobic activities (7 exercises, 3 difficulty levels with 3
38
39 352 duration objectives); objective: every day

40
41
42 353 ■ inspiratory muscle training with Voldyne® and Triflo II® devices;
43
44 354 objective: 3 sessions per day for a total duration of 30 minutes

45
46
47 355 ■ general nutritional counselling adapted to the older population: food
48
49 356 enrichment, inter-meal collations, oral nutritional supplements.

50
51 357 ○ Fulfil a 3-day food statement that allows, in the 7 days after inclusion, to deliver
52
53 358 a dietician-driven personalised nutritional counselling. If needed, in case of
54
55 359 unfavourable nutritional parameters, artificial nutrition is introduced.

56
57
58 360 - Prescription, if needed:
59
60

- 1
2
3 361 ○ of home physiotherapy according to the PROADAPT programme for respiratory
4
5 362 training sessions and physical activity training sessions
6
7
8 363 ○ of oral nutritional supplements
9
10 364 ○ of usual medicines, adapted following pharmaceutical review
11
12 365 - For patients requiring inpatient follow-up, hospital admission for a few days in a
13
14 366 rehabilitation unit for a physiotherapeutic programme and/or artificial nutrition (enteral
15
16
17 367 preferred).

18
19 368 During the pre-intervention period, phone calls by a dedicated paramedic are planned (once a
20
21 369 week for the first 4 weeks and then once a month until the intervention). Calls are semi-directed
22
23 370 interviews focused on the patient's autonomy, physical activity, appetite, and sleep over the last
24
25 371 period (week/month). A special attention is paid to encouraging patient motivation and
26
27 372 compliance to the programme.

28
29
30 373 *The pre-therapeutic visit* is scheduled when possible within the 5 days before the day of the
31
32 374 intervention. This visit is performed in the surgery or radiotherapy unit only if the visit is
33
34 375 necessary before the intervention and does not modify standard therapeutic care; it collects:

- 35
36
37 376 - Clinical, laboratory, and paraclinic data
38
39 377 - All concomitant treatments and drug conciliation
40
41 378 - Data concerning pain, nutrition, fitness, and physical tests (Table 2 and 3)

42
43
44 379 During the post-intervention period, paramedics trained in clinical research will resume follow-
45
46 380 up phone calls as before the intervention once a week for 12 weeks after day 0 (D0), and once
47
48 381 a month up to 12 months after D0. D0 is defined as the last day of surgery (day of the last
49
50 382 resumption of surgery in the limit of 30 days after the first intervention) or the last day of
51
52 383 radiotherapy. For weekly calls, a margin of ± 2 days is allowed, and for monthly calls a margin
53
54 384 of ± 7 days is allowed.
55
56
57
58
59
60

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2
3 385 *Visits at 1, 3, and 6 months after the intervention (± 7 days):* The patient may have started an
4
5 386 antineoplastic treatment according to standard of care. The visit could be with the surgeon, the
6
7 387 radiotherapist, or the oncologist according local habits. The data to be collected are:

- 8
9
10 388 - Clinical (blood pressure, heart rate, ECOG scale (38)), laboratory (albumin, prealbumin,
11
12 389 C-reactive protein), and patient characteristics (weight, body mass index)
13
14 390 - All concomitant treatments and drug conciliation
15
16
17 391 - Patient care (surgery and complications, treatment for the cancer)
18
19 392 - Radiological disease assessments (date and nature)
20
21
22 393 - Quality of life, pain, nutrition, fitness, physical performance through questionnaires and
23
24 394 tests regarding (Table 2 and 3)
25
26 395 - Hospital costs related to complications

27
28 396 *The end of study visit* is planned at 12 months (per-protocol) or at the date of trial premature
29
30 397 discontinuation (± 7 days) for the collection of the data listed above. In addition, and in case of
31
32 398 omission of one or more of the intermediate visits, data relating to complications occurring
33
34 399 during the post-therapeutic period are collected.
35
36

37
38 400

40 401 **Outcomes and measurements**

41 42 402 *Primary outcome*

43
44 403 The main outcome measure will be the proportion of patients who have completed at least one
45
46 404 item in the PROADAPT programme after 12 months after D0. The workshops of the
47
48 405 programme are:

- 49
50
51 406 - Physical and respiratory rehabilitation
52
53 407 - Re-nutrition session
54
55 408 - Telephone nurse follow-up
56
57

58 409
59
60

1
2
3 410 ***Secondary outcomes***
4

5 411 The secondary outcomes of the study are:

6
7 412 - The feasibility of each stage of the programme independently of each other (rate of
8
9 413 achievement of all or part of the instructions)

10
11
12 414 ○ Pre-operative physical rehabilitation including (Figure 1):

13
14
15 415 ● Muscle strengthening

16
17 416 ● Respiratory rehabilitation

18
19 417 ● Endurance work

20
21
22 418 ○ Pre-operative nutrition counselling (Figure 1)

23
24 419 ○ Drug reconciliation / iatrogenic prevention

25
26 420 ○ Pre-therapeutic follow-up calls

27
28 421 ○ Post-surgery or post-radiotherapy follow-up calls
29
30
31 422

32
33 423 - Patient satisfaction with the overall programme at the end of the study (end of follow-up or
34
35 424 study discontinuation) estimated using a questionnaire (Supplementary file 1).

