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Supplemental information

Immunity to SARS-CoV-2

up to 15 months after infection

Harold Marcotte, Antonio Piralla, Fanglei Zuo, Likun Du, Irene Cassaniti, Hui Wan, Makiko Kumagai-Braesh, Juni Andréll, Elena Percivalle, Josè Camilla Sammartino, Yating Wang, Stelios Vlachiotis, Janine Attevall, Federica Bergami, Alessandro Ferrari, Marta Colaneri, Marco Vecchia, Margherita Sambo, Valentina Zuccaro, Erika Asperges, Raffaele Bruno, Tiberio Oggionni, Federica Meloni, Hassan Abolhassani, Federico Bertoglio, Maren Schubert, Luigi Calzolai, Luca Varani, Michael Hust, Yintong Xue, Lennart Hammarström, Fausto Baldanti, and Qiang Pan-Hammarström

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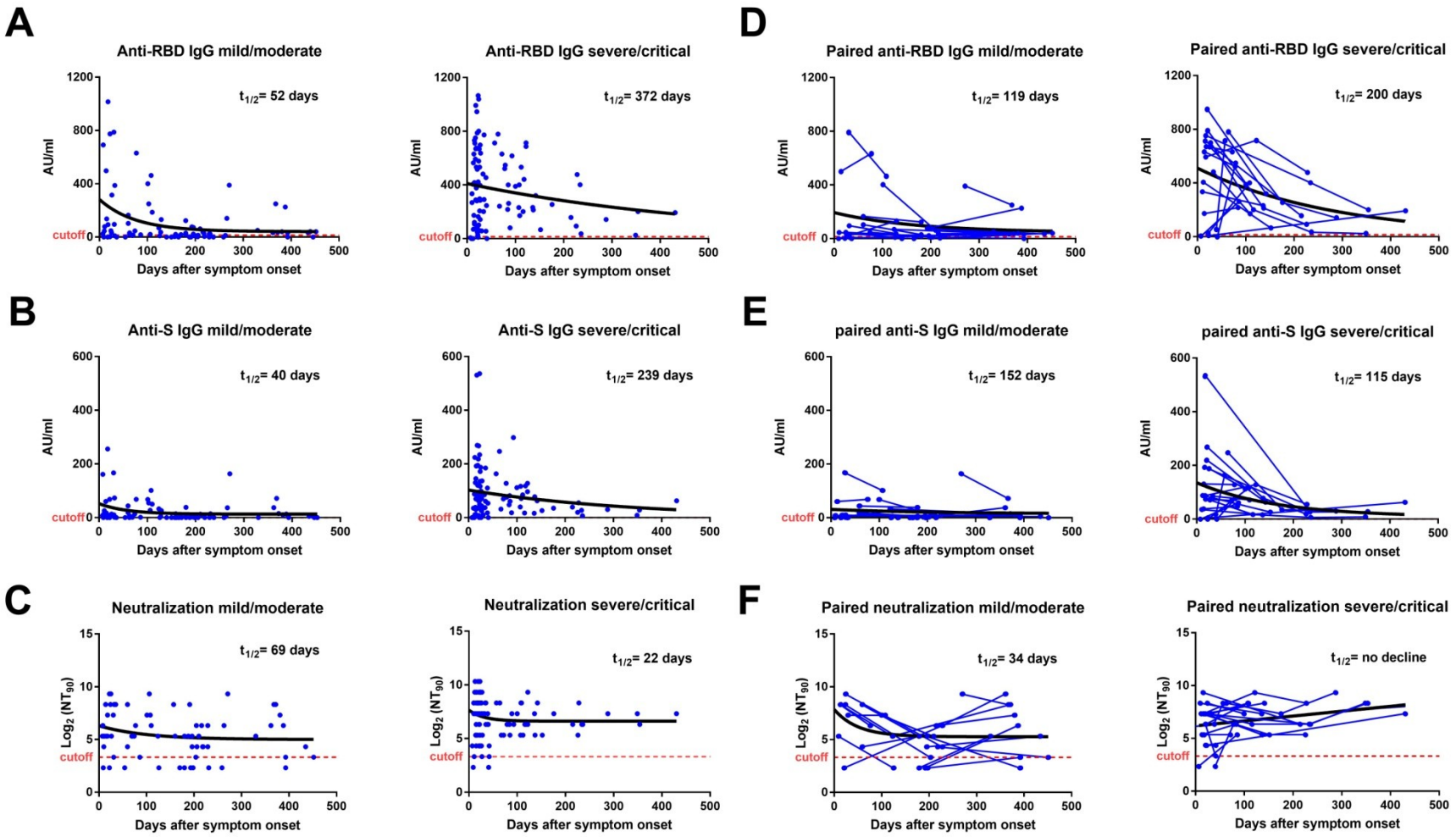

