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Supplementary appendix

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SARS-CoV-2 Omicron (B.1.1.529) related sequelae in vaccinated and unvaccinated patients with cancer: results from the OnCovid registry.

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Supplementary Files

Supplementary Methods

Study design and procedures

OnCovid (NCT04393974) is an active European registry study that, since the beginning of the pandemic, has collected consecutive patients fulfilling the following inclusion criteria: 1) age ≥18 years; 2) diagnosis of SARS-CoV-2 infection confirmed by RT-PCR of a nasopharyngeal swab; 3) history of solid or hematologic malignancy, at any time during the patients' past medical history, either active or in remission at the time of COVID-19 diagnosis. Patients with a history of non-invasive/premalignant lesions or with low malignant potential (i.e., basal cell carcinoma of the skin, non-invasive carcinoma in situ of the cervix, ductal carcinoma in situ) were excluded. For hematologic malignancies, only patients with a history of oncologic diseases with defined malignant behavior (lymphoma, leukaemia, multiple myeloma) were included.

The overarching subgrouping of demographics, oncological and COVID-19 related features has been consistently utilised in all the publications from our registry (Cancer Discov. 2020 Jul 31;10(10):1465–74; Eur J Cancer. 2021 Jun;150:190-202; J Immunother Cancer. 2021 Mar;9(3):e002277; Cancers. 2020 Jul 8;12(7):1841; Lancet Oncol. 2021 Nov 3;S1470-2045(21)00573-8; JAMA Oncol. 2021 Nov 24; J Natl Cancer Inst. 2022 Jul 11; Eur J Cancer. 2022 Jul; Lancet Oncol. 2022 Jul; Eur J Cancer. 2022 Aug) and was made necessary by the wide heterogeneity oncological diagnoses included in the registry.

The following key variables were considered as baseline key demographic and tumour characteristics:

- Country (United Kingdom, Spain, Italy),
- Biological sex (male vs female),
- Age (≥65 vs < 65 years),
- Number of co-morbidities (0-1 vs ≥ 2),
- Tumour stage at COVID-19 (defined as advanced vs non-advanced) at COVID-19. In details, we defined as “advanced” stage any patient with distant metastatic disease, to differentiate them from “non-advanced” patients. Disease-specific criteria (i.e. Rai, Binet criteria etc.) were utilised as appropriate to define advanced haematological malignancies.
- Smoking status at COVID-19 (Never vs ever smokers),
- Primary tumour (clustered as: breast, gastro-intestinal, gynaecological/genito-urinary, thoracic, others, and haematologic),
- Receipt of any systemic anticancer therapy within 4 weeks prior to SARS-CoV-2 infection (yes vs no),

The following surrogates of COVID-19 severity were tested for their association with the prevalence of COVID-19 sequelae:

- Experience of at least one COVID-19 complications including acute respiratory failure, ARDS, kidney injury, secondary infections, sepsis, septic shock, acute cardiac injury, acute liver injury and others (yes vs no);
- Receipt of any COVID-19 oriented therapy, including antivirals, antimalarials, antibiotics, corticosteroids, interleukin-6 inhibitors and others (yes vs no);
- Oxygen therapy requirement (yes vs no);
- Hospitalization requirement (pre-existent/due to COVID-19 vs not required).

Oncological and disease specific variables were collected at baseline, defined at the moment of diagnosis of SARS-CoV-2 by PCR test. Characteristics of severity, complications and therapy

against COVID-19 were collected throughout the observation period until full clinical resolution of COVID-19 or patients' mortality.

Considering the variety of dosing intervals between the first and second vaccination across the participating countries, which prevented a unique definition of complete vaccination starting from the first dose, in the main analysis patients were categorized as fully vaccinated at the time of COVID-19 diagnoses if they had received two doses for the BNT162b2, mRNA-1273, and AZD1222 vaccines or in case the breakthrough infection diagnosis was diagnosed at least 28 days after a single dose of the Ad.26.COV2.S vaccine. Patients who received at least one vaccination, without meeting the above-mentioned criteria, were considered partially vaccinated.