36
37 425 - To assess the change over time before surgery of: physical parameters and exercises,
38
39 426 inspiratory parameters and exercises (Voldyne[®], Triflo[®]), as well as weight and food intake
40
41 427 (qualitative and quantitative assessments).
42
43

44
45 428 - To assess the change over 1 year of:

46
47 429 ○ physical performance (SPPB, gate speed, TUG test) and functional independence on
48
49 430 ADL (27), IADL (39), AIPVQ (42)

50
51 431 ○ nutritional parameters of the patient (weight, albuminemia, appetite)

52
53 432 ○ health-related QoL for patients based on QLQ-C30 and ELD14 (5 dimensions: mobility,
54
55 433 disease burden, emotional and physical functioning, tiredness) (54,55)

56
57 434 ○ pharmaceutical conciliation
58
59
60

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2
3 435 - Estimate the rate and nature of post-operative complications at 30 days (NCI-CTCAE)
4
5 436 - Estimate the rate and nature of post-operative complications according to the CCI at 30 and
6
7 437 90 days
8
9 438 - Estimate post-operative mortality at 30 and 90 days
10
11 439 - Estimate the one-year overall survival (OS) rate
12
13 440 - Estimate the one-year progression-free survival (PFS) rate
14
15 441 - Estimate the longitudinal change of QoL according to QLQ C30, ELD14, and EQ-5D
16
17 442 - Estimate treatment costs (health system)
18
19 443 - Study therapeutic strategies (treatment completion rate)
20
21 444 - Estimate the change of geriatric covariates over 1 year.
22
23
24
25
26
27

28 446 **Sample size calculation**

29
30 447 The programme will be considered feasible, at the patient level, if all or part of the programme
31
32 448 is implemented in at least 50% of the included patients (= alternative hypothesis). This threshold
33
34 449 was defined in line with previous studies on prehabilitation for older cancer patients, that
35
36 450 reported compliance rates between 16 and 95% (56,57). Considering that the PROADAPT
37
38 451 programme is complex even if tailored to older patients, we anticipate modest compliance rates.
39
40 452 To reject the null hypothesis of programme feasibility in less than 35% of patients, with an
41
42 453 alpha risk of 5% and a power of 90% (beta=10%, bilateral test), the number of subjects required
43
44 454 is 111; accounting for 10% non-treatable patients, a total of 122 patients should be included.
45
46 455 The included patients will be analysed according to the intention-to-treat principle.
47
48
49
50

51 456

52 53 457 **Data management and statistical analyses**

1
2
3 458 Data are monitored by a clinical research assistant (CRA). Inconsistencies will be reported to
4
5 459 the study investigators in order to decide whether the data should be corrected or considered as
6
7 460 missing. Any changes in the data will be reported.
8
9

10 461 Data analyses will be performed by the data management and analysis centre. The analyses will
11
12 462 be carried out by an independent statistician with the latest version of the R software
13
14 463 environment (R Core Team. R: A language and environment for statistical computing. R
15
16 464 Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>). All
17
18 465 of the characteristics collected will be subjected to a descriptive analysis.
19
20
21 466

22 23 24 467 ***Descriptive analyses***

25
26 468 A flow diagram will describe the data available for the patient population at baseline, and during
27
28 469 each follow-up visit. Eligibility criteria for treated patients will be verified, as well as follow-
29
30 470 up and end of study visits. Reasons for premature end of study will be provided.
31
32

33 471 Characteristics of the study population, numbers and proportions of missing values will be
34
35 472 reported. Patient characteristics will be described using mean and standard deviation or median
36
37 473 and interquartile range for quantitative variables, and frequencies and distribution for
38
39 474 categorical variables. A comparison of baseline characteristics between patients with complete
40
41 475 follow-up and those with attrition will be performed. If needed, methods for handling missing
42
43 476 data (multiple imputation, mixed model, or auxiliary variable) will be used when appropriate.
44
45
46
47 477

48 49 478 ***Primary analysis***

50
51 479 The proportion of patients who have completed at least one PROADAPT programme activity
52
53 480 12 months after the start of treatment will be estimated using mean and standard deviation.
54
55

56 481 ***Secondary analyses***

57
58 482
59
60

1
2
3 483 **Time-to-event variables: follow-up, overall survival, progression-free survival**

4
5 484 The probabilities of events at specific measurement times will be estimated according to the
6
7
8 485 Kaplan-Meier method. Medians of event-free survival will be reported by treatment arm with
9
10 486 its 95 % confidence interval [95% CI], if the number of events allows estimation of the median.
11
12 487 OS and PFS probabilities at 12 months (after the day of the last revision of surgery or the last
13
14 488 day of radiotherapy) will be provided with 95% CI.

15
16
17 489

18
19 490 **Quality of life**

20
21 491 Analyses of the QoL data will be performed according to the modified intention-to-treat (mITT)
22
23 492 principle: all included patients, regardless of compliance with the eligibility criteria and whether
24
25 493 or not they were followed-up, and for whom the QoL scores are available at inclusion will be
26
27 494 included in the analysis. Patient QoL, linked to health, will be analysed after 3 months through
28
29 495 5 dimensions: mobility, disease burden, emotional and physical functioning, and fatigue.

