

SUPPLEMENTARY MATERIALS

Immunogenicity of two doses of BNT162b2 and mRNA-1273 vaccines for solid cancer patients on treatment with or without a previous SARS-CoV-2 infection.

Nicla La Verde, Agostino Riva, Maria Silvia Cona, Arianna Gabrieli, Monica Cattaneo, Cinzia Fasola, Giuseppe Lipari, Claudia De Stradis, Valentina Favorito, Benedetta Lombardi Stocchetti, Davide Chizzoniti, Alice Covizzi, Eliana Rulli, Francesca Galli, Lorenzo Ruggieri, Anna Gambaro, Sabrina Ferrario, Davide Dalu, Maciej S. Tarkowski.

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Table S1. Demographic and clinical characteristics of cancer patients

	Group 1 N=28	Group 2 N=65	Group 3 N=69	Group 4 N=24	Group 5 N=9
Age at tumor diagnosis					
Mean (SD)	61.5 (9.8)	58.4 (12.8)	56.8 (11.4)	60.5 (12.8)	60.6 (8.1)
Median (Q1 - Q3)	64.0 (52.1-68.9)	59.9 (49.4-69.5)	58.2 (47.9-65.8)	63.0 (54.0-69.2)	62.4 (59.2-65.1)
Min - Max	39.9 - 75.8	24.0 - 78.4	33.6 - 78.6	27.2 - 78.5	42.9 - 71.1
Tumor site					
Breast	19 (67.9)	29 (44.6)	38 (55.1)	0 (0.0)	0 (0.0)
Gastroenteric	5 (17.9)	19 (29.2)	2 (2.9)	10 (41.7)	4 (44.4)
Lung	0 (0.0)	4 (6.2)	12 (17.4)	4 (16.7)	0 (0.0)
Genitourinary	3 (10.7)	2 (3.1)	5 (7.2)	8 (33.3)	0 (0.0)
Gynaecological	0 (0.0)	8 (12.3)	8 (11.6)	0 (0.0)	5 (55.6)
Head and neck	1 (3.6)	0 (0.0)	1 (1.4)	1 (4.2)	0 (0.0)
Other	0 (0.0)	3 (4.6)	3 (4.3)	1 (4.2)	0 (0.0)
Tumor stage					
Limited	26 (92.9)	21 (32.3)	9 (13.0)	6 (25.0)	0 (0.0)
Advanced	2 (7.1)	43 (66.2)	59 (85.5)	18 (75.0)	9 (100.0)
Not applicable	0 (0.0)	1 (1.5)	1 (1.4)	0 (0.0)	0 (0.0)
>1 line of cancer treatment	18 (64.3)	40 (61.5)	55 (79.7)	15 (62.5)	7 (77.8)
Patients out of treatment	27 (96.4)	2 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)
Patients on treatment	1 (3.6)	63 (96.9)	69 (100.0)	24 (100.0)	9 (100.0)
Neoadjuvant	0 (0.0)	6 (9.2)	0 (0.0)	2 (8.3)	0 (0.0)
Adjuvant	1 (3.6)	17 (26.2)	10 (14.5)	3 (12.5)	0 (0.0)
Metastatic	0 (0.0)	40 (61.5)	54 (78.3)	19 (79.2)	9 (100.0)
Maintenance	0 (0.0)	0 (0.0)	5 (7.2)	0 (0.0)	0 (0.0)
Treatment schedule					

1w	0 (0.0)	13 (20.6)	1 (1.4)	4 (16.7)	0 (0.0)
2w	0 (0.0)	5 (7.9)	1 (1.4)	2 (8.3)	0 (0.0)
3w	1 (100.0)	35 (55.6)	29 (42.0)	15 (62.5)	0 (0.0)
4w	0 (0.0)	1 (1.6)	13 (18.8)	0 (0.0)	6 (66.7)
Daily	0 (0.0)	9 (14.3)	25 (36.2)	3 (12.5)	3 (33.3)
Comorbidity					
No	9 (32.1)	33 (50.8)	30 (43.5)	13 (54.2)	1 (11.1)
= 1	12 (42.9)	16 (24.6)	26 (37.7)	7 (29.2)	4 (44.4)
>1	7 (25.0)	16 (24.6)	13 (18.8)	4 (16.7)	4 (44.4)
Steroids	1 (3.6)	56 (86.2)	8 (11.6)	20 (83.3)	3 (33.3)
G-CSF	0 (0.0)	13 (20.0)	1 (1.4)	1 (4.2)	0 (0.0)