Patient observation time started from date of first PCR/SARS-CoV-2 infection confirmation until patient death or loss to follow-up. Being a retrospective, observational study, the entirety of the OnCovid cohort was followed up at intervals dictated by the routine clinical practice in each participating institutions, as deemed clinically indicated by the treating physicians. All-cause of mortality was retrieved and validated by investigators at each centre by accessing patients' electronic medical records and death certificates. Timing of follow-up was not standardized but dictated by the discretion of treating physicians as per standard of care. To avoid incurring into bias, by mislabelling patients that were lost to follow-up as potentially deceased, we decided to exclude all patients with incomplete/missing follow up data to preserve the integrity of our results. Patients were lost to follow-up when for any reason failed to attend planned follow-up appointments scheduled by the treating clinicians. Given the pragmatic nature of this registry, based on standard of care clinical practice, we could not accurately reconstruct the reasons to explain why a proportion of patients did not attend for follow-up

Supplementary Table 1. Patient disposition across participating centres. PI: principal Investigator.

Institution	Eligible Patients		Site PI
	N	%	
Vall d'Hebron University Hospital, Barcelona (Spain)	372	19.5	Josep Tabernero
University College London, London (UK)	251	13.1	Alvin JX Lee
Chelsea and Westminster Hospital, London (UK)	231	12.1	Mark Bower
Ospedale Maggiore della Carità, Novara (Italy)	155	8.1	Alessandra Gennari
Guy's and St Thomas' NHS Foundation Trust, London (UK)	142	7.4	Ailsa Sita-Lumsden
ICO L'Hospitalet, L'Hospitalet de Llobregat, Barcelona (Spain)	138	7.2	Ramon Salazar
IRCCS Humanitas Research Hospital, Rozzano - Milan (Italy)	125	6.5	Lorenza Rimassa
Policlinico San Matteo, Pavia (Italy)	75	3.9	Paolo Pedrazzoli
ICO Girona (Spain)	73	3.8	Joan Brunet
ICO Badalona (Spain)	62	3.2	Andrea Plaja
Imperial College London, London (UK)	58	3.0	David Pinato
IRCCS AOU San Martino, Genova (Italy)	54	2.8	Matteo Lambertini
Manresa Hospital (Spain)	43	2.3	Clara Martinez-Vila
Careggi University Hospital, Florence (Italy)	35	1.8	Francesca Mazzoni
Università Campus Bio-Medico, Rome (Italy)	23	1.2	Bruno Vincenzi
Istituto Europeo di Oncologia, Milano (Italy)	17	0.9	Paola Queirolo
Azienda Ospedaliera S. Andrea, Rome (Italy)	16	0.8	Raffaele Giusti
Istituto Tumori, Milan (Italy)	14	0.7	Rossella Bertulli
Northumbria Healthcare NHS (UK)	13	0.7	Avinash Aujayeb
Santa Maria Goretti Hospital, Latina (Italy)	12	0.6	Federica Zoratto
Ospedale Antonio e Biagio e Cesare Arrigo, Alessandria (Italy)	-	-	Maura Rossi
Ospedali Riuniti di Ancona, Universitá Politecnica delle Marche (Italy)	-	-	Rossana Berardi
Hospital Clinic, Barcelona (Spain)	-	-	Aleix Prat
University of Bari 'Aldo Moro', Bari (Italy)	-	-	Marco Tucci
Ospedale Papa Giovanni XXIII, Bergamo (Italy)	-	-	Alberto Zambelli
Azienda Ospedaliera Spedali Civili, Brescia (Italy)	-	-	Salvatore Grisanti
Fondazione Poliambulanza Istituto Ospedaliero, Brescia (Italy)	-	-	Michela Lubertini
Institut Jules Bordet, Brussels (Belgium)	-	-	Angela Loizidou
Velindre Cancer Centre, Cardiff (UK)	-	-	Sarah Townsend
Azienda Istituti Ospitalieri di Cremona, Cremona (Italy)	-	-	Daniele Generali
University of L'Aquila, L'Aquila (Italy)	-	-	Alessandro PArisi
Hospital Universitario 12 de Octubre, Madrid (Spain)	-	-	Ana Sanchez de Torre
University of Munich (Germany)	-	-	Nadia Harbeck
Palma de Mallorca Hospital, Palma de Mallorca, (Spain)	-	-	Maria Iglesias
Azienda Ospedaliera S Maria, Terni (Italy)	-	-	Sergio Bracarda
Barts Health NHS Trust, London (UK)	-	-	Nikolaos Diamantis
Institut Gustave Roussy, Villejuif (France)	-	-	Fanny Pommeret
Total	**1909**	**100%**	

Supplementary Table 2. Rate of overall COVID-19 sequelae across the pre-defined pandemic phases. Unvaccinated (including partially vaccinated) and Vaccinated (including patients who received either a double dose or a booster dose) patients from the Alpha-Delta and Omicron phases are presented separately.