30
31
32 496

33
34
35 497 ***Data monitoring***

36
37 498 The successful completion of the database is ensured by the hospital CRA. The hospital CRA
38
39 499 also ensures compliance with the study protocol. The sponsor CRA verifies that the rights of
40
41 500 the participants are respected.

42
43
44 501

45
46
47 502 ***End of study***

48
49 503 Patients leave the study either on a per-protocol basis during the “end of study visit” on month
50
51 504 12 after the intervention or at any time during the conduct of the study if they no longer wish
52
53 505 to participate. However, as indicated in the information letter to the patients/caregivers, the data
54
55 506 collected before exclusion may be used as part of the study.

56
57
58 507

59
60

1
2
3 508 ***Confidentiality***
4

5 509 Correspondence tables will be kept in a separate file that does not contain clinical data. The
6
7
8 510 access to the nominative information is protected by a password and confidentiality is
9
10 511 guaranteed by the study.
11

12 512

13
14 513 ***Protocol amendments***
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16
17 514 Any important modification requiring a new ethics committee approval will be communicated
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19 515 in future publications. Any potential impact of protocol modifications on the results will be
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21 516 discussed as appropriate.
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26 518 ***Trial status***
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28 519 Patient enrolment began on 3 July 2018. Data are currently being collected.
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33 521 ***Patient and public involvement***
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35 522 Patients were involved at different steps of the trial: during the development of the PROADAPT
36
37 523 booklet, several (n=30) patients were asked to answer an anonymous questionnaire in order to
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39 524 improve its ergonomics; the information letter and consent form for the study were reviewed
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41 525 by the patients committee of the *Ligue Nationale de Lutte contre le Cancer* (a French
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43 526 association of cancer patients).
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49 528 **Discussion**
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51 529 **Discussion of the intervention**
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53 530 Prehabilitation has long been conceptualised as an effective means of improving the functional
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55 531 capacity of the individual to enable them to resist various stressors. Originally developed in the
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57 532 military as the association of physical training to improve strength and endurance, improvement
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3 533 of nutritional intake, and general education (58), it has been transposed into medicine and major
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5 534 surgery – initially when an ICU admission is planned – at the beginning of the century (59).
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7 535 Despite a growing interest in the medical community for prehabilitation, and particularly cancer
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9 536 prehabilitation, the level of evidence for specific interventions remains too low for it to be
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11 537 implemented in everyday practice. Among the main limitations include the heterogeneity of
12
13 538 programmes, sometimes poor patient compliance, and the fact that most studies were small pilot
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15 539 studies developed for patients fitter and younger than those who are likely to benefit the most
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17 540 from prehabilitation. Another point to emphasise is that most programmes include only one
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19 541 intervention – physical, nutritional, or psychological rehabilitation – while multimodal
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21 542 interventions are often considered to be more effective in older populations.
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23 543 Considering these points, the PROADAPT intervention was developed according to an
24
25 544 innovative management strategy since it started in 2016 by multi-professional meetings
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27 545 conceived as brainstorming sessions in order to develop a multidisciplinary programme
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29 546 dedicated to prehabilitation and follow-up of older patients. The multidisciplinary conception
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31 547 of the intervention, the particular attention paid to older patients’ specificities and the previous
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33 548 experience of the participants in various fields, including patient education, cognition, and
34
35 549 physiotherapy, are hopefully the warrants of the most tailored approach to the target population.
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37 550 For example, a large font was used in the booklet and the illustrations highly schematic and
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39 551 highly contrasted, and, furthermore, each sentence was verified by a panel of patients in order
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41 552 to ensure correct understanding. This resulted in high rate of satisfaction regarding the booklet
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43 553 that was evaluated by 30 patients (unpublished data).
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45 554 This pilot study is the first step towards an ambitious programme, since the PROADAPT
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47 555 programme will be evaluated in the future in two randomized studies, PROADAPT-
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49 556 ovary/EWOC-2 (NCT04284969) and PROADAPT sus-mesocolic, designed to evaluate the
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51 557 impact of the PROADAPT programme on post-treatment complications versus usual practice.
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3 558 In order to favour patient compliance and follow-up, an eHealth tool, ID-PROADAPT®, has
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5 559 been developed that will help supervise the course of patients' care.
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7 560 **Discussion of the study design**

