

Supplemental table 1 – Clinical trials studying implementation of nutritional preconditioning in cancer treatment being chemotherapy, surgery or radiotherapy. DR, dietary restriction; FMD, fasting-mimicking diet; KD, ketogenic diet; QoL, quality of life; STF, short-term fasting; NA, not available. *Trials referred to in main text.

Cancer type	Nutritional intervention	Effect on	Study focus	Patient group	Study name, description	Study ID ^a	Location	Status
Advanced or metastatic cancer	KD	Tumor growth	Safety and tolerability of KD in advanced cancer patients	Male and female adults	Ketogenic Diet in Advanced Cancer	NCT01716468	Pennsylvania, USA, 1 center	Completed*
Advanced LKB1-inactive lung adenocarcinoma	FMD +- metformin	Tumor growth	Effect on progression-free survival	Male and female adults	Metformin Plus/Minus Fasting Mimicking Diet to Target the Metabolic Vulnerabilities of LKB1-inactive Lung Adenocarcinoma (FAME)	NCT03709147	Italy, 1 center	Not yet recruiting
Brain tumour	Ketogenic diet	Acute toxicity, Tumor growth	Feasibility, tolerability and tumour response	Boys and girls up to 21 yrs	Therapeutic Targeting of Sex Differences in Pediatric Brain Tumor Glycolysis	NCT03591861	Missouri, USA, 1 center	Recruiting
Breast cancer	Low-carb diet	NA	Effect on aromatase inhibitor therapy	Adult females	BREADS: Breast Adjuvant Diet Study: <20 g carbohydrates/day, 6 months	NCT04189263	California, USA, 1 center	Recruiting
Breast cancer	Low-fat diet	Tumor growth	Effect on disease-free and overall survival	Postmenopausal females	Nutrition Intervention in Treating Women With Breast Cancer: Total fat intake <15% of calories	NCT00002564	USA, 37 centers	Completed

Breast cancer	Low-carb diet	Tumor growth	Effect on preoperative endocrine prognostic index (PEPI)	Adult females	NEOBREADS: Neoadjuvant Breast Diet Study (NEOBREADS): <20 g carbohydrates/day, 6 months	NCT03822715	California, USA, 1 center	Recruiting
Breast cancer	DR	Tumor growth (Acute toxicity)	Evaluate feasibility of DR and effect on tumour progression	Adult females	Caloric Restriction in Treating Patients With Stage 0-I Breast Cancer Undergoing Surgery and Radiation Therapy (CAREFOR): 25% CR	NCT01819233	Pennsylvania, USA, 1 center	Completed, results available
Breast cancer	Low carb (ketogenic) diet, low fat diet	Tumor growth	Evaluation of proliferation and apoptosis markers	Adult females	Comparison of Healthy Diets on Breast Cancer Markers (KetoBreast)	NCT02744079	New York, USA, 1 center	Recruiting
Breast cancer	FMD	Acute toxicity, Tumor growth	Grade III/IV toxicity	Female adults	Dietary Restriction as an Adjunct to Neoadjuvant ChemoTherapy for HER2 Negative Breast Cancer (DIRECT)	NCT02126449	The Netherlands, 15 centers	Completed
Breast cancer (HER2-positive)	Fasting	Acute toxicity, Tumor growth	Safety of fasting, decrease in chemo-induced side effects, tumor shrinkage	Female adults	Fasting on Newly Diagnosed Breast Cancer (STEFNE): fasting 24 h before and 24 h after chemotherapy	NCT02379585	Arizona, USA, 1 center	Terminated
Breast cancer	Fasting	Acute toxicity	Effect of STF on tolerance to adjuvant chemotherapy in	Female adults	Effects of Short-term Fasting on Tolerance to Chemotherapy: 24 h	NCT01304251	The Netherlands, 1 center	Completed*