	Overall Population			
	Overall population (N=1909)	**Prevaccination (N=1000)**	**Alpha-Delta (N=653)**	**Omicron (N=256)**
	N (Rate, 95%CI)	**N (Rate, 95%CI)**	**N (Rate, 95%CI)**	**N (Rate, 95%CI)**
COVID-19 sequelae	317 **16.6%** (14.8-18.5)	191 **19.1%** (16.4-22.0)	110 **16.8%** (13.8-20.3)	16 **6.2%** (3.5-10.2)
P-value *(comparison)* *(Pre-vaccination phase)*			*0.24*	*<0.0001*
	Unvaccinated			
	Alpha-Delta (N=458)		**Omicron (N=32)**	
	N (Rate, 95%CI)		**N (Rate, 95%CI)**	
COVID-19 sequelae	84 **18.3%** (14.6-22.7)		3 **9.4%** (1.9-27.3)	
P-value *(comparison)* *(Pre-vaccination phase)*	*0.73*		*0.16*	
	Vaccinated			
	Alpha-Delta (N=123)		**Omicron (N=196)**	
COVID-19 sequelae	16 **13.0%** (7.4-21.1)		12 **6.1%** (3.2-10.7)	
P-value *(comparison)* *(Alpha-Delta/Omicron phase Unvaccinated)*	*0.16*		*0.49*	

Supplementary Table 3. Summary of baseline characteristics' distribution before to and after the propensity score matching between unvaccinated patients from the Omicron phase (32 patients) and patients from the Pre-vaccination phase (1000 patients). Variability of included characteristics is estimate through the standardized mean difference (SMD). SACT: systemic anticancer therapy.

Unvaccinated patients Omicron (N=32)	**Unmatched cohorts 32 vs 1000 patients**	**Matched cohorts 30 vs 118 patients**
	SMD	**SMD**
Country		
United Kingdom	0.11	0.12
Spain	-0.09	-0.09
Italy	-0.04	-0.05
Sex	-0.02	-0.02
Age (≥ vs < 65 years)	-0.05	-0.05
Comorbidities	0.04	0.04
Primary Tumour		
Breast	0.07	0.07
Gastrointestinal	0.09	0.09
Gynaecological/Genito-Urinary	0.08	0.04
Thoracic	-0.04	-0.04
Others	0.03	0.03
Haematological	-0.21	-0.21
Tumour stage		
Non-advanced	-0.12	-0.12
Advanced	-0.09	0.17
Missing	-0.04	-0.09
Status at COVID-19 diagnosis	0.00	0.00
SACT at COVID-19 diagnosis		
No	0.02	0.02
Yes	0.08	0.09
Missing	-0.13	-0.14

Supplementary Table 4. Propensity score matching fitted multivariable logistic regression model for COVID-19 sequelae comparing unvaccinated patients from the Omicron phase (30 patients) with 118 patients from the pre-vaccination phase. Country, tumour stage, primary tumour, SACT at COVID-19 were included in the multivariable analysis due to their respective SMD at the propensity score matching. *Clustered robust correction of 95%CI for participating centre. SACT: systemic anticancer therapy; UK: United Kingdom; Unk: unknown; GI: gastro-intestinal; GU: genito-urinary; GY: gynaecological; Unk: unknown; aOR: adjusted odds ratio; CI: confidence intervals.

COVID-19 sequelae	aOR	95%CI		95%CI*	
Pandemic phase: Omicron unvaccinated vs Pre-vaccination	0.35	0.09	3.79	0.08	3.64
Country: Italy vs UK	0.48	0.15	1.50	0.21	1.12
Country: Spain vs UK	0.45	0.10	2.07	0.15	1.32
Tumour stage: Advanced vs Non-advanced	0.97	0.36	2.65	0.55	1.72
Tumour stage: Unk vs Non-advanced	0.41	0.06	2.60	0.12	1.41
Primary Tumour: GI vs Breast	0.71	0.05	9.34	0.03	13.2
Primary Tumour: GU/GY vs Breast	0.99	0.07	13.1	0.07	12.2
Primary Tumour: Thoracic vs Breast	4.54	0.38	53.5	0.38	53.15
Primary Tumour: Others vs Breast	0.84	0.03	21.4	0.02	25.64
Primary Tumour: Haematological vs Breast	2.39	0.17	32.2	0.20	28.47
SACT at COVID-19: Yes vs No	0.85	0.27	2.68	0.46	1.56
SACT at COVID-19: Unk vs No	1.61	0.43	5.93	0.39	6.50

Supplementary Table 5. Summary of vaccine type administered according to vaccination category among the study population.

