

Supplementary Tables

Supplementary Table 1. ICI cohort: Tumor therapy history according to SARS-CoV-2 test status

Supplementary Table 2. ICI cohort: Hematological variables at serologic test according to SARS-CoV-2 status

Supplementary Table 3. SARS-CoV-2 testing

Supplementary Table 4. Adverse reactions: trend test - ICI cohort by SARS-CoV-2 test results and overall

Supplementary Table 5. Univariable logistic regression models for SAE- SARS-CoV-2 positive patients within ICI cohort

Supplementary Table 6: Summary statistics of AEs, SAEs and deaths – Sensitivity analysis according to nasal swab SARS-CoV-2 status

Supplementary Table 7: Evaluation of AEs, SAEs and deaths by SARS-CoV-2 positivity – Sensitivity analysis according to nasal swab SARS-CoV-2 status

Supplementary Table 1 ICI cohort: Tumor therapy history according to SARS-CoV-2 test status

	SARS-CoV-2 Negative N=107	SARS-CoV-2 Positive N=52	OVERALL N=159
Number of patients using Corticosteroids or other types of immunosuppressant	40 (37.4)	16 (30.8)	56 (35.2)
Tumor treatment characteristics			
First line adjuvant therapy	21 (19.6)	13 (25.0)	34 (21.4)
First line therapy for advanced treatment	53 (49.5)	24 (46.2)	77 (48.4)
Subsequent line for advanced treatment	33 (30.8)	15 (28.8)	48 (30.2)
Type of immunotherapy*			
Anti CTLA4	2 (1.9)	0 (0.0)	2 (1.3)
Anti PD1/PDL-1	91 (85.0)	46 (88.5)	137 (86.2)
Combined therapies	14 (13.1)	6 (11.5)	20 (12.6)
Duration of last anti-cancer therapy (months from start to last dose prior to serology test)			
Mean (SD)	8.6 (9.5)	9.0 (13.9)	8.7 (11.1)
Median (Q1 - Q3)	5.1 (1.5-13.0)	3.0 (0.9-11.5)	4.8 (1.4-12.0)
Min - Max	0.0 - 53.3	0.0 - 78.8	0.0 - 78.8
Missing	3	1	4
Tumor response (at serology test)**			
CR	8 (12.3)	6 (21.4)	14 (15.1)
PD	11 (16.9)	6 (21.4)	17 (18.3)
PR	14 (21.5)	6 (21.4)	20 (21.5)
SD	32 (49.2)	10 (35.7)	42 (45.2)
Missing	42	24	66
ORR (at serology test)**			
CR+PR	22 (33.8)	12 (42.9)	34 (36.6)
SD+PD	43 (66.2)	16 (57.1)	59 (63.4)
Missing	42	24	66

Legend:Positive:one positive result from serologic test or nasal swab.

(*) Combined therapy refers to the following combinations of therapies: Anti PD-1 and Anti CTLA4, Anti PD-1 and Relatlimab, Anti PD-1 and chemotherapy, Anti PD-1 and Levantinib, Anti PD-1 and Ribociclib, Anti VEGFR and chemotherapy. (***)Out of 66 missing responses, 30 are from patients treated with adjuvant chemotherapy.

Supplementary Table 2. ICI cohort: Hematological variables at serologic test according to SARS-CoV-2 status

	SARS-CoV-2 negative N=107	SARS-CoV-2 positive N=52	OVERALL N=159
Neutrophil count (10L)			
Mean (SD)	4.8 (2.2)	4.7 (1.9)	4.8 (2.1)
Median (Q1 - Q3)	4.5 (3.2-6.0)	4.6 (3.4-6.1)	4.5 (3.2-6.0)
Min - Max	0.0 - 11.1	1.7 - 9.9	0.0 - 11.1
Missing	18	7	25
Values out of normal range (2-6.7)	16 (18.0)	9 (20.0)	25 (18.7)
Missing	18	7	25
Lymphocyte count (10L)			
Mean (SD)	2.0 (0.9)	1.7 (0.7)	1.9 (0.9)
Median (Q1 - Q3)	1.9 (1.5-2.6)	1.6 (1.2-2.2)	1.8 (1.3-2.4)
Min - Max	0.5 - 5.2	0.4 - 4.2	0.4 - 5.2
Missing	21	8	29
Values out of normal range (1.13-3.4)	19 (22.1)	10 (22.7)	29 (22.3)
Missing	21	8	29
Neutrophil/Lymphocyte ratio			
Mean (SD)	2.7 (2.0)	3.4 (2.8)	3.0 (2.3)
Median (Q1 - Q3)	2.1 (1.4-3.4)	2.7 (1.7-4.2)	2.2 (1.6-3.7)
Min - Max	0.0 - 13.2	0.7 - 17.5	0.0 - 17.5
Missing	21	8	29
Platelet count (10L)			
Mean (SD)	237.1 (74.9)	254.0 (96.4)	242.7 (82.6)
Median (Q1 - Q3)	225.0 (192.0-266.0)	224.5 (195.5-275.5)	225.0 (194.0-270.0)
Min - Max	78.0 - 471.0	136.0 - 626.0	78.0 - 626.0
Missing	18	8	26
Values out of normal range (150-400)	9 (10.1)	7 (15.9)	16 (12.0)
Missing	18	8	26