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9
10 561 In line with the previous points, this pilot study was designed to answer the critical question: is
11
12 562 a multidomain prehabilitation programme feasible in an older cancer population? This question
13
14 563 encompasses several points: Is the programme physically adapted to an older population? Is
15
16 564 such a program applicable in ambulatory care? How to build pedagogical tools adapted for such
17
18 565 ambulatory use? Are such pedagogical tools understandable? What is the compliance of the
19
20 566 patients to each domain of the intervention programme?... Another point is to understand is
21
22 567 whether the patient's care team accepts such intervention; however, this point was previously
23
24 568 evaluated by Ghignone *et al.* who demonstrated through an international survey that surgeons
25
26 569 are generally in favour for such programmes since 71% of them would accept to prehabilitate
27
28 570 their elderly patients four weeks before surgery, if such intervention is proven to be effective
29
30 571 (60). Nevertheless, the participation of surgeons and anaesthetists during initial brainstorming
31
32 572 sessions was of major interest since they greatly enriched the structure of the programme.
33
34 573 Thus, the construct of this trial may appear as highly complex with overabundant secondary
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36 574 endpoints, but this design encompasses as much as possible the complexity of preventive care
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38 575 in an older population, which has to mix adaptation to the target population and the ability to
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40 576 maintain compliance over time.
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49 578 **Ethics and dissemination**

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51 579 The study sponsor is the Hospices Civils de Lyon, responsible for study insurance and
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53 580 pharmacovigilance. The study protocol (V2) was approved by the Ile de France 8 ethics
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55 581 committee on 5 June 2018 and cover all sites involved in this study. The amended versions
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57 582 were as follows: V3 dated 23 October 2018 (change in the recruitment period, addition of new
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3 583 investigation centres), V4 dated 17 May 2019 (request for an additional 12 months extension,
4
5 584 update with the General Data Protection Regulations (GPDR) and update of the patient
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7 585 booklet), V5 dated 17 July 2020 (addition of a cohort of 30 patients to test the follow-up
8
9 586 programme with the ID-PROADAPT® eHealth tool, Supplementary file 2, request for an
10
11 587 additional 8 months extension). The current version is the V5 dated 17 July 2020, authorised
12
13 588 on 10 September 2020. The research will be carried out in accordance with the Helsinki
14
15 589 Declaration and ICH GCP (International Conference on Harmonisation-Good Clinical Practice)
16
17 590 Guidelines. The trial protocol fulfils the SPIRIT 2013 checklist (Supplementary table 1) and
18
19 591 World Health Organization trial registration data set (Supplementary table 2). The study
20
21 592 complies with the principles of the data protection act in France and with the GPRD in force in
22
23 593 Europe. Each investigator must collect a written informed consent at the beginning of the
24
25 594 procedure. This consent is retained in the patient's medical chart. The patient can stop
26
27 595 participation in the study at any time with an oral instruction given to the investigator or CRA.
28
29 596 Patients will be informed of additional amendments according to the law in force.
30
31 597 The results of the primary and secondary objectives will be published in peer-reviewed journals.
32
33 598 All authors of future publications will have to meet the criteria for authorship stated in the
34
35 599 Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International
36
37 600 Committee of Medical Journal Editors.
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602 Total words count: 4771

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604 **Abbreviations**

605 ADL: Activities of Daily Living; AIPVQ: Physical Instrumental activities of daily living (in
606 French: Activités Instrumentales Physiques de la Vie Quotidienne); CRA: Clinical Research
607 Assistant; EORTC: European organisation for research and treatment of cancer; ESPEN:

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3 608 European Society for Clinical Nutrition and Metabolism; FSS: Fatigue Severity Scale; GDS:
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5 609 Geriatric Depression Scale; IADL: Instrumental Activities of Daily Living; ICU: Intensive Care
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8 610 Unit; mITT: Modified Intention To Treat; MNA: Mini Nutritional Assessment; QLQ-C30:
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10 611 quality of life questionnaire core 30 of the EORTC; QLQ-ELD14: Older patients- specific
11
12 612 quality of life questionnaire in 14 items of the EORTC; RAPA: Rapid Assessment of Physical
13
14 613 Activity; SF-36: short form 36 health survey questionnaire; SPPB: Short Physical Performance
15
16
17 614 Battery
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19 615

21 616 **Declarations**

24 617

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29
30 620 older people with cancer.

33 621 *PROADAPT working group*

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32
33 646 assistants.

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36 647

37 38 648 **Availability of data and materials**

39
40 649 The final dataset of the PROADAPT pilot study will be available on reasonable request after
41
42 650 publication of the primary objective. Data requests can be submitted to the corresponding
43
44 651 author.

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48 49 653 **Competing interest**

50
51 654 The authors declare that they have no competing interests.

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55 56 656 **Consent for publication**

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3 657 Not applicable
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7
8 659 **Author contributions**
9

10 660 All authors participated to the PROADAPT intervention conception. Study protocol was
11
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13
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18
19 664 reviewed and approved the final version of the protocol.
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peer review only

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3 852 **Illustrations' legends**
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5 853 Figure 1: PROADAPT program: interventions at the patient's level
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7 854 Table 1: PROADAPT programme: tasks according to the different domains and the
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10 855 successive chronological steps (before, during, and after complex medical-surgical
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12 856 procedures)
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14 857 Table 2: PROADAPT pilot trial: questionnaires and screening tests
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17 858 Table 3: PROADAPT pilot trial study: flow diagram
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861 Table 1: PROADAPT programme: tasks according to the different domains and the
 862 successive chronological steps (before, during, and after complex medical-surgical
 863 procedures)