SARS-CoV-2 vaccinations			
	Partially vaccinated N (%)	**Double-dosed N (%)**	**Boosted N (%)**
BNT162b2	23 (35.4)	77 (42.1)	67 (49.3)
mRNA-1273	17 (26.2)	40 (21.9)	36 (26.5)
Ad.26.COV2.S	-	4 (2.2)	1 (0.7)
ChAdOx1-S	12 (18.5)	39 (21.3)	24 (17.6)
Not specified	13 (20.0)	23 (12.6)	8 (5.9)
Total	65	183	136

Supplementary Table 6. Distribution of baseline patients, tumour and COVID-19 characteristics among the vaccinated (including both patients who received 2 vaccinal doses and a booster dose) and unvaccinated patients (including partially vaccinated patients) prior to COVID-19. SACT: systemic anticancer therapy.

	Unvaccinated patients	Vaccinated patients	P value
	N = 1489 (%)	N = 319 (%)	
Country			
United Kingdom	520 (34.9)	125 (39.2)	0.018
Spain	556 (37.3)	130 (40.8)	
Italy	413 (27.7)	64 (20.1)	
Sex			
Male	728 (49.1)	160 (50.3)	0.69
Females	755 (50.9)	158 (49.7)	
Missing	6	1	
Age			
<65 years	694 (46.9)	153 (48.7)	0.54
≥65 years	787 (53.1)	161 (51.3)	
Missing	8	5	
Comorbidities			
0-1	890 (59.8)	183 (57.4)	0.42
≥2	599 (40.2)	136 (42.6)	
Smoking history			
Never smokers	654 (51.9)	113 (43.3)	0.011
Former/current smokers	606 (48.1)	148 (56.7)	
Missing	229	58	
Primary Tumour			
Breast	280 (19.0)	51 (16.1)	0.063
Gastrointestinal	370 (25.1)	74 (23.3)	
Gynaecological/Genito-Urinary	281 (19.0)	48 (15.1)	
Thoracic	192 (13.0)	59 (18.6)	
Others	101 (6.8)	23 (7.3)	
Haematological	253 (17.1)	62 (19.6)	
Missing	12	2	
Tumour stage			
Local/loco-regional	666 (51.8)	110 (38.1)	<0.0001
Advanced	619 (48.2)	179 (61.9)	
Missing	204	30	
Tumour status at COVID-19 diagnosis			
Remission/non measurable disease	702 (47.5)	116 (36.5)	0.0003
Active malignancy	775 (52.5)	202 (63.5)	
Missing	12	1	
SACT at COVID-19 diagnosis			
No	795 (56.2)	125 (42.1)	<0.0001
Yes	619 (43.8)	172 (57.9)	
Missing	75	22	

Supplementary Table 7: Distribution of baseline characteristics before and after the IPTW procedure between vaccinated (including both patients who received 2 vaccinal doses and a booster dose) and unvaccinated patients (including partially vaccinated patients). Variability of included characteristics is estimated through the standardized mean difference (SMD). SACT: systemic anticancer therapy; Gy: gynecological; Gu: genito-urinary.

	Unvaccinated (%)	Vaccinated (%)	P value	SMD	Unvaccinated Weighted (%)	Vaccinated Weighted (%)	P value	SMD Weighted
Country								
United Kingdom	34.9	39.2	0.018	0.18	35.8	37.6	0.63	0.06
Spain	37.3	40.8			**37.9**	38.7		
Italy	27.7	20.1			26.3	23.7		
Sex								
Male	50.7	49.5	0.74	0.02	50.4	49.8	0.85	0.01
Age								
≥65 years	52.9	50.5	0.47	0.04	52.4	51.9	0.88	0.01
Comorbidities								
≥2	40.2	42.6	0.46	0.05	40.6	40.3	0.924	0.01
Status at COVID-19								
Active malignancy	55.0	53.6	0.69	0.02	54.8	55.2	0.91	0.01
Tumour stage								
Non-advanced	42.3	45.8	0.24	0.13	42.9	43.1	0.85	0.03
Advanced	44.5	44.2			44.5	45.4		
Unknown	13.2	20.1			12.6	11.4		
SACT at COVID-19								
No	53.4	39.2	<0.001	0.28	50.8	48.8	0.78	0.04
Yes	41.6	53.9			43.8	45.3		
Unknown	5.0	6.9			5.4	5.9		
Primary tumour								
Breast	20.0	15.7	0.096	0.18	19.2	18.3	0.99	0.04
Gastrointestinal	24.4	24.1			24.4	24.0		
Gy-Gu	17.9	17.2			17.8	19.0		
Thoracic	14.3	16.3			14.7	15.4		
Others	6.1	10.0			6.8	6.8		
Haematological	17.3	16.6			17.1	16.5		