			breast cancer patients		before and 24 h after chemotherapy			
Breast cancer	FMD +/- metformin	Tumor growth (Acute toxicity)	Effect on treatment response	Female adults	Calorie Restriction With or Without Metformin in Triple Negative Breast Cancer (BREAKFAST): every three weeks classical FMD	NCT04248998	Italy, 1 center	Not yet recruiting
Breast cancer, ovarian cancer	Fasting + vegan diet vs. vegan diet	Acute toxicity, Tumor growth	Effect on Functional Assessment of Cancer Therapy - General (FACT-G) score	Adult females	Intermittent Fasting Accompanying Chemotherapy in Gynecological Cancers (FIT2): Modified fasting 36-48h before and 24h after chemo 350-400 kcal per day. Between chemotherapies time-restricted feeding	NCT03162289	Germany, 8 centers	Recruiting
Breast cancer	DR	Acute toxicity	Effect on heart function (anthracycline treatment)	Adult females	Caloric Restriction and Exercise for Protection From Anthracycline Toxic Effects (CREATE): 50% CR for 48h. Also includes exercise arm	NCT03131024	Alberta, Canada, 1 center	Recruiting
Breast cancer, colorectal cancer	FMD	Tumor growth	Safety and feasibility of FMD	Male and female adults	Fasting-mimicking Diet in Patients Undergoing Active Cancer Treatment	NCT03595540	Italy, 1 center	Recruiting

Breast cancer, melanoma	FMD	Tumor growth	Analysis of immunological and metabolic changes induced by FMD in pre- and post-operative setting	Male and female adults	Impact of Dietary Intervention on Tumor Immunity: the DigesT Trial (DigesT)	NCT03454282	Italy, 1 center	Recruiting
Breast and prostate cancer	DR	Acute toxicity, Tumor growth	Effect on toxicity and efficacy of chemotherapy	Male and female adults	Controlled Low Calorie Diet in Reducing Side Effects and Increasing Response to Chemotherapy in Patients With Breast or Prostate Cancer: 3 d prior to chemo, 12 wks during chemo, 2 d after chemo	NCT01802346	California & Minnesota, USA, 3 centers	Recruiting
Breast cancer, head and neck cancer, rectal cancer	KD	Acute toxicity	Effect of KD on body composition in patients undergoing RT	Male and female adults	Impact of a Ketogenic Diet Intervention During Radiotherapy on Body Composition (KETOCOMP): One group received a ketogenic breakfast in the form of a drink, other group followed full KD	NCT02516501	Germany, 1 center	Recruiting, some data available*
Cancer	FMD	Acute toxicity	Safety of FMD	Male and female adults	Safety, Feasibility and Metabolic Effects of the Fasting Mimicking Diet (FMD) in Cancer Patients	NCT03340935	Italy, 1 center	Active, not recruiting

Cancer patients receiving taxol/carboplatin treatment	FMD	Acute toxicity	Effect on nausea grade	Male and female adults	Can Fasting Decrease the Side Effects of Chemotherapy?	NCT04027478	California, USA, 1 center	Enrolling by invitation
Colorectal cancer	STF	Acute toxicity, Tumor growth	Effect on toxicity	Male and female adults	Short-term Fasting as an Enhancer of Chemotherapy: Pilot Clinical Study on Colorectal Carcinoma Patients (CHEMOFAST): 44-48h fast, start 24h before chemotherapy	NCT04247464	Spain, 1 center	Enrolling by invitation
Glioblastoma	KD	Tumor growth	Feasibility of KD	Male and female adults	Ketogenic Diet for Recurrent Glioblastoma (ERGO)	NCT00575146	Germany, 2 centers	Completed*
Glioblastoma	KD + fasting	Tumor growth	Progression-free survival rates 6 months after reirradiation	Male and female adults	Calorie-restricted, Ketogenic Diet and Transient Fasting During Reirradiation for Patients With Recurrent Glioblastoma (ERGO2): On day 1-3 and day 7-9, restriction of carbohydrates to < 60 g and of calories to 21-23 kcal/kg per day, on day 4-6 fasting.	NCT01754350	Germany, 2 centers	Completed, abstract oral presentation available
Glioblastoma	KD	Acute toxicity	Adherence to KD	Male and female adults (≥16 yrs)	Ketogenic Diets as an Adjuvant Therapy in	NCT03075514	UK, 1 center	Completed*