Legend: SD: standard deviation. Q1 – Q3: first-third quartile.

Group 1: patients in complete remission after surgery, untreated or pre-treated with adjuvant chemotherapy (CT) completed since at least 12 months. Adjuvant hormone therapy (HT) was allowed.

Group 2: patients in active treatment with CT.

Group 3: patients treated with biological therapy (immunotherapy, CDK4/6 inhibitors, TKI and monoclonal antibody).

Group 4: patients in treatment with a combination of CT and biological treatment.

Group 5: patients receiving only HT in metastatic setting.

Table S2. Vaccines and antibodies measurement

	Group 1 N=28	Group 2 N=65	Group 3 N=69	Group 4 N=24	Group 5 N=9	Healthy subjects N=20
Age at vaccine first dose						
Mean (SD)	64.1 (10.0)	61.4 (12.9)	61.8 (11.2)	64.3 (12.6)	71.9 (6.6)	34.0 (12.6)
Median (Q1 - Q3)	66.5 (54.6-70.7)	63.7 (51.5-71.1)	61.6 (53.9-71.6)	67.0 (58.2-73.5)	72.1 (67.0-75.6)	28.5 (25.0-42.0)
Min - Max	40.7 - 79.0	26.9 - 84.3	36.8 - 81.8	27.9 - 79.0	61.2 - 83.2	21.0 - 63.0
Sex						
Male	7 (25.0)	19 (29.2)	17 (24.6)	9 (37.5)	5 (55.6)	9 (45.0)
Female	21 (75.0)	46 (70.8)	52 (75.4)	15 (62.5)	4 (44.4)	11 (55.0)
Anti-SARS-CoV-2 vaccine*						
mRNA-1273	8 (28.6)	19 (29.7)	19 (27.5)	8 (33.3)	1 (11.1)	0 (0.0)
BNT162b2	20 (71.4)	45 (70.3)	50 (72.5)	16 (66.7)	8 (88.9)	20 (100.0)
Missing	0	1	0	0	0	0
Timing of vaccine in relation to anticancer treatments administration (n=166)						
At first cycle	0 (0.0)	13 (20.6)	4 (5.8)	3 (12.5)	2 (22.2)	-
After first cycle	1 (100.0)	50 (79.4)	65 (94.2)	21 (87.5)	7 (77.8)	-
IgG anti-N1						
Negative both at T0 and T1	27 (96.4)	54 (83.1)	54 (78.3)	21 (87.5)	9 (100.0)	20 (100.0)
Negative at T0, positive at T1	0 (0.0)	1 (1.5)	3 (4.3)	1 (4.2)	0 (0.0)	0 (0.0)
Positive at T0, negative at T1	1 (3.6)	2 (3.1)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
Positive both at T0 and T1	0 (0.0)	8 (12.3)	11 (15.9)	2 (8.3)	0 (0.0)	0 (0.0)

Legend: SD: standard deviation. Q1 – Q3: first-third quartile. T0: at first dose of the vaccine. T1: 30 days after second dose of vaccine.

Group 1: patients in complete remission after surgery, untreated or pre-treated with adjuvant chemotherapy (CT) completed since at least 12 months. Adjuvant hormone therapy (HT) was allowed.

Group 2: patients in active treatment with CT.

Group 3: patients treated with biological therapy (immunotherapy, CDK4/6 inhibitors, TKI and monoclonal antibody).

Group 4: patients in treatment with a combination of CT and biological treatment.