Figure S1. Antibody and neutralization titers in relation to severity. Related to Figures 2-4. Levels of anti-RBD, anti-S and neutralization activity according to severity using cross-sectional (all samples) (A-C) and longitudinal (paired samples) (D-F) analysis. The antibody titers and NT_{90} decay curves (in black) together with corresponding half-lives ($t_{1/2}$) were estimated by a one-phase decay model. Symbols represent individual subjects. The dashed red line indicates the cutoff value. The cutoff-value is not visible in some graphs because it is very close to the X-axis.

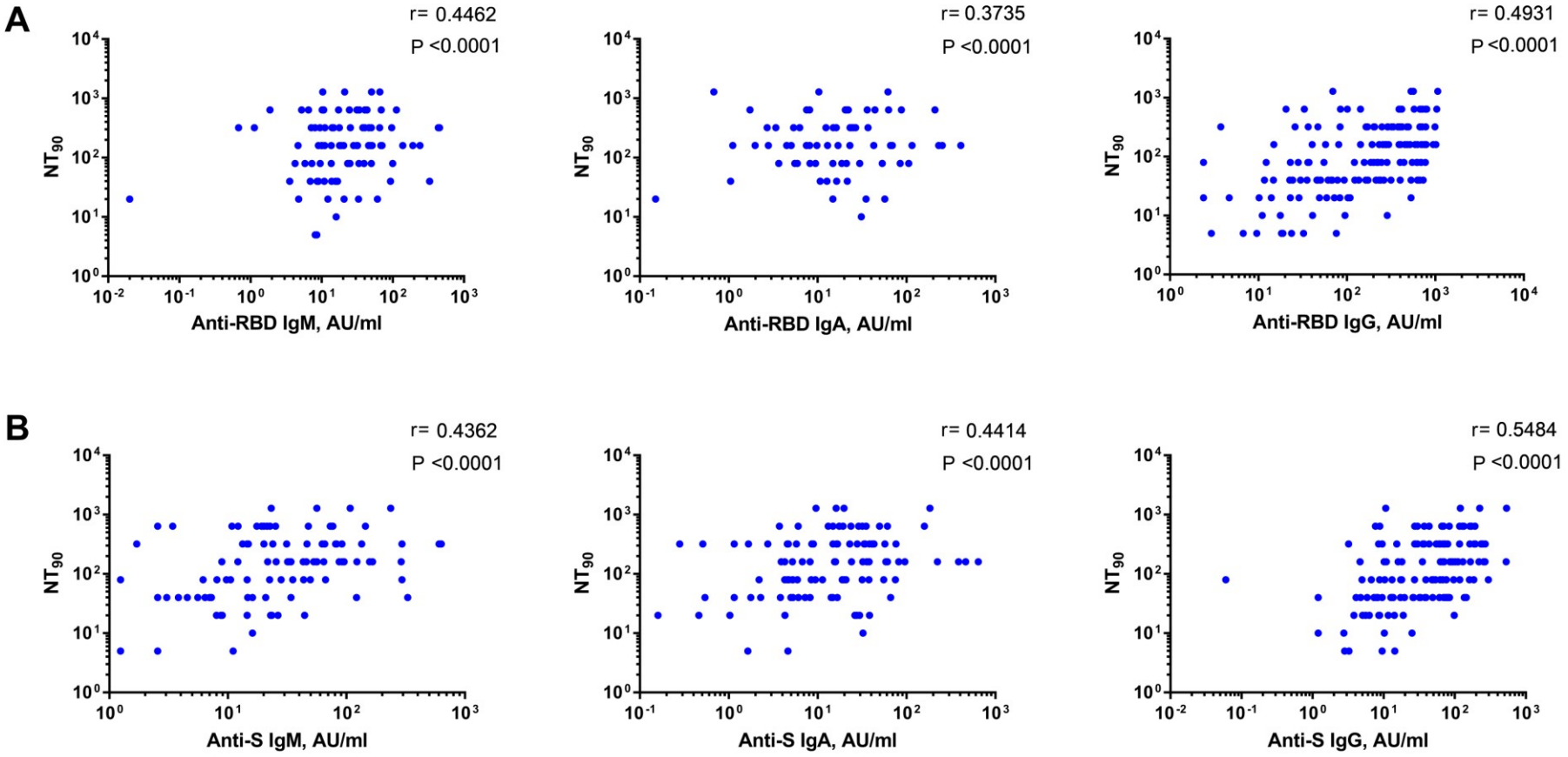

Figure S2. Correlation between the level of anti-SARS-CoV-2 antibodies and neutralizing antibody titers. Related to Figures 2 and 4. Levels of anti-RBD (A) and anti-S (B) IgM, IgA, and IgG antibodies significantly correlated with neutralization antibody titers measured against SARS-CoV-2 virus in COVID-19 patient samples (n=168 for each antibody isotype). Symbols represent individual subjects. Spearman's rank correlation. Significant if $p < 0.05$.