Supplementary Table 8: Distribution of baseline characteristics before and after the IPTW procedure between patients who received two SARS-CoV-2 vaccinal doses prior to COVID-19 and unvaccinated patients (including partially vaccinated patients). Variability of included characteristics is estimated through the standardized mean difference (SMD). SACT: systemic anticancer therapy; Gy: gynecological; Gu: genito-urinary.

	Unvaccinated (%)	Vaccinated (%)	P value	SMD	Unvaccinated Weighted (%)	Vaccinated Weighted (%)	P value	SMD Weighted
Country								
United Kingdom	34.9	48.6	<0.001	0.42	36.5	381	0.89	0.04
Spain	37.3	39.3			37.5	37.3		
Italy	27.7	12.0			26.0	24.5		
Sex								
Male	50.7	48.6	0.65	0.04	50.4	49.3	0.80	0.02
Age								
≥65 years	52.9	49.2	0.38	0.07	52.4	50.0	0.58	0.04
Comorbidities								
≥2	40.2	43.7	0.41	0.07	40.6	38.4	0.59	0.04
Status at COVID-19								
Active malignancy	55.0	54.1	0.87	0.02	54.9	54.0	0.84	0.02
Tumour stage								
Non-advanced	42.3	51.4	0.041	0.20	43.3	43.8	0.55	0.09
Advanced	44.5	39.9			44.0	46.5		
Unknown	13.2	8.7			12.7	9.7		
SACT at COVID-19								
No	53.4	43.7	0.039	0.19	52.3	49.5	0.76	0.06
Yes	41.6	49.2			42.5	45.3		
Unknown	5.0	7.1			5.3	5.2		
Primary tumour								
Breast	20.0	17.5	0.010	0.26	19.7	18.9	0.99	0.04
Gastrointestinal	24.4	24.6			24.5	24.8		
Gy-Gu	17.9	16.9			17.8	17.9		
Thoracic	14.3	13.1			14.2	15.4		
Others	6.1	13.7			7.0	7.1		
Haematological	17.3	14.2			16.9	15.9		

Supplementary Table 9: Distribution of baseline characteristics before and after the IPTW procedure between patients who received a SARS-CoV-2 vaccine booster dose prior to COVID-19 and unvaccinated patients (including partially vaccinated patients). Variability of included characteristics is estimated through the standardized mean difference (SMD). SACT: systemic anticancer therapy; Gy: gynecological; Gu: genito-urinary.

	Unvaccinated (%)	Vaccinated (%)	P value	SMD	Unvaccinated Weighted (%)	Vaccinated Weighted (%)	P value	SMD Weighted
Country								
United Kingdom	34.9	26.5	0.13	0.18	34.2	37.7	0.32	0.14
Spain	37.3	42.6			37.8	40.5		
Italy	27.7	30.9			28.0	21.7		
Sex								
Male	50.7	50.7	1.00	0.00	50.7	49.7	0.84	0.02
Age								
≥65 years	52.9	52.2	0.95	0.01	52.8	50.1	0.60	0.06
Comorbidities								
≥2	40.2	41.2	0.90	0.02	40.3	39.0	0.79	0.02
Status at COVID-19								
Active malignancy	55.0	53.6	0.69	0.02	54.9	57.8	0.55	0.06
Tumour stage								
Non-advanced	42.3	38.2	0.47	0.11	42.0	43.1	0.78	0.07
Advanced	44.5	50.0			45.0	46.2		
Unknown	13.2	11.8			13.0	10.7		
SACT at COVID-19								
No	53.4	33.1	<0.001	0.42	51.7	53.2	0.94	0.02
Yes	41.6	60.3			43.1	41.8		
Unknown	5.0	6.6			5.2	5.0		
Primary tumour								
Breast	20.0	13.2	0.22	0.23	19.5	20.9	0.99	0.07
Gastrointestinal	24.4	23.5			24.4	22.7		
Gy-Gu	17.9	17.6			17.9	19.5		
Thoracic	14.3	20.6			14.8	14.0		
Others	6.1	5.1			6.0	6.3		
Haematological	17.3	19.9			17.5	16.6		