					Glioblastoma (KEATING): Modified ketogenic diet (MKD): 80% fat and 5% carbohydrate of total kcal/day. Medium chain triglyceride (MCT) diet: 75% fat (30% of which medium chain fatty acids) and 5% carbohydrates.			
Glioblastoma	Energy-restricted KD	Tumor growth	Change in brain tumor size	Male and female adults	Pilot Study of a Metabolic Nutritional Therapy for the Management of Primary Brain Tumors (Ketones)	NCT01535911	Michigan, USA, 1 center	Active, not recruiting
Gynecological cancer	Fasting	Acute toxicity	QoL	Adult females	Short-Term Fasting During Chemotherapy in Patients With Gynecological Cancer- a Randomized Controlled Cross-over Trial (FIT): Modified fasting (<400kcal/day) 36-48h before chemotherapy and 24h after chemotherapy	NCT01954836	Germany, 1 center	Completed*
Malignant neoplasm	Fasting	Acute toxicity	Safety and feasibility of STF	Male and female adults	Short-Term Fasting Before Chemotherapy in	NCT01175837	Minnesota, USA, 1 center	Completed; No results available

					Treating Patients With Cancer: 24 h fasting before chemotherapy, can be escalated to 36-48 h			
Non-small-cell lung cancer	KD	Tumor growth	Safety of KD during chemoradiation for lung cancer	Male and female adults	Ketogenic Diet With Chemoradiation for Lung Cancer (KETOLUNG)	NCT01419587	Iowa, USA, 1 center	Terminated, has results*
Non-small-cell lung cancer	FMD	Tumor growth, Acute toxicity	Effect on circulating tumor cells and its DNA damage	Male and female adults	Fasting-mimicking Diet With Chemo-immunotherapy in Non-small Cell Lung Cancer (NSCLC): Plant-based FMD ~300 kcal/ fasting day	NCT03700437	Indiana, USA, 3 centers	Recruiting
Ovarian cancer, endometrial cancer	KD	NA	Changes in fasting glucose, fasting insulin and beta-hydroxybutyrate. Effect on body composition.	Adult females	Targeted Disruption to Cancer Metabolism and Growth Through Dietary Macronutrient Modification	NCT03171506	Alabama, USA, 1 center	Completed*
Pancreatic cancer	KD	Tumor growth	Frequency of adverse events	Male and female adults	Ketogenic Diet With Concurrent Chemoradiation for Pancreatic Cancer (KETOPAN)	NCT01419483	Iowa, USA, 1 center	Terminated, has results*
Prostate cancer	FMD	Acute toxicity, 3 months after FMD	Changes in body weight, blood pressure, waist circumference and cholesterol levels	Adult males	Fasting Mimicking Diet in Prostate Cancer and Metabolic Syndrome: 3 cycles of 5 days FMD	NCT04292041	Ireland, 1 center	Active, not recruiting

Prostate cancer	Fasting/FMD	Acute toxicity	QoL, reduction of side effects, reduction in tumor progression	Adult males	Fasting and Nutritional Therapy in Patients With Advanced Metastatic Prostate Cancer: 36 h before and 24 h after chemotherapy modified fasting (<400 kcal/day) or if fasting is not feasible FMD	NCT02710721	Germany, 1 center	Recruiting
Sarcoma	DR	Surgery	Effect on surgical wound complications	Male and female adults	Effects Of Caloric Restriction On Post-Operative Complications In Sarcoma Patients Treated With Pre-Operative Radiation Therapy: Nutritional supplement (Scandishake) providing 30% of caloric needs with 45% fat, 46% carbohydrates, 8% protein. Shake will be used 3 days before surgery.	NCT02792270	Massachusetts, USA, 1 center	Not yet recruiting
Solid tumor	Fasting	Acute toxicity	Safety/feasibility of STF, toxicity profile	Male and female adults	Short-Term Fasting: Impact on Toxicity: 24, 48 or 72 hours fasting before platinum-based chemotherapy	NCT00936364	California, USA, 1 center	Recruiting