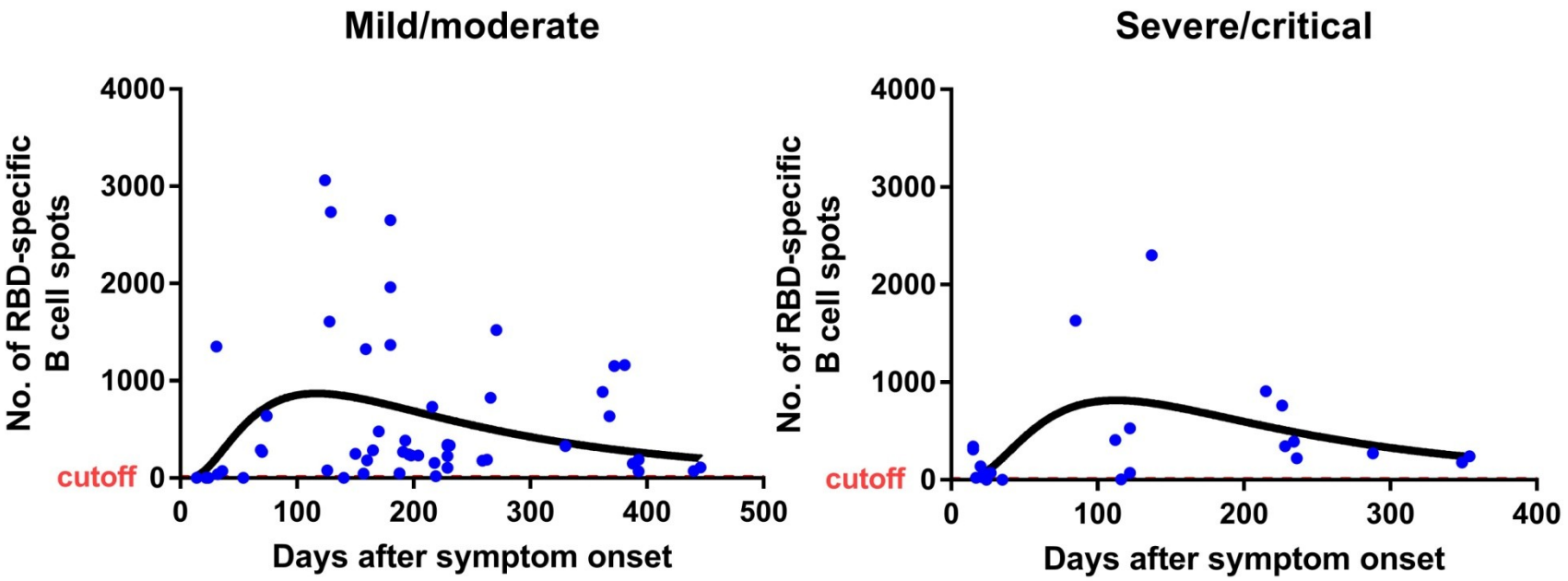

Figure S3. Cross-sectional analysis of SARS-CoV-2-specific memory B cell responses in COVID-19 patients in relation to disease severity. Related to Figure 5. Dynamics of RBD-specific memory B cells levels in samples from COVID-19 patients with mild/moderate (A) and severe/critical (B) symptoms with the corresponding log-normal fitting curve (in black). The results were expressed as the number of spots per 300,000 seeded cells after subtracting the background spots of the negative control. Symbols represent individual subjects. The cutoff value (dashed red line) was set at the highest number of specific B cell spots for the negative controls (> 12 spots / 300,000 cells). The cutoff-value is not visible because it is very close to the X-axis.