Group 5: patients receiving only HT in metastatic setting.

Table S3. Antibody response in subject groups

	Anti-S1 antibodies		P-value ^a	P-value ^b	Anti-RBD antibodies		P-value ^a	P-value ^b
Group 1 (N=28)								
Antibody titres		G1 vs G2:	0.6212	0.0331		G1 vs G2:	0.8670	0.6643
Mean (SD)	1991.6 (1620.5)	G1 vs G3:	0.3683	0.7861	12878.7 (6121.0)	G1 vs G3:	0.2719	1.0000
Median (Q1 - Q3)	1559.5 (728.8-2366.3)	G1 vs G4:	0.4628	0.5104	12956.8 (7616.5-17319.5)	G1 vs G4:	0.4628	1.0000
Min - Max	13.0 - 6613.0	G1 vs G5:	0.3956	0.3727	34.0 - 24549.0	G1 vs G5:	0.5240	0.4324
Responders – n (%)	23 (82.1)	G1 vs HS:	0.0192	0.3787	27 (96.4)	G1 vs HS:	0.0032	1.0000
Group 2 (N=65)								
Antibody titres								
Mean (SD)	2731.2 (3411.4)	G2 vs G3:	0.1085	0.0159	12384.5 (8093.4)	G2 vs G3:	0.2109	0.4835
Median (Q1 - Q3)	1352.0 (280.0-3967.0)	G2 vs G4:	0.1492	0.3334	13715.0 (4364.0-19513.5)	G2 vs G4:	0.3271	0.3181
Min - Max	6.0 - 12322.5	G2 vs G5:	0.6374	0.7307	7.0 - 25900.0	G2 vs G5:	0.5136	0.5541
		G2 vs HS:	0.0373	0.0022		G2 vs HS:	0.0167	0.3342
Responders – n (%)	38 (58.5)				60 (92.3)			
Group 3 (N=69)								
Antibody titres								
Mean (SD)	3192.2 (3478.2)	G3 vs G4:	0.9370	0.5777	13215.6 (7309.9)	G3 vs G4:	0.9720	0.5661
Median (Q1 - Q3)	1838.0 (819.0-4288.0)	G3 vs G5:	0.1970	0.4234	14023.5 (7330.0-19905.0)	G3 vs G5:	0.1480	0.3939
Min - Max	5.0 - 15649.0	G3 vs HS:	0.1813	0.1071	7.0 - 25900.0	G3 vs HS:	0.0802	1.0000
Responders – n (%)	54 (78.3)				66 (95.7)			
Group 4 (N=24)								
Antibody titres								
Mean (SD)	3195.0 (3391.8)				14292.0 (7105.8)			
Median (Q1 - Q3)	1949.0 (653.5-4300.3)	G4 vs G5:	0.1693	1.0000	17075.5 (6571.8-20001.8)	G4 vs G5:	0.1456	0.2727
Min - Max	339.0 - 12689.0	G4 vs HS:	0.2679	0.0544		G4 vs HS:	0.1716	NE
					3515.0 - 25981.0			
Responders – n (%)	17 (70.8)				24 (100.0)			
Group 5 (N=9)								

	Anti-S1 antibodies		P-value ^a	P-value ^b	Anti-RBD antibodies		P-value ^a	P-value ^b
Antibody titres								
Mean (SD)	1558.4 (1457.1)				10734.2 (6466.5)			
Median (Q1 - Q3)	1095.0 (351.0-2335.5)	G5 vs HS:	0.0162	0.0760	10298.0 (7745.0-16107.0)	G5 vs HS:	0.0040	0.3103
Min - Max	9.0 - 4190.0				133.0 - 18967.0			
Responders – n (%)	6 (66.7)				8 (88.9)			
Healthy subjects (N=20)								
Antibody titres								
Mean (SD)	3003.1 (1533.0)				17717.7 (3581.0)			
Median (Q1 - Q3)	2590.0 (1731.8-4253.0)				18088.8 (15661.3-20097.5)			
Min - Max	663.0 - 5961.0				8267.0 - 21954.5			
Responders – n (%)	19 (95.0)				20 (100.0)			

Legend: SD: standard deviation. Q1 – Q3: first-third. HS: healthy subjects.

a. Kruskal-Wallis test

b. Fisher test

Table S4. Effect on IgG anti-S1 response to vaccine in cancer patients according to G-CSF administration. Multivariable linear regression analysis.