Legend: Positive: one positive result from serologic test or nasal swab. **Note:** Hematological variables were measured at the time of serologic testing

Supplementary Table 3 SARS-CoV-2 testing

	CT N=50	TTs N=84	ICIs N=159	OVERALL N=293				
Testing strategy								
Both	17 (34.0)	29 (34.5)	58 (36.5)	104 (35.5)				
Only serology test*	33 (66.0)	53 (63.1)	92 (57.9)	178 (60.8)				
Only nasal swab	0 (0.0)	2 (2.4)	9 (5.7)	11 (3.8)				
For patients with only nasal swab – results – n(%)								
Negative	-	2 (100.0)	1 (11.1)	3 (27.3)				
Positive	-	0 (0.0)	8 (88.9)	8 (72.7)				
Number of patients positive by serology testing – n(%)								
	13 (26.0)	24 (29.3)	44 (29.3)	81 (28.7)				
Nasal swab test results in patients with previous positive serological test								
Negative	10 (76.9)	16 (66.7)	4 (9.1)	30 (37.0)				
Positive	3 (23.1)	8 (33.3)	40 (90.9)	51 (63.0)				
Overall SARS-COV 2 status								
Negative	37 (74.0)	60 (71.4)	107 (67.3)	204 (69.6)				
Positive	13 (26.0)	24 (28.6)	52 (32.7)	89 (30.4)				
Comparison of patients test results:								
Chi squared test pvalue	0.610							
Legend: N: number of subjects; CT: chemotherapy, TTs: targeted therapy, ICIs: immune checkpoint inhibitors								
(*) patients with only serology test are all negative for SARs-CoV-2 since in case of positive result nasal swab was also performed								

Supplementary Table 4: Adverse reactions: trend test - ICI cohort by SARS-CoV-2 test results and overall

Toxicity - N=159	G0 n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)	G3+G4+G5 n (%)	Chi square for trend (exact pvalue)
OVERALL								0.849
SARS-CoV-2 Negative	70 (65.4)	20 (18.7)	15 (14.0)	2 (1.9)	0 (0.0)	0 (0.0)	2 (1.9)	
SARS-CoV-2 Positive	39 (75.0)	1 (1.9)	9 (17.3)	2 (3.8)	1 (1.9)	0 (0.0)	3 (5.8)	
Cardiac AE								0.034
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	49 (94.2)	1 (1.9)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Elevation of the troponin								0.327
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Hypertension								0.106
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Endocrinological AE								0.071
SARS-CoV-2 Negative	90 (84.1)	14 (13.1)	3 (2.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	1 (1.9)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Hyperthyroidism								1.000
SARS-CoV-2 Negative	103 (96.3)	3 (2.8)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	1 (1.9)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Hypothyroidism								0.050
SARS-CoV-2 Negative	98 (91.6)	8 (7.5)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Pituitary								1.000
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Vitiligo								0.551
SARS-CoV-2 Negative	104 (97.2)	3 (2.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Gastrointestinal AE								0.630

Toxicity - N=159	G0 n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)	G3+G4+G5 n (%)	Chi square for trend (exact pvalue)
SARS-CoV-2 Negative	91 (85.0)	6 (5.6)	8 (7.5)	2 (1.9)	0 (0.0)	0 (0.0)	2 (1.9)	
SARS-CoV-2 Positive	48 (92.3)	0 (0.0)	3 (5.8)	0 (0.0)	1 (1.9)	0 (0.0)	1 (1.9)	
-Colitis								1.000
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (0.9)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Diarrhea								0.101
SARS-CoV-2 Negative	95 (88.8)	5 (4.7)	7 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Hepatitis								0.779
SARS-CoV-2 Negative	105 (98.1)	1 (0.9)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Immuno-mediated hepatitis								0.327
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Lipase increased								1.000
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	1 (0.9)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Mucositis								1.000
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Serum creatine increased								0.327
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Transaminitis								0.178
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	0 (0.0)	1 (1.9)	0 (0.0)	1 (1.9)	0 (0.0)	1 (1.9)	
Lung related AE								1.000
SARS-CoV-2 Negative	103 (96.3)	0 (0.0)	4 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

Toxicity - N=159	G0 n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)	G3+G4+G5 n (%)	Chi square for trend (exact pvalue)
SARS-CoV-2 Positive	50 (96.2)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Pneumonia								1.000
SARS-CoV-2 Negative	103 (96.3)	0 (0.0)	4 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Other								-
-Asthenia								0.080
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	49 (94.2)	0 (0.0)	2 (3.8)	1 (1.9)	0 (0.0)	0 (0.0)	1 (1.9)	
-Plantar dysaesthesia								0.327
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Staphylococcus Infection								0.327
SARS-CoV-2 Negative	107 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	1 (1.9)	
Skin related AE								0.407
SARS-CoV-2 Negative	94 (87.9)	11 (10.3)	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Lichen dermatosis								1.000
SARS-CoV-2 Negative	106 (99.1)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	52 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Pruritus								0.425
SARS-CoV-2 Negative	98 (91.6)	8 (7.5)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	51 (98.1)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
-Rash								0.464
SARS-CoV-2 Negative	97 (90.7)	9 (8.4)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
SARS-CoV-2 Positive	50 (96.2)	1 (1.9)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