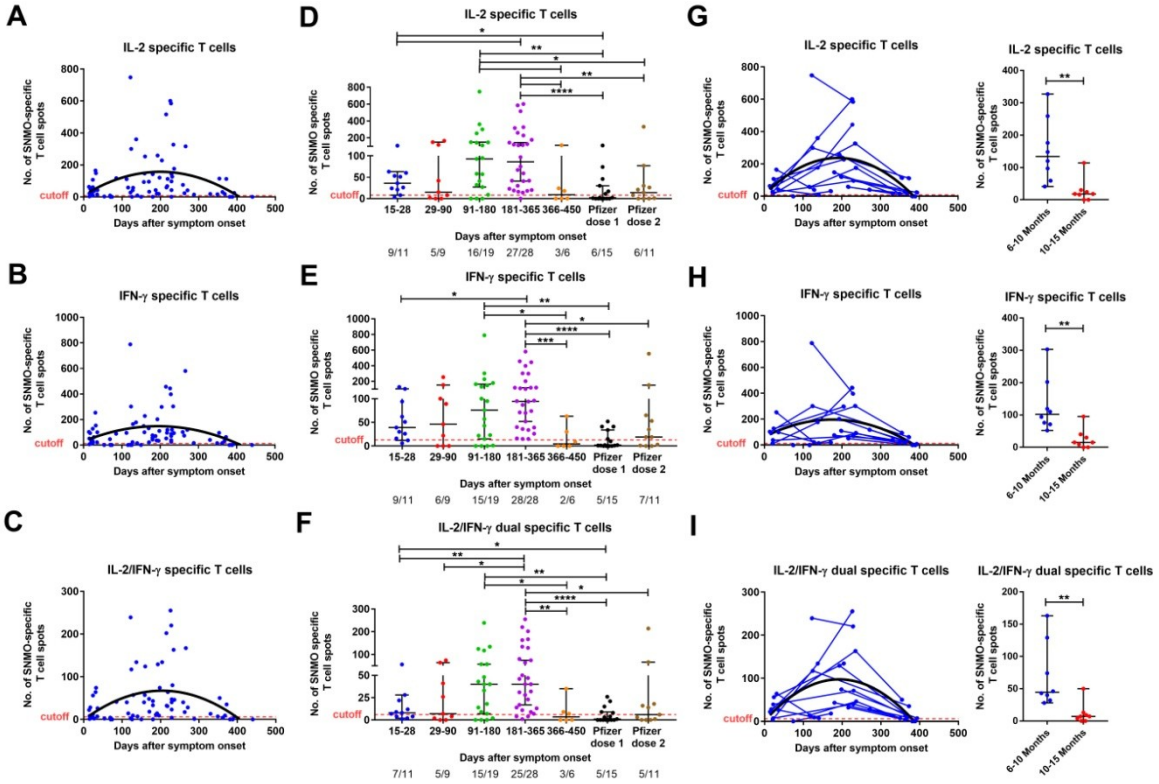

Figure S4. Cross-sectional and longitudinal analysis of S N M O-specific memory T cell responses in COVID-19 patients. Related to Figure 6. (A-C) Dynamics of S N M O-specific memory IL-2, IFN-γ, and IL-2/IFN-γ-producing T cells with the corresponding second order polynomial fitting curve (in black). (D-F) T cells were measured in control (n =11), COVID-19 samples at 5 study periods: 14-30 days (n = 11), 31-90 (n = 9), 91-180 days (n = 19), 181-365 (n = 28), and 366-452 (n = 6) days after symptom onset, as well as vaccinee samples after first (n = 15) and second (n = 11) dose. For longitudinal analysis, samples were taken at two (n = 10) or more (n = 5) time points, and further comparisons were made between paired samples (n = 8) at two time points ranging from 6 to 15 months (TP1: 181-300 and TP2: 301-452 days after symptoms onset; right panel). The results were expressed as the number of spots per 300,000 seeded cells after subtracting the background spots of the negative control. The horizontal black lines indicate the median value and 95% CI of the group (D-I). The cutoff value (dashed red line) was set at the highest number of specific T cell spots for the negative controls (> 6 to 13 spots / 300 000 seeded cells depending of the T cell population). Mann-Whitney U test. **p ≤ 0.01, ***p ≤ 0.001, and ****p ≤ 0.0001. The cutoff-value is not visible because it is very close to the X-axis.