Nurse coaching & education Bridging interventions	Coaching nurse self-presentation Delivery of a personalised patient booklet Care according to best practice guidelines: - Confirm and document patient goals and treatment preferences, including advance directives. - Confirm and document patient's healthcare proxy or surrogate decision-maker. - In patients with existing advance directives, discuss new risks associated with the surgical procedure and an approach for potentially life-threatening problems consistent with the patient's values and preferences ("required reconsideration"). Weekly phone calls	Coaching nurse visits / phone calls Communication of patient's preference to the staff	Coaching nurse visit in the rehabilitation ward Communication of patient's preference and care difficulties to the staff (checklist): - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - pressure ulcers prevention	Coaching nurse bi-weekly phone call Communication of patient's care difficulties to the staff
Nutrition	W-4: nutritional evaluation Nutritional plan based on measured intake W-3: nutritional follow up - weight W-2: nutritional follow up-weight W-1: nutritional follow up-weight + pre-operative immunonutrition	If surgery: care according to best practice guidelines: - Consider shortened fluid fastin (clear liquids up to 2 hours before anaesthesia).(36) - Normal food intake or enteral feeding should start as early as possible	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain	Nutritional plan based on - Weight curve - Measured intake Optimal management of - Nausea/vomiting - Abdominal pain
Physical activity	W-4: physical performance evaluation Physical activity plan W-3 group physical activity W-2 + W-1 functional follow-up	If surgery: care according best practice guidelines: - Early physical and/or occupational therapy. - Check for orthostatic hypotension. - Review physical environment to reduce injury risk. - Assistive walking devices (e.g. walkers) at bedside if used as outpatient	(to the discretion of the rehabilitation unit)	Pursuing of the pre-operative physical activity plan
Medication conciliation	Centralised medication conciliation and treatment optimisation (STOPP/START guidelines)	Centralised medication conciliation Advices for care according best practice guidelines (16): - Adhere to existing best practices regarding antibiotic and venous thromboembolism prophylaxis. - Ensure nonessential medications have been stopped and essential medications have been taken.	Centralised medication conciliation	Centralised medication conciliation
Standardisation of surgical procedures		If surgery: consider antiseptic toothpaste If surgery: care according to best practice guidelines (16): - Consideration of regional techniques to avoid postoperative complications and improve pain control. - Directed pain history. - Multi-modal or opioid-sparing techniques. - Postoperative nausea risk stratification and prevention strategies. - Strategies to avoid pressure ulcers and nerve damage. - Prevention of postoperative pulmonary complications and hypothermia. - Judicious use of intravenous fluids. - Appropriate haemodynamic management. - Continuation of indicated cardiac medications. - Daily post-operative rounding checklist: - delirium/cognitive impairment - peri-operative acute pain - pulmonary complications - fall risk - ability to maintain adequate nutrition - urinary tract infection prevention - functional decline monitoring - Pressure ulcers prevention If surgery: consider IV iron supplementation		

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866 Table 2: PROADAPT pilot trial: questionnaires and screening tests

Domain	
Autonomy	ADL, IADL
Geriatric screening	G8
Physical activity	RAPA, AIPVQ
Quality of life	QLQ-C30, QLQ-ED14, EQ-5D-3L, SF-36
Locomotion and balance	TUG test, SPPB
Pain	Pain scale
Nutrition	Nutrition scale
Tiredness severity	FSS
Depression/anxiety	MNA, GDS4/GDS15
Cognitive assessment	Mini-COG
Fall risk assessment	Tinetti test
Breathlessness	Borg scale

867 Abbreviations: Abbreviations: ADL: Activities of Daily Living; AIPVQ: Physical Instrumental
868 activities of daily living (in French: Activités Instrumentales Physiques de la Vie Quotidienne); EQ-
869 5D-3L: EUROQOL evaluation of quality of life in five dimensions and three levels; FSS: Fatigue
870 Severity Scale; GDS: Geriatric Depression Scale; IADL: Instrumental Activities of Daily Living;
871 MNA: Mini Nutritional Assessment; QLQ-C30: quality of life questionnaire core 30 of the European
872 organisation for research and treatment of cancer (EORTC); QLQ-ELD14: Older patients- specific
873 quality of life questionnaire in 14 items of the EORTC; RAPA: Rapid Assessment of Physical
874 Activity; SF-36: Short Form 36 Health Survey Questionnaire; SPPB: Short Physical Performance
875 Battery
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877 **Table 3:** PROADAPT pilot study: flow diagram

	Baseline	Pre-therapeutic visit (0-5 days before intervention)	M1, M3, M6	M12	End of study visit
<i>Comprehensive geriatric assessment</i>					
G8	X			X	X
ADL/IADL	X			X	X
GDS4/GDS15	X			X	X
Mini COG	X			X	X
MNA	X			X	X
QLQ-C30	X		X	X	X
QLQ-ELD14	X		X	X	X
EQ-5D-3L	X		X	X	X
Pain scale	X	X	X	X	X
Nutrition scale	X	X	X	X	X
Socio-economic evaluation	X				
<i>Physical and respiratory assessments</i>					
FSS	X		X	X	X
SF-36	X		X	X	X
Timed Up and Go	X			X	X
SPPB	X		X	X	X
Borg scale	X			X	X
RAPA questionnaire	X		X	X	X
AIPVQ scale	X		X	X	X
Tinetti test	X			X	X
Equimog evaluation	X			X	X
Triflo II	X	X			
Voldyne	X	X			
Physical activity data collection		X	X	X	X
<i>Patient satisfaction</i>					
Standardised questionnaire					X