Supplementary Table 10: Inverse Probability of Treatment Weighting (IPTW) fitted multivariable logistic regression model for COVID-19 sequelae comparing patients who received a SARS-CoV-2 vaccine booster dose prior to COVID-19 and unvaccinated patients (including partially vaccinated patients). Country was included as covariate because of the >0.10 SMD at the IPTW. *Clustered robust correction of 95%CI for participating centre. SACT: systemic anticancer therapy; UK: United Kingdom; Unk: unknown; aOR: adjusted odds ratio; CI: confidence intervals; SMD: standardized mean difference.

COVID-19 sequelae	aOR	95%CI		95%CI*	
SARS-CoV-2 vaccination status: Booster dose vs Unvaccinated	0.47	0.35	0.35	0.18	1.18
Country: Italy vs UK	0.61	0.45	0.45	0.25	1.50
Country: Spain vs UK	0.33	0.22	0.22	0.13	0.81

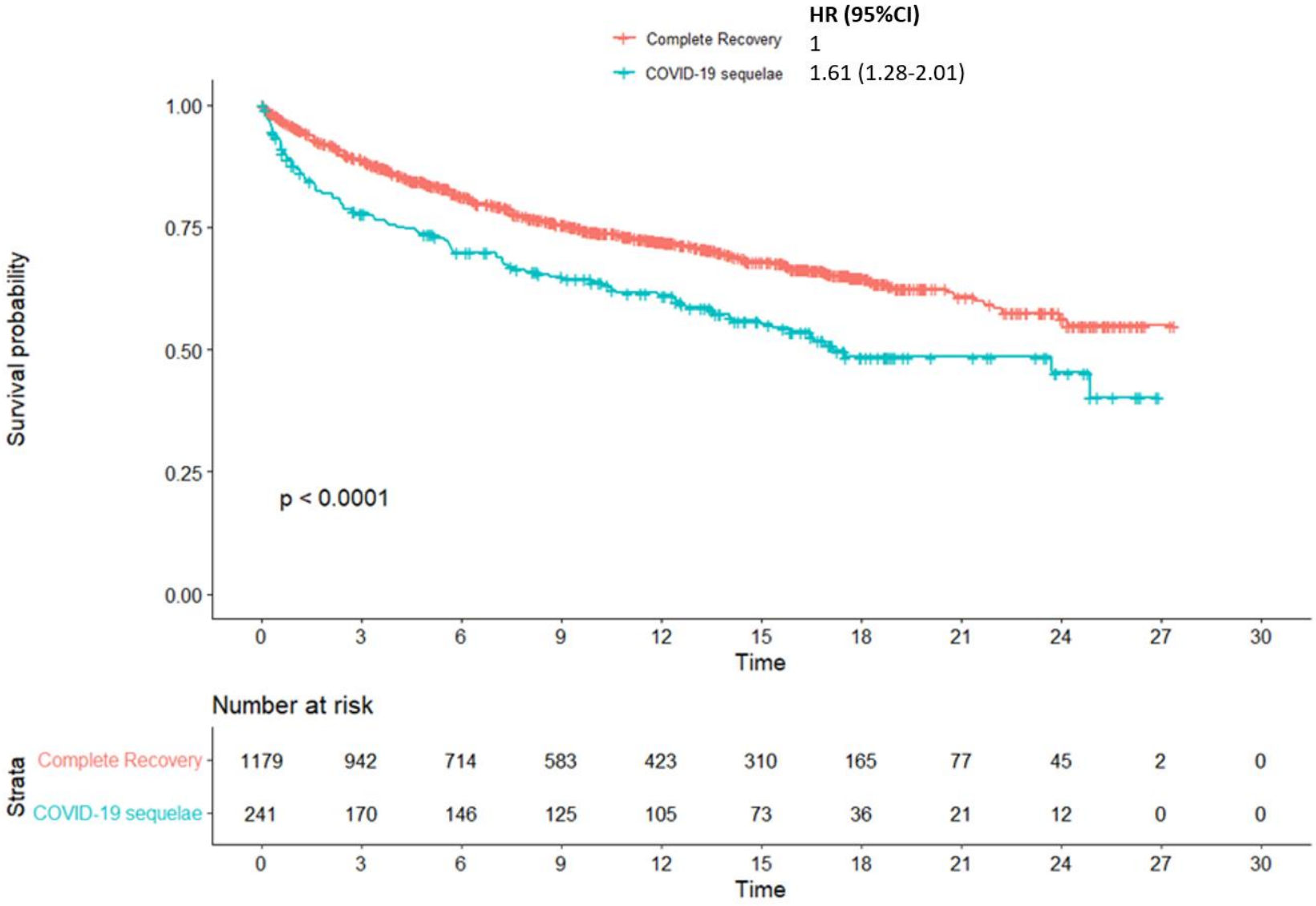
Supplementary Table 11: Restricted mean survival time (RMST) analysis of post COVID-19 survival at 2-, 4- and 6-months reporting difference in months according to key covariates. SACT: systemic anticancer therapy.