No G-CSF (N=179)			G-CSF (N=15)	
Parameter	Exp(Estimate [95 % CI])	P-value	Exp(Estimate [95 % CI])	P-value
Intercept	2481.32		1661.46	
Group 2 (vs 1)	0.92 (0.43-1.99)	0.8328	NE	
Group 3 (vs 1)	0.89 (0.49-1.61)	0.6998	1.44 (0.01-186.11)*	0.8703
Group 4 (vs 1)	1.54 (0.65-3.66)	0.3294	1.01 (0.01-94.10)*	0.9973
Group 5 (vs 1)	0.80 (0.29-2.21)	0.6664	NE	
Post-hoc contrasts:				
Group 2 (vs 3)	1.03 (0.55-1.94)	0.9161	NE	
Group 2 (vs 4)	0.60 (0.31-1.15)	0.1236	NE	
Group 3 (vs 4)	0.58 (0.27-1.22)	0.1507	NE	
Group 2 (vs 5)	1.15 (0.42-3.11)	0.7833	NE	
Group 3 (vs 5)	1.11 (0.43-2.86)	0.8257	NE	
Group 4 (vs 5)	1.92 (0.65-5.62)	0.2340	NE	
Steroids	0.69 (0.39-1.23)	0.2032	NE	
BNT162b2 vaccine (vs mRNA-1273)	0.44 (0.29-0.69)	0.0004	0.13 (0.01-1.51)	0.0919
One comorbidity (vs none)	1.03 (0.66-1.63)	0.8871	0.84 (0.07-10.04)	0.8766
More than one comorbidity (vs none)	0.61 (0.37-1.01)	0.0539	0.45 (0.01-35.58)	0.6908
Previous SARS-CoV-2 infection	5.90 (3.44-10.11)	<0.0001	NE	

Note. Antibody titres were analyzed as on the logarithmic scale. The p-value for interaction vaccine type/G-CSF is 0.0652. The association with antibody response of some patient categories, of steroids taking and of a previous SARS-CoV-2 infection was not estimable for patients who took G-CSF (grey area).

Legend: *The reference level is the second patient category. NE: not estimable.

Group 1: patients in complete remission after surgery, untreated or pre-treated with adjuvant chemotherapy (CT) completed since at least 12 months. Adjuvant hormone therapy (HT) was allowed.

Group 2: patients in active treatment with CT.

Group 3: patients treated with biological therapy (immunotherapy, CDK4/6 inhibitors, TKI and monoclonal antibody).

Group 4: patients in treatment with a combination of CT + biological treatment.

Group 5: patients receiving only HT in metastatic setting.

Table S5. Effect on anti-S1 IgG response to SARS-CoV-2 vaccine in cancer patients according to the exposition to SARS-CoV-2. Multivariable linear regression analysis.