Legend: SARS-CoV-2 positive: one positive result from serologic test or nasal swab, N: number of subjects; G: Grade

Supplementary Table 5 Univariable logistic regression models for SAE- SARS-CoV-2 positive patients within ICI cohort

	N	P-value of variable	OR (95% CI)	P-value of contrasts
Age	52	0.511	1.02 (0.96 - 1.10)	-
Sex	52	0.334		
Male			reference	
Female			2.07 (0.47 - 9.03)	0.334
Comorbidity	52	0.910		
No			reference	
Yes			1.09 (0.26 - 4.61)	0.910
Platelet count	44	0.992	1.00 (0.99 - 1.01)	-
Lymphocyte count	44	0.056	0.09 (0.01 - 1.06)	-
Neutrophils/Lymphocyte ratio	44	0.021*	2.76 (1.16 - 6.54)	-

Legend: OR: Odds ratio; CI: Confidence Interval

Supplementary Table 6: Summary statistics of AEs, SAEs and deaths – Sensitivity analysis according to nasal swab SARS-CoV-2 status

	CT N=50	TT N=84	ICI N=159	OVERALL N=293
Number of patients with positive nasal swab test result – n(%)	3 (6.0)	8 (9.5)	48 (30.2)	59 (20.1)
Evaluation of AEs				
SARS-CoV-2 positive patients	3 (6.0)	8 (9.5)	48 (30.2)	59 (20.1)
No occurrence of AEs	3 (100.0)	7 (87.5)	36 (75.0)	46 (78.0)
Occurrence of AEs	0 (0.0)	1 (12.5)	12 (25.0)	13 (22.0)
SARS-CoV-2 negative patients	47 (94.0)	76 (90.5)	111 (69.8)	234 (79.9)
No occurrence of AEs	26 (55.3)	53 (69.7)	73 (65.8)	152 (65.0)
Occurrence of AEs	21 (44.7)	23 (30.3)	38 (34.2)	82 (35.0)
Evaluation of SAEs				
SARS-CoV-2 positive patients	3 (6.0)	8 (9.5)	48 (30.2)	59 (20.1)
No occurrence of SAE	3 (100.0)	8 (100.0)	39 (81.3)	50 (84.7)
Occurrence of SAE	0 (0.0)	0 (0.0)	9 (18.8)	9 (15.3)
SARS-CoV-2 negative patients	47 (94.0)	76 (90.5)	111 (69.8)	234 (79.9)
No occurrence of SAE	44 (93.6)	76 (100.0)	107 (96.4)	227 (97.0)
Occurrence of SAE	3 (6.4)	0 (0.0)	4 (3.6)	7 (3.0)
Evaluation of mortality				
SARS-CoV-2 positive patients	3 (6.0)	8 (9.5)	48 (30.2)	59 (20.1)
Alive	3 (100.0)	8 (100.0)	42 (87.5)	53 (89.8)
Dead	0 (0.0)	0 (0.0)	6 (12.5)	6 (10.2)
SARS-CoV-2 negative patients	47 (94.0)	76 (90.5)	111 (69.8)	234 (79.9)
Alive	44 (93.6)	76 (100.0)	109 (98.2)	229 (97.9)
Dead	3 (6.4)	0 (0.0)	2 (1.8)	5 (2.1)

Legend: N: number of subjects; SARS-CoV-2 positive: positive result from nasal swab, CT: chemotherapy, TTs: targeted therapy, ICIs: immune checkpoint inhibitors.

Supplementary Table 7: Evaluation of AEs, SAEs and deaths by SARS-CoV-2 positivity – Sensitivity analysis according to nasal swab SARS-CoV-2 status

	SARS-CoV-2 negative N=234	SARS-CoV-2 positive N=59	Overall N=293
Evaluation of AEs			
No occurrence of AEs	152 (65.0)	46 (78.0)	198 (67.6)
Occurrence of AEs	82 (35.0)	13 (22.0)	95 (32.4)
Fisher exact test pvalue			
		0.063	
Evaluation of SAEs			
No occurrence of SAEs	227 (97.0)	50 (84.7)	277 (94.5)
Occurrence of SAEs	7 (3.0)	9 (15.3)	16 (5.5)
Fisher exact test pvalue			
		0.001*	
Evaluation of mortality			
Alive	229 (97.9)	53 (89.8)	282 (96.2)
Dead	5 (2.1)	6 (10.2)	11 (3.8)
Fisher exact test pvalue			
		0.011*	
Legend: N: number of subjects; SARS-CoV-2 positive: positive result from nasal swab, AEs: adverse events, SAEs: serious adverse events			