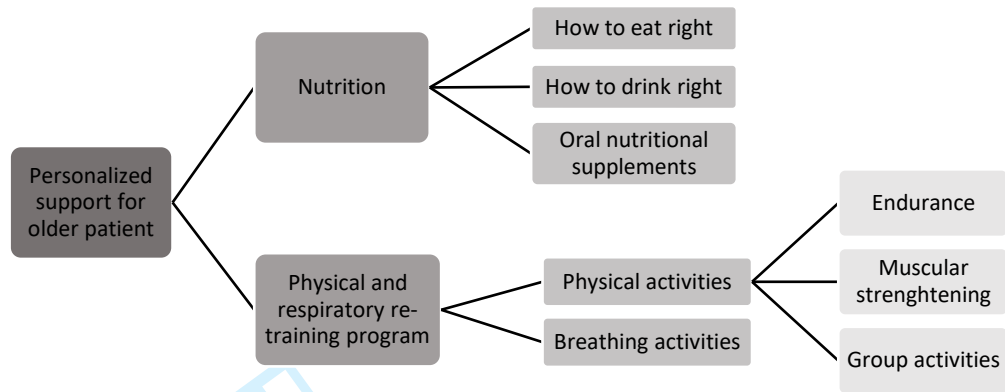
878 Abbreviations: ADL: Activities of Daily Living; AIPVQ: Physical Instrumental activities of daily living (in
879 French: Activités Instrumentales Physiques de la Vie Quotidienne); EQ-5D-3L: EUROQOL evaluation of quality
880 of life in five dimensions and three levels; FSS: Fatigue Severity Scale; GDS: Geriatric Depression Scale; IADL:
881 Instrumental Activities of Daily Living; MNA: Mini Nutritional Assessment; QLQ-C30: quality of life
882 questionnaire core 30 of the European organisation for research and treatment of cancer (EORTC); QLQ-ELD14:
883 Older patients- specific quality of life questionnaire in 14 items of the EORTC; RAPA: Rapid Assessment of
884 Physical Activity; SF-36: Short Form 36 Health Survey Questionnaire; SPPB: Short Physical Performance Battery
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Figure 1 : PROADAPT program : interventions at the patient’s level



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Supplementary file 1: Patient satisfaction assessment of the PROADAPT programme

 Hospices Civils de Lyon Direction de la Recherche Clinique et de l'Innovation	<h2>PATIENT ASSESSMENT OF THE PROADAPT PROGRAMME</h2>
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Dear Sir or Madam,

You have been part of the PROADAPT - pilot study and we thank you for your involvement. In order to assess and improve this study, we would like to collect your opinion. This opinion is anonymous and does not affect your healthcare.

The following questions are concerning the patient booklet that was given to you as part of the study

If you consider the booklet overall

- | | | | |
|---|-------------------------------------|-----------------------------------|-------------------------------------|
| • Did the explanations seem appropriate to you? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | Absolutely <input type="checkbox"/> |
| • Did the information seem clear to you? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | Absolutely <input type="checkbox"/> |
| • Did the pages seem readable enough? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | Absolutely <input type="checkbox"/> |
| • Did the illustrations seem clear to you? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | Absolutely <input type="checkbox"/> |

How would you rate the booklet?

(useless = 0 ; very useful = 10)

0 1 2 3 4 5 6 7 8 9 10

The following questions are concerning the overall PROADAPT programme (breathing and physical exercises, booklet, calls, and follow-up visits)

Did you have difficulty in understanding the explanations given by the medical staff

- | | | | |
|---|-------------------------------------|-----------------------------------|--------------------------------|
| • for breathing exercises? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | A lot <input type="checkbox"/> |
| • for physical exercises? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | A lot <input type="checkbox"/> |
| • for nutritional advices? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | A lot <input type="checkbox"/> |
| • during the assessment with the physician of the different drugs you are taking? | Not at all <input type="checkbox"/> | A little <input type="checkbox"/> | A lot <input type="checkbox"/> |

Did you encounter any difficulties

- for the realisation of breathing exercises ? Not at all A little A lot
- for the realisation of physical exercises ? Not at all A little A lot
- for the application of nutritional advice? Not at all A little A lot
- for the recording of activities? Not at all A little A lot

How do you estimate nursing phone calls

- at the beginning of your healthcare before your surgery / radiotherapy Useless Of little importance Needed
- after your surgery / radiotherapy Useless Of little importance Needed

Would you have liked to have more information? No Yes

If yes, on which aspect

.....

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What would you propose to make the programme more suitable for patients?

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Thank you for your time, we will use your opinions to improve the PROADAPT programme and the patient booklet.