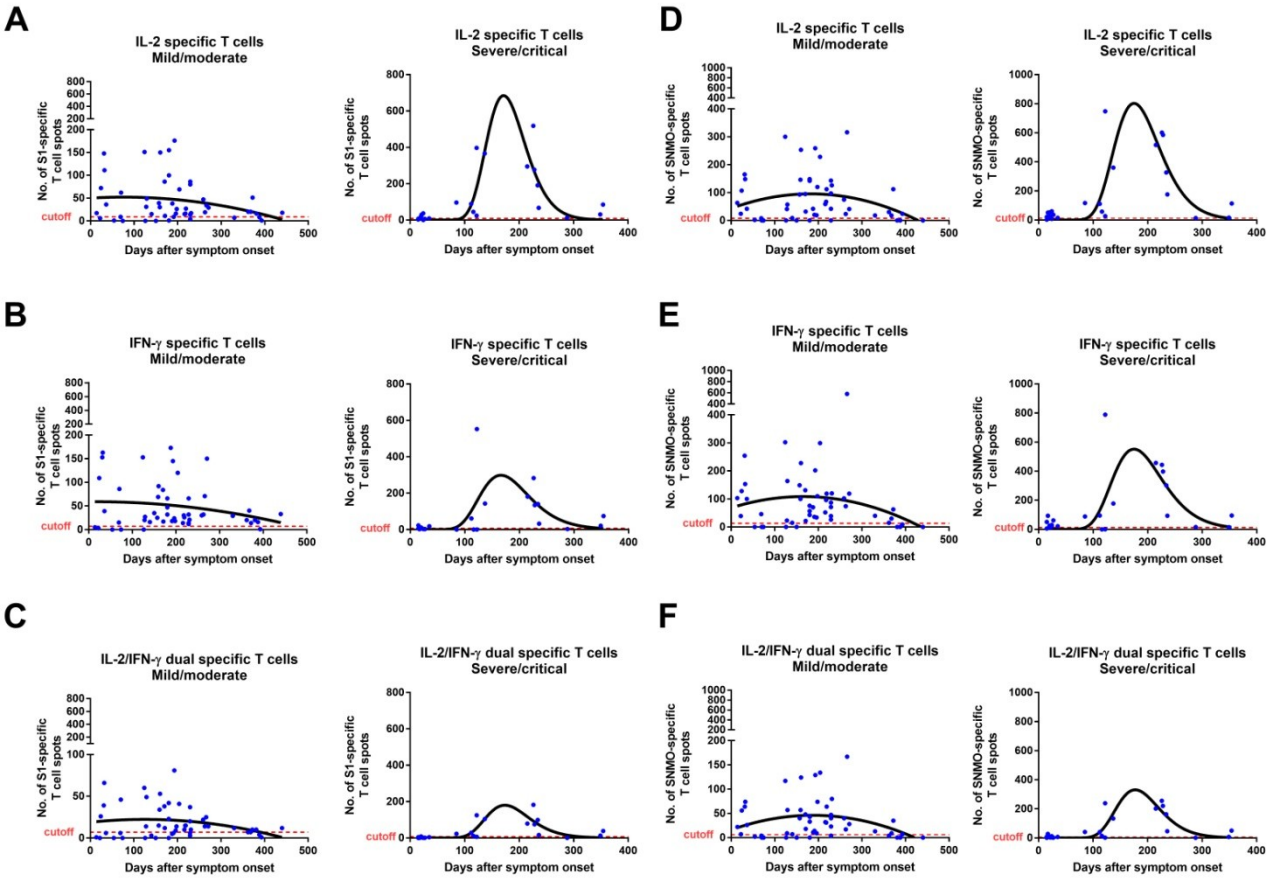

Figure S5. Cross-sectional analysis of SARS-CoV-2-specific memory T cell responses in COVID-19 patients in relation to disease severity. Related to Figures 6 and S4. Dynamics of S1 (A-C) and S N M O (D-F) peptide pools-specific memory IL-2, IFN-γ, and IL-2/IFN-γ-producing T cells in samples from COVID-19 patients with mild/moderate (A) and severe/critical (B) symptoms with the corresponding second order polynomial (mild/moderate) or log-normal (severe/critical) fitting curve (in black). The results were expressed as the number of spots per 300,000 seeded cells after subtracting the background spots of the negative control. Symbols represent individual subjects. The cutoff value (dashed red line) was set at the highest number of specific T cell spots for the negative controls (> 6 to 13 spots / 300 000 seeded cells depending on the T cell population). Mann-Whitney U test. The cutoff-value is not visible because it is very close to the X-axis.