Solid tumor	Fasting	Tumor growth	Response to therapy	Male and female adults	Short-term Starvation vs. Normal Diet Before Chemotherapy of Solid Tumors: fasting 24 h before and 6 h after chemotherapy	NCT02607826	Not provided	Unknown
Prostate cancer, endometrial cancer, breast cancer	DR	Surgery	Changes in expression of miR-21 in serum	Male and female adults	Caloric Restriction Before Surgery in Treating Patients With Endometrial, Prostate, or Breast Cancer: 25% DR for 3-12 weeks prior to surgery	NCT02983279	Pennsylvania, USA, 1 center	Active, not recruiting

^a Study ID refers to clinical trials registered at clinicaltrials.gov

Supplemental table 2 – Clinical trials implementing nutritional preconditioning to study a.o. cancer prevention. DR, dietary restriction.

Subjects	Nutritional intervention	Effect on	Patient group	Study name, description	Study ID ^a	Location	Status
Overweight subjects	DR	Aging and incidence of age-related diseases including cancer	Males and females between 25 - 50 years	CALERIE (PBRC, Baton Rouge) - Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy: 6 months of DR	NCT00099151	USA, 3 centers	Completed
Healthy subjects	DR	Aging and incidence of age-related diseases including cancer	Males and females between 21 - 50 years	CALERIE: Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy: 25% DR for two years	NCT00427193	USA, 3 centers	Completed
Healthy, slightly overweight subjects	DR	Aging and incidence of age-related diseases including cancer	Males and females between 25 - 50 years	CALERIE (Tufts) - Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy: 10 % or 30 % DR for one year	NCT00099099	USA, 3 centers	Completed
Overweight or obese subjects with increased risk of developing colorectal cancer	DR	Energy balance	Adult males and females >50 years	Energy Balance Interventions for Colorectal Cancer Prevention	NCT00653484	Tennessee, USA, 1 center	Completed
Obese subjects	DR	Inflammation levels (and potentially breast cancer risk)	Postmenopausal females	Diet Induced Weight Loss to Reduce Inflammation in Obese Women: diet of 800 kcal/day until 10% of initial baseline body weight was lost	NCT01699906	New York, USA, 1 center	Completed
Overweight or obese subjects	DR	Obesity-related health risks including cancer	Adult males, overweight or obese	Nutrition and Energy Restriction for Cancer Prevention (HELENA): Continuous 20 % DR or 25 % DR for two days per week combined with 5 days normal intake	NCT02449148	Germany, 1 center	Completed

Subjects previously diagnosed with breast cancer	Reduced caloric intake + exercise	Breast cancer recurrence	Adult females	Prevention of Breast Cancer Recurrence Through Weight Control, Diet, and Physical Activity Intervention (PREDICOP)	NCT02035631	Spain, 5 centers	Not yet recruiting
Moderately overweight subjects	DR	Cancer risk	Males and females (35-65 years)	Effect of Daily Calorie or Alternate-day Calorie Reductions on Risk for Cardiovascular Disease and Cancer (1072): continuous DR or alternate-day DR for 3 months	NCT00467220	California, 1 center	Completed
Subjects with metabolic syndrome	Lifestyle intervention and/or metformin	Age-related diseases including cancer	Males and females (55-74 years)	Metformin and Dietary Restriction to Prevent Age-related Morbid Events in People With Metabolic Syndrome (MeMeMe): lifestyle intervention consists of moderate exercise and moderate reduction of calorie and protein intake	NCT02960711	Italy, 1 center	Unknown

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