Prof Claire Falandry, study coordinator

Supplementary file 2: Patient satisfaction assessment of ID-PROADAPT® eHealth device

 <p>Hospices Civils de Lyon Direction de la Recherche Clinique et de l'Innovation</p>	<p>ASSESSMENT OF THE ID-PROADAPT® DEVICE, COMPANION OF THE PROADAPT PROGRAMME</p>
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Dear Sir or Madam,

You have been part of the PROADAPT-pilot study and we thank you for your involvement. In order to assess and improve this study, we would like to collect your opinion. This opinion is anonymous and does not affect your healthcare.

The following questions are concerning your experience with the PROADAPT programme as proposed in the ID-PROADAPT® device

If you consider the PROADAPT programme provided using ID-PROADAPT® device overall

- Did the font appear easy to read? Not at all A little Absolutely
- Did you manage to use the stylus easily? Not at all A little Absolutely
- Did you experience any visual fatigue after watching the program? Not at all A little Absolutely
- Were you tired at the end of filling out the various questionnaires? Not at all A little Absolutely
- Have you encountered connection problems? Not at all A little Absolutely
- Were you bothered by certain colors? Not at all A little Absolutely

If yes: which ones?

.....

The following questions concern the overall PROADAPT programme (breathing and physical exercises, booklet, calls, and follow-up visits)

Did you have difficulty in understanding the explanations given proposed in the ID-PROADAPT® device?

- for breathing exercises? Not at all A little A lot
- for physical exercises? Not at all A little A lot
- for nutritional advices? Not at all A little A lot

Ergonomics evaluation of the ID-PROADAPT® device

We now ask you to focus on your ergonomics (ease of use) of the PROADAPT program that was proposed on the provided tablet. Please indicate on this scale how you rate each statement.

	Not agree at all	Somewhat agree	Neither agree nor disagree	Somewhat agree	Totally agree
I have used the PROADAPT program regularly	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I find the PROADAPT program unnecessarily complex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I find the PROADAPT program easy to use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I regularly needed help from technical support to be able to use the PROADAPT program	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I find that the different functions of the PROADAPT program have been well integrated	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I find there are too many inconsistencies in the PROADAPT program	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I find the PROADAPT program very restrictive to use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel very confident using the PROADAPT program	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I needed to learn a lot before I could use the PROADAPT program effectively	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

User experience evaluation

We now ask you to focus on your overall experience with the PROADAPT interface. We offer two opposite terms and a 7-point scale. Please indicate on this scale where your impression is located.

Annoying	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Cheering
Incomprehensible	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Understandable
Creative	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Monotone
Easy to use	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Difficult to use
Precious	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Poor
Boring	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Captivating
Uninteresting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Interesting
Unpredictable	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Predictable

Fast	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Slow
Original	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Conventional
Handicapping	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Helping
Good	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Bad
Complicated	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Simple
Repulsive	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Attractive
Common	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Unpublished
Unpleasant	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Pleasant

Would you have liked to have more information? No Yes

If yes, on which aspect?

.....

What would you propose to make the programme more suitable for patients?

.....

How would you rate the contents of the tablet?

(not adapted = 0 ; very suitable = 10)

0 1 2 3 4 5 6 7 8 9 10

How would you rate the overall organisation of the program?

(not adapted = 0 ; very suitable = 10)

0 1 2 3 4 5 6 7 8 9 10

How would you rate the intuitive nature of the tablet?

(not adapted = 0 ; very suitable = 10)

0 1 2 3 4 5 6 7 8 9 10

How would you rate the videos on the tablet?

(not adapted = 0 ; very suitable = 10)

0 1 2 3 4 5 6 7 8 9 10

Thank you for your time, we will use your opinions to improve the ID-PROADAPT® device and the PROADAPT programme.

Prof Claire Falandry, study coordinator

Supplementary table 1: SPIRIT 2013 checklist of the trial



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Reported on page #
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary table 2 Ref 24
Protocol version	3	Date and version identifier	17 (Ethics and Consent to participate)
Funding	4	Sources and types of financial, material, and other support	17-18 (Funding)
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1 (Authors' list) 18 (Authors' contributions)
	5b	Name and contact information for the trial sponsor	Supplementary table 2 Ref 24
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	10 (Ethical and legal considerations) 17 (Funding)

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	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13 (Data management and statistical analyses) 14 (Data monitoring)
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Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6

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4		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)
5			14 (End of protocol)
6			And N/4 (no dose modifications)
7			
8		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)
9			6 (two turns of validations of the PROADAPT booklet by candidate patients)
10			
11			
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13		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial
14			N/A
15			
16	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
17			11-12
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22	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)
23			8-9
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26	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations
27			12-13 (Sample size calculation)
28			
29			
30	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size
31			N/A (no problem for accrual)
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33	Methods: Assignment of interventions (for controlled trials)		N/A
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35	Allocation:		
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Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	-
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial	-

Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 3
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13 (Data management and statistical analyses)

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4	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13-14 (Data management and statistical analyses)
5				
6		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
7				
8		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
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12	Methods: Monitoring			
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14	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	14 (Data Monitoring)
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16		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
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23	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11 (Secondary outcomes: NCI CTCAE, QOL)
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28	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
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31	Ethics and dissemination			
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33	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	10 (Ethical and legal considerations)
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36	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	10 (Ethical and legal considerations) 14 (Protocol amendments)
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4	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10-11 (Ethical and legal considerations)
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6		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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9	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14 (Confidentiality)
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13	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	17 (Competing interests)
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16	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17 (Availability of data and materials)
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19	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
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22	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15 (Dissemination policy)
23				
24		31b	Authorship eligibility guidelines and any intended use of professional writers	15 (Dissemination policy), N/A
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26		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
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34	Appendices			
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36	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Annex 1 (in French)
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4	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for
5			genetic or molecular analysis in the current trial and for future use in ancillary
6			studies, if applicable
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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons “[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)” license.

