**Supplemental Material**

Table S1. Descriptive detail data of reactive interpretation of T-SPOT.*COVID*

Table S2. Missing data of reactive interpretation of T-SPOT.*COVID*

Table S3. Details of the information and results of the previously infected participants

Table S4. Descriptive data of reactive interpretation of T-SPOT.*COVID*

Figure S1. Difference in anti-SARS-COV-2 IgG titer between non-reactive & borderline and reactive group

of T-SPOT.*COVID*

**Table S1. Descriptive detail data of reactive interpretation of T-SPOT.*COVID.***

| Variables | N=1089 | Reactive Interpretation | | |
| --- | --- | --- | --- | --- |
| | | Non-Reactive (n =250) | Reactive (n =700) | Borderline (n =139) |
| **Comorbidities** | | | | |
| At least one | 616 (56.4) | 182 (72.8) | 355 (50.7) | 79 (56.8) |
| DETAILS | | | | |
| Hypertension | 295 (27.0) | 102 (41.0) | 152 (21.8) | 41 (29.5) |
| Dyslipidemia | 95 (8.7) | 22 (8.8) | 59 (8.5) | 14 (10.1) |
| Heart disease | 96 (8.8) | 35 (14.1) | 46 (6.6) | 15 (10.8) |
| Diabetes | 88 (8.1) | 36 (14.5) | 42 (6.0) | 10 (7.2) |
| Allergic disease | 54 (4.9) | 9 (3.6) | 39 (5.6) | 6 (4.3) |
| Asthma | 43 (3.9) | 10 (4.0) | 28 (4.0) | 5 (3.6) |
| Liver disease | 69 (6.3) | 22 (8.8) | 38 (5.4) | 9 (6.5) |
| Cancer | 42 (3.8) | 17 (6.8) | 19 (2.7) | 6 (4.3) |
| Gout | 23 (2.1) | 9 (3.6) | 10 (1.4) | 4 (2.9) |
| Thyroid disease | 30 (2.7) | 5 (2.0) | 22 (3.2) | 3 (2.2) |
| Lung disease | 23 (2.1) | 10 (4.0) | 11 (1.6) | 2 (1.4) |
| Mental disease | 20 (1.8) | 11 (4.4) | 6 (0.9) | 3 (2.2) |
| Rheumatism | 21 (1.9) | 11 (4.4) | 7 (1.0) | 3 (2.2) |
| Kidney disease | 8 (0.7) | 2 (0.8) | 4 (0.6) | 2 (1.4) |
| Anaphylaxis | 8 (0.7) | 3 (1.2) | 4 (0.6) | 1 (0.7) |
| Collagen disease | 8 (0.7) | 3 (1.2) | 3 (0.4) | 2 (1.4) |
| Immune deficiency | 4 (0.4) | 1 (0.4) | 2 (0.3) | 1 (0.7) |
| Others | 197 (18.0) | 68 (27.4) | 109 (15.6) | 20 (14.4) |
| **Drug** | | | | |
| At least one | 180 (16.5) | 62 (24.8) | 87 (12.4) | 31 (22.3) |
| DETAILS | | | | |
| Steroid | 32 (2.9) | 15 (6.1) | 14 (2.1) | 3 (2.2) |
| NSAIDs | 83 (7.6) | 27 (11.0) | 43 (6.3) | 13 (9.6) |
| Acetaminophen | 34 (3.1) | 9 (3.7) | 18 (2.6) | 7 (5.1) |
| Antihistamine | 50 (4.6) | 16 (6.5) | 27 (3.9) | 7 (5.1) |
| Biologics | 14 (1.3) | 5 (2.0) | 8 (1.2) | 1 (0.7) |
| Anticancer agent | 5 (0.5) | 0 (0) | 4 (0.6) | 1 (0.7) |
| Immunosuppressants | 4 (0.4) | 2 (0.8) | 2 (0.3) | 0 (0) |
| **Adverse reaction after 2nd dose** | | | | |
| At least once | 825 (75.5) | 137 (54.8) | 587 (84.0) | 101 (73.2) |
| DETAILS | | | | |
| Local Pain | 563 (51.6) | 88 (35.3) | 405 (58.0) | 70 (50.7) |
| Fever over 37.5 degree | 154 (14.1) | 18 (7.2) | 123 (17.6) | 13 (9.4) |
| Fever under 37.5 degree | 265 (24.3) | 18 (7.2) | 217 (31.1) | 30 (21.6) |
| Fatigue | 514 (47.1) | 59 (23.7) | 396 (56.7) | 59 (42.4) |
| Joint pain | 273 (25.0) | 24 (9.6) | 222 (31.8) | 27 (19.4) |
| Headache | 317 (29.0) | 43 (17.3) | 240 (34.4) | 34 (24.5) |
| Dizziness | 52 (4.8) | 6 (2.4) | 45 (6.4) | 1 (0.7) |
| Nausea | 46 (4.2) | 3 (1.2) | 38 (5.4) | 5 (3.6) |
| Diarrhea | 27 (2.5) | 1 (0.4) | 24 (3.4) | 2 (1.4) |
| Others | 55 (5.0) | 10 (4.0) | 36 (5.2) | 9 (6.5) |
| **Adverse reaction after 3rd dose** | | | | |