	2 months Univariable model		4 months Univariable model		6 months Univariable model	
	RMST difference days (95% CI)	p-value	RMST difference days (95% CI)	p-value	RMST difference days (95% CI)	p-value
COVID-19 sequelae						
Yes vs No	-0.13 (-0.21 / -0.06)	<0.001	-0.34 (-0.52 / -0.16)	<0.001	-0.54 (-0.83 / -0.25)	<0.001
Vaccination status						
Vaccinated vs Unvaccinated	-0.03 (-0.09 / 0.02)	0.27	-0.12 (-0.29 / 0.04)	0.13	-0.34 (-0.62 / -0.05)	0.020
Country						
Spain vs UK	0.01 (-0.04 / 0.07)	0.58	0.04 (-0.09 / 0.19)	0.53	0.13 (-0.11 / 0.38)	0.26
Italy vs UK	0.07 (0.02 / 0.13)	0.007	0.22 (0.08 / 0.36)	0.002	0.46 (0.22 / 0.71)	<0.001
Sex						
Males vs Females	-0.04 (-0.08 / 0.01)	0.060	-0.12 (-0.22 / -0.01)	0.023	-0.22 (-0.41 / -0.05)	0.013
Age						
≥65 vs <65 years	-0.05 (-0.09 / -0.01)	0.021	-0.13 (-0.24 / -0.03)	0.012	-0.27 (-0.45 / -0.08)	0.004
Comorbidities						
≥2 vs 0-1	-0.05 (-0.10 / -0.01)	0.015	-0.13 (-0.25 / -0.02)	0.019	-0.29 (-0.48 / -0.09)	0.003
Primary tumour						
Breast vs Gasttrointestinal	0.03 (-0.02 / 0.09)	0.21	0.15 (0.01 / 0.31)	0.038	0.31 (0.06 / 0.57)	0.014
Gynaecological/Genito-Urinary vs Gasttrointestinal	-0.09 (-0.17 / -0.01)	0.030	-0.23 (-0.44 / -0.03)	0.021	-0.37 (-0.71 / -0.03)	0.029
Thoracic vs Gasttrointestinal	0.06 (0.01 / 0.12)	0.019	0.16 (0.01 / 0.31)	0.035	0.26 (0.01 / 0.53)	0.046
Others vs Gasttrointestinal	0.11 (0.08 / 0.15)	<0.001	0.40 (0.30 / 0.30)	<0.001	0.41 (-0.02 / 0.86)	0.06
Haematological vs Gasttrointestinal	0.01 (-0.06 / 0.07)	0.91	0.03 (-0.13 / 0.21)	0.65	0.10 (-0.18 / 0.38)	0.48
Tumour stage						
Advanced vs Local/loco-regional	-0.01 (-0.05 / 0.04)	0.80	-0.07 (-0.19 / 0.04)	0.19	-0.13 (-0.33 / 0.05)	0.16
Tumour status						
Active malignancy vs Remission/non measurable disease	-0.02 (-0.06 / 0.02)	0.41	-0.03 (-0.14 / 0.06)	0.47	-0.04 (-0.22 / 0.14)	0.64
SACT at COVID-19						
Yes vs No	0.04 (-0.01 / 0.08)	0.063	0.09 (-0.08 / 0.20)	0.070	0.14 (-0.03 / 0.32)	0.12
Unkown vs No	-0.08 (-0.21 / 0.05)	0.25	-0.28 (-0.61 / 0.54)	0.27	-0.55 (-1.11 / 0.01)	0.050

Supplementary Table 12. Distribution of baseline patients, tumour and COVID-19 characteristics according to the SACT resumption pathways. Only patients who were on SACT within 4 weeks prior to COVID-19 were included and categorized as those who resumed/continued SACT without changes and those who permanently discontinued SACT/resumed SACT following dose/regimen adjustments. SACT: systemic anticancer therapy.