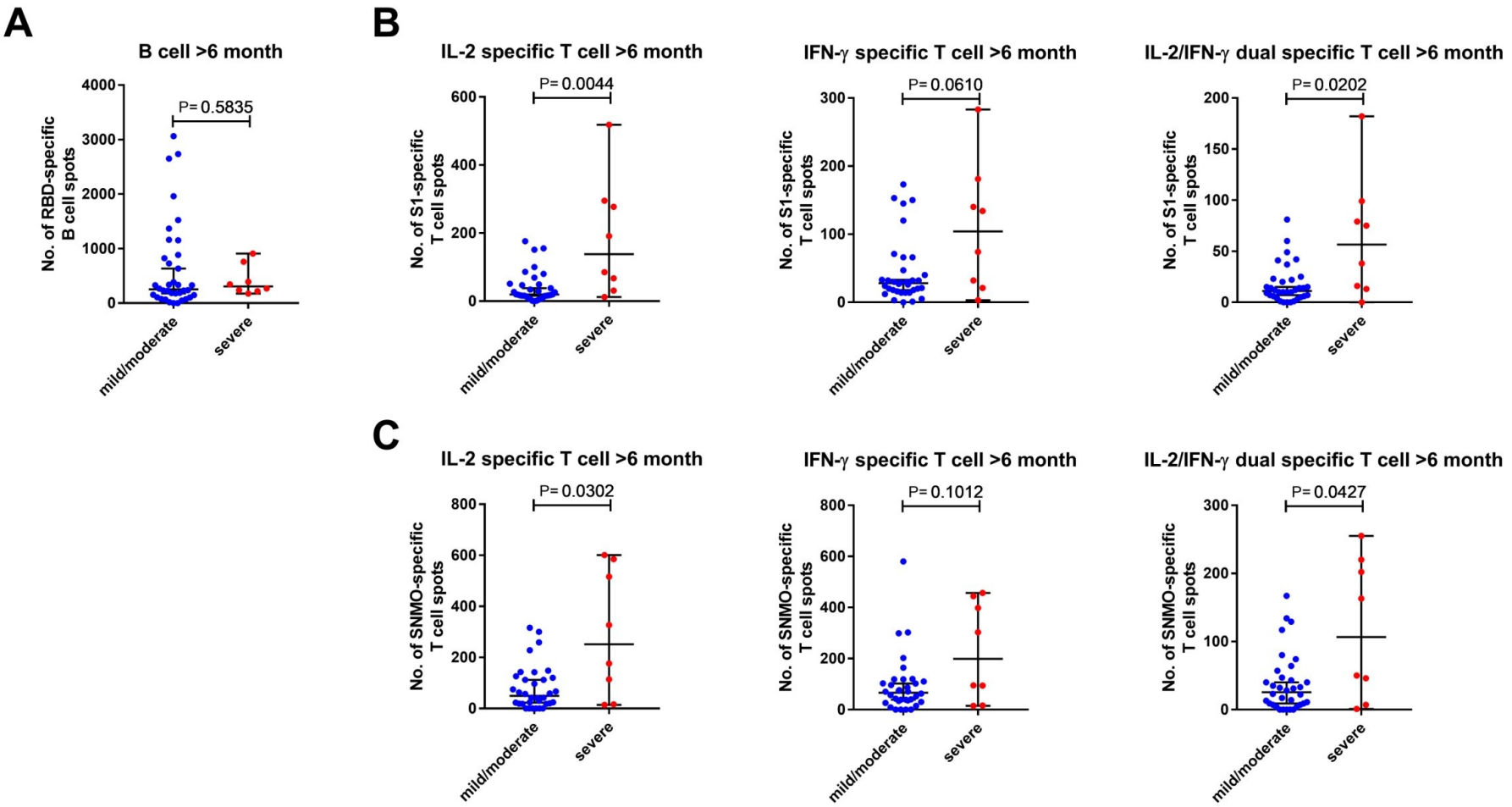

Figure S6. Comparison of SARS-CoV-2-specific memory B and T cells in COVID-19 patients according to longevity and severity. Related to Figures 5, 6, and S4. Number of B cells (A), and S1 (B) and S N M O (C) peptide pools - specific T cells in mild/moderate and severe/critical COVID-19 patients between 6 and 15 months after symptoms onset. Symbols represent individual subjects. The horizontal black lines indicate the median value and 95% CI of the group. Mann-Whitney U test.

Table S2. Summary of demographic and clinical characteristics in convalescent patients. Related to Figure 1.

	Italian cohort	Swedish cohort
No.	98	38
Age (Median, range), year	66 (22-89)	44 (18-75)
Male, %	58 (59.2%)	16 (42.1%)
Female, %	40 (40.8%)	22 (57.9%)
Disease severity, %		
Mild	8 (8.2%)	38 (100%)
Moderate	17 (17.3%)	0
Severe	67 (68.4%)	0
Critical	6 (6.1%)	0

Table S3. Patient characteristics for each time interval used in the cross-sectional analysis. Related to Figures 2, and 4-6.

		Number of patients per category			
	Total	Gender		Severity	
Time interval (Days)		Male	Female	Mild/moderate	Severe/critical
7-14	19	10	9	7	12
15-28	52	31	21	9	43
29-90	35	17	18	16	19
91-180	35	19	16	20	15
181-365	33	18	15	25	8
366-452	11	5	6	10	1

Table S4. Characteristics of the cohort of vaccinated recipients sampled after the first and second dose. Related to Figure 1.

	1 dose	2 doses
No. of samples	15[a]	15 [a]
Age (Median, range)	38 (23-62)	41 (25-64)
Male, %	9 (47%)	8 (40%)
Female, %	10 (53%)	12 (60%)

[a]Seven individuals were sampled after the first and second dose and 16 were sampled either after the first (n=8) or second (n=8) dose for a total of 15 samples after each dose.