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Supplementary table 2: All items from the World Health Organization Trial Registration Data Set (SPIRIT item 2b)

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT03659123
Date of registration in primary registry	6 September 2018
Secondary identifying numbers	69HCL16_0701 ID RCB N° 2018-A001026-49
Source(s) of monetary or material support	Agence Régionale de Santé Auvergne Rhône Alpes
Primary sponsor	Hospices Civils de Lyon
Secondary sponsor(s)	
Contact for public queries	David Dayde, +33.4.78.86.37.74, david.dayde@chu-lyon.fr
Contact for scientific queries	Claire Falandry, +33.4.78.86.66.34, claire.falandry@chu-lyon.fr
Public title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer
Scientific title	Prehabilitation & Rehabilitation in Oncogeriatrics: Adaptation to Deconditioning Risk and Accompaniment of Patients' With Cancer, a Multicentre Pilot Study
Countries of recruitment	France
Health condition(s) or problem(s) studied	Old Injury
Intervention(s)	<p>Behavioural: standardised geriatric intervention</p> <p>Nutritional care is based on:</p> <ul style="list-style-type: none"> • A personalised evaluation of nutritional balance and nutritional needs of the patient • A weekly follow-up of weight and nutritional intake <p>Total-body rehabilitation is based on:</p> <ul style="list-style-type: none"> • 2 to 3 times a week: strength exercise • 2 to 3 times a week: endurance exercise, 20 to 45 min each sequence • 2 times a week: respiratory physiotherapy <p>Pharmaceutical conciliation and optimisation according to the STOPP/START criteria During peri-operative time, the nurse contacts the surgical team for transmission of the patient's personal data, physical medication conciliation results During rehabilitation time and hospital-home transition time, the nurse contacts the rehabilitation team for transmission of the patient's personal data and care course, physical (nutritional, functional, and/or comorbidities), medication conciliation results.</p>

Data category	Information
Key inclusion and exclusion criteria	<p>Inclusion criteria: Patient aged ≥ 70 years OR patient aged ≥ 60 years with significant comorbid condition (modified Charlson index ≥ 3) or disability (ADL score $< 6/6$); Histologically or cytologically proven cancer. Life expectancy > 3 months. Written informed consent obtained Covered by a Health System where applicable.</p> <p>Exclusion Criteria: Other malignancy within the previous 5 years, except for adequately treated carcinoma <i>in situ</i> of the cervix or squamous carcinoma of the skin, or adequately controlled limited basal cell skin cancer. Patient unable to be regularly followed for any reason (geographical, familial, social, psychological). Any mental or physical handicap at risk of interfering with the appropriate treatment. Any administrative or legal supervision where applicable</p>
Study type	Interventional Allocation: N/A Intervention model: Single Group Assignment Masking: None (Open Label) Primary purpose: Health Services Research Phase II
Date of first enrolment	3 July 2018
Target sample size	122
Recruitment status	Recruiting
Primary outcome(s)	<p>Implementation of at least one item of PROADAPT standardised geriatric intervention of the PROADAPT programme pilot study [Time Frame: 12 months]:</p> <ul style="list-style-type: none"> • Preoperative physical activity including strength and endurance exercise assessed by physical exercises accomplished under the supervision of a physiotherapist. Number of patients with at least 1 intervention achieved in the domain. • Nutrition guidelines before and after physical activity assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain. • Patient education and coaching assessed by questionnaires and visits. Number of patients with at least 1 intervention achieved in the domain • Achievement of standardized intervention procedures, according to the checklist established in consensus with surgeons. Number of patients with at least 1 intervention achieved in the domain • Rehabilitation assessed by questionnaires. Number of patients with at least 1 intervention achieved in the domain

Data category	Information
	<ul style="list-style-type: none"> • Accomplishment of pharmaceutical medication conciliation and treatment optimisation. Number of patients with at least 1 intervention achieved in the domain • Bridging interventions for hospital-to-home transition. Number of patients with at least 1 intervention achieved in the domain
Key secondary outcomes	<ul style="list-style-type: none"> • Post-operative morbidity [Time Frame: 30 and 90 days] according to the Clavien-Dindo classification • Post-operative morbidity [Time Frame: 90 days] according to NCI CTC v4.4 • Therapeutic strategy [Time Frame: 12 months]: Treatment plan completion rate: Number of patients for whom the treatment plan was completed. • Progression-free survival [Time Frame: 12 months] • Post-treatment complication [Time Frame: 12 months]: Post-treatment complication grade ≥ 3 according the National Cancer Institute Common Toxicity Criteria version 4 (NCI-CTC-v4)

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