	SACT unchanged	**SACT adjustments /discontinuations**	**P value**
	N=506 (%)	**N=332 (%)**	
COVID-19 sequelae			
No	445 (87.9)	271 (81.6)	0.011
Yes	61 (12.1)	61 (18.4)	
SARS-CoV-2 vaccination status			
No	365 (77.5)	254 (79.4)	0.52
Yes	106 (22.5)	66 (20.6)	
Missing	35	12	
Country			
United Kingdom	118 (23.3)	70 (21.1)	0.0154
Spain	191 (37.7)	158 (47.6)	
Italy	197 (38.9)	104 (31.3)	
Sex			
Male	279 (55.2)	184 (55.8)	0.88
Females	226 (44.8)	146 (44.2)	
Missing	1	2	
Age			
<65 y	262 (52.0)	169 (51.1)	0.79
≥65 y	242 (48.0)	162 (48.9)	
Missing	2	1	
Comorbidities			
0-1	336 (66.4)	226 (68.1)	0.61
≥2	170 (33.6)	106 (31.9)	
Smoking history			
Never smokers	240 (56.9)	149 (50.3)	0.083
Former/current smokers	182 (43.1)	147 (49.7)	
Missing	84	36	
Primary Tumour			
Breast	148 (29.4)	72 (21.8)	0.0081
Gastrointestinal	112 (22.3)	87 (26.4)	
Gynaecological/Genito-Urinary	82 (16.3)	41 (12.4)	
Haematological	74 (14.7)	51 (15.5)	
Thoracic	27 (5.4)	15 (4.5)	
Others	60 (11.9)	64 (19.4)	
Missing	3	2	
Tumour stage			
Local/loco-regional	181 (37.2)	91 (30.7)	0.06
Advanced	306 (62.8)	205 (69.3)	
Missing	19	36	
Tumour status at COVID-19 diagnosis			
Remission/non measurable disease	207 (41.0)	112 (33.7)	0.034
Active malignancy	298 (59.0)	220 (66.3)	
Missing	1	0	
COVID-19 therapy			
No	270 (57.2)	143 (45.5)	0.0014
Yes	202 (42.8)	171 (54.5)	
Missing	34	18	
Oxygen therapy requirement			
No	348 (73.6)	205 (64.9)	0.0090
Yes	125 (26.4)	111 (35.1)	
Missing	33	16	
Complicated COVID-19			
0	417 (82.4)	238 (71.7)	0.0002
≥ 1	89 (17.6)	94 (28.3)	
Hospitalization			
Not required	246 (48.8)	116 (35.2)	0.0005
Required	184 (36.5)	149 (45.2)	
Pre-existing	74 (14.7)	65 (19.7)	
Missing	2	2	

Supplementary Figure 1. Kaplan-Meier survival estimate for post COVID-19 survival according to the experience of COVID-19 sequelae. Patients who did not experienced sequelae: not reached (316 events); patients who experienced COVID-19 sequelae: 17.2 months (95%CI: 14.1-NA; 241 events). Log-rank: p<0.0001; HR: 1.61 (95%CI: 1.28-2.01). HR: hazard ratio; CI: confidence intervals.



Supplementary Figure 2. Kaplan-Meier survival estimate for post COVID-19 survival according to SACT resumption pathways. Only patients on SACT within 4 weeks prior to COVID-19 diagnosis were included. Patients who continued/resumed SACT without changes: not reached (86 events); patients who resumed SACT following dose/regimen adjustments: not reached (62 events); patients who permanently discontinued SACT: 4.7 months (95%CI: 2.5-17.5; 42 events). Log-rank: p<0.0001; HR for the risk of death (unchanged group set as reference): dose/regimen adjustments: HR=0.92 (95%CI: 0.71-1.21), permanent discontinuation: HR=3.17 (95%CI: 2.29-4.38). HR: hazard ratio; CI: confidence intervals; cessation: permanent discontinuation.