Parameter	Patients without previous SARS-CoV-2 infection (N=164)		Patients with previous SARS-CoV-2 infection (N=30)	
	Exp(Estimate [95%CI])	P-value	Exp(Estimate [95%CI])	P-value
Intercept	3326.09		2238.93	
Group 2 (vs 1)	0.78 (0.33-1.80)	0.5503	11.77 (0.73-189.49)	0.0792
Group 3 (vs 1)	0.92 (0.48-1.75)	0.7945	3.53 (0.38-32.94)	0.2540
Group 4 (vs 1)	1.48 (0.58-3.77)	0.4099	12.73 (0.77-210.54)	0.0732
Group 5 (vs 1)	0.83 (0.28-2.44)	0.7389	NE	
Post-hoc contrasts:				
Group 2 (vs 3)	0.84 (0.42-1.71)	0.6365	3.34 (0.78-14.33)	0.1001
Group 2 (vs 4)	0.52 (0.25-1.08)	0.0784	0.92 (0.23-3.77)	0.9081
Group 3 (vs 4)	0.62 (0.27-1.41)	0.2519	0.28 (0.04-1.89)	0.1787
Group 2 (vs 5)	0.93 (0.32-2.70)	0.8924	NE	
Group 3 (vs 5)	1.10 (0.40-3.00)	0.8498	NE	
Group 4 (vs 5)	1.77 (0.56-5.60)	0.3256	NE	
Steroids	0.65 (0.35-1.23)	0.1884	0.36 (0.08-1.68)	0.1837
G-CSF	0.49 (0.21-1.13)	0.0953	0.01 (0.00-0.11)	0.0003
BNT162b2 vaccine (vs mRNA-1273)	0.36 (0.23-0.58)	<0.0001	0.39 (0.14-1.13)	0.0807
One comorbidity (vs none)	0.91 (0.55-1.50)	0.7159	2.08 (0.83-5.23)	0.1123
More than one comorbidity (vs none)	0.51 (0.29-0.90)	0.0201	1.79 (0.65-4.90)	0.2443

Note. Antibody titres were analyzed as on the logarithmic scale. The p-value for interaction vaccine type/previous SARS-CoV-2 infection is 0.6207.

The association with antibody response of the Group 5 was not estimable for patients previously exposed to SARS-CoV-2 (grey area).

Legend: NE: not estimable.

Group 1: patients in complete remission after surgery, untreated or pre-treated with adjuvant chemotherapy (CT) completed since at least 12 months. Adjuvant hormone therapy (HT) was allowed.

Group 2: patients in active treatment with CT.

Group 3: patients treated with biological therapy (immunotherapy, CDK4/6 inhibitors, TKI and monoclonal antibody).

Group 4: patients in treatment with a combination of CT + biological treatment.

Group 5: patients receiving only HT in metastatic setting.

Table S6. Effect on IgG anti-RBD response to vaccine in cancer patients according to steroids administration. Multivariable linear regression analysis.

Parameter	No steroids (N=107)		Steroids (N=87)	
	Exp(Estimate [95% CI])	P-value	Exp(Estimate [95% CI])	P-value
Intercept	11596.08		18072.51	
BNT162b2 vaccine (vs mRNA-1273)	0.79 (0.50-1.26)	0.3209	0.35 (0.19-0.66)	0.0013
More than one comorbidity (vs none)	0.71 (0.41-1.21)	0.2061	0.37 (0.18-0.76)	0.0074
More than one comorbidity (vs none)	0.71 (0.41-1.21)	0.2061	0.37 (0.18-0.76)	0.0074
Previous SARS-CoV-2 infection	1.76 (1.03-3.00)	0.0396	3.41 (1.45-8.00)	0.0054

Note. Antibody titres were analyzed as on the logarithmic scale. The p-value for interaction vaccine type/steroids is 0.0865.

Table S7. Effect on IgG anti-RBD response in cancer patients according to exposition to SARS-CoV-2. Multivariable linear regression analysis.

Parameter	Patients without previous SARS-CoV-2 infection (N=164)		Patients with previous SARS-CoV-2 infection (N=30)	
	Exp(Estimate [95% CI])	P-value	Exp(Estimate [95% CI])	P-value
Intercept	14397.46		23971.23	
BNT162b2 vaccine (vs mRNA-1273)	0.56 (0.37-0.86)	0.0083	0.67 (0.30-1.47)	0.3005
One comorbidity (vs none)	1.01 (0.64-1.58)	0.9709	1.14 (0.55-2.36)	0.7206
More than one comorbidity (vs none)	0.51 (0.31-0.84)	0.0086	0.65 (0.28-1.48)	0.2929

Note. Antibody titres were analyzed as on the logarithmic scale. The p-value for interaction vaccine type/steroids is 0.7370.