| | | | | |
|---|---|---|---|---|
| At least once | 876 (80.2) | 153 (62.2) | 612 (88.3) | 111 (81.0) |
| DETAIL | | | | |
| Local Pain | 663 (60.7) | 115 (46.0) | 454 (65.2) | 94 (67.6) |
| Fever over 37.5 degree | 135 (12.4) | 16 (6.4) | 97 (13.9) | 22 (15.8) |
| Fever under 37.5 degree | 285 (26.1) | 16 (6.4) | 253 (36.4) | 16 (11.5) |
| Fatigue | 474 (43.4) | 43 (17.2) | 377 (54.2) | 54 (38.8) |
| Joint pain | 323 (29.6) | 37 (14.8) | 251 (36.1) | 35 (25.2) |
| Headache | 294 (26.9) | 29 (11.6) | 239 (34.3) | 26 (18.7) |
| Dizziness | 51 (4.7) | 7 (2.8) | 40 (5.7) | 4 (2.9) |
| Nausea | 46 (4.2) | 4 (1.6) | 36 (5.2) | 6 (4.3) |
| Diarrhea | 31 (2.8) | 4 (1.6) | 25 (3.6) | 2 (1.4) |
| Others | 69 (6.3) | 5 (2.0) | 57 (8.2) | 7 (5.0) |

Number (percentage) are shown for continuous or categorical variables. Abbreviations; NSAIDs: Non-

Steroidal Anti-Inflammatory Drugs.

**Table S2. Missing data of reactive interpretation of T-SPOT.*COVID***

| Variables | Reactive Interpretation | | |
|---|---|---|---|
| | Non-Reactive (n =250) | Reactive (n =700) | Borderline (n =139) |
| Age | 0 (0) | 0 (0) | 0 (0) |
| Sex | 0 (0) | 0 (0) | 0 (0) |
| Blood type | 33 (13.2) | 27 (3.9) | 3 (2.2) |
| Days between booster vaccination and blood collection | 0 (0) | 0 (0) | 0 (0) |
| Vaccine type | 0 (0) | 0 (0) | 0 (0) |
| Previous infection | 0 (0) | 0 (0) | 0 (0) |
| IgG (S) | 0 (0) | 0 (0) | 0 (0) |
| Smoking | 8 (3.2) | 13 (1.9) | 4 (2.9) |
| Drinking Habits | 11 (4.4) | 20 (2.9) | 8 (5.8) |
| Comorbidities | 0 (0) | 0 (0) | 0 (0) |
| Drug | 0 (0) | 0 (0) | 0 (0) |
| Adverse reaction after 2nd and 3rd dose vaccination | 4 (1.6) | 8 (1.1) | 3 (2.2) |
| Adverse reaction after 2nd dose vaccination | 0 (0) | 1 (0.1) | 1 (0.7) |
| Adverse reaction after 3rd dose vaccination | 4 (1.6) | 7 (1.0) | 2 (1.4) |

Number (percentage) are shown for continuous or categorical variables.

**Table S3. Details of the information and results of the previously infected participants**

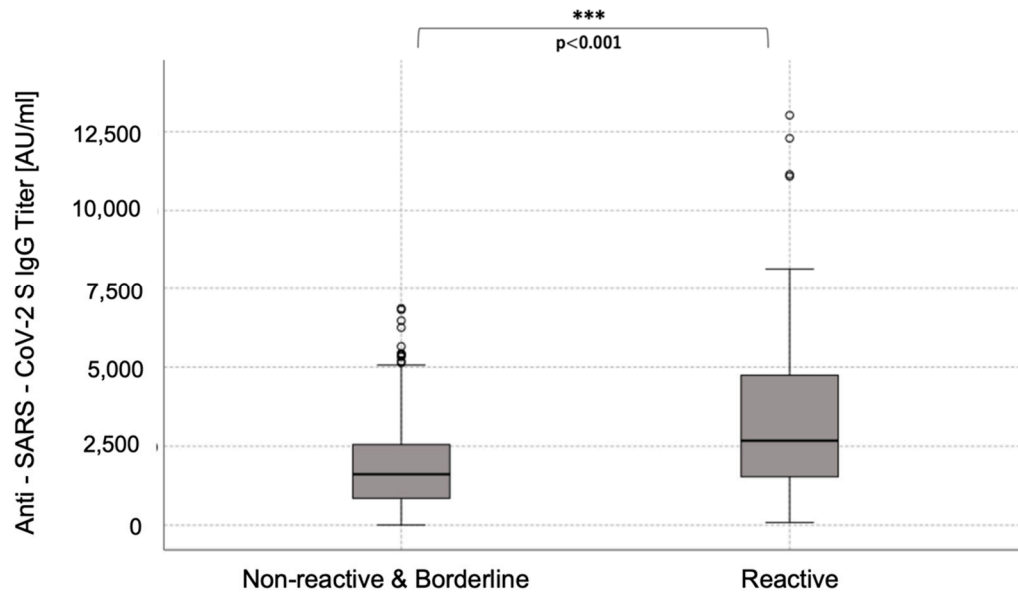| # | sex | age | comorbidity | AR after 2nd / 3rd dose | Days between booster vaccination and blood collection | T-SPOT.*COVID* | Nab (AU/ml) | IgG (S) (AU/ml) |
|---|-----|-----|-------------|------------------------|-------------------------------------------------------|----------------|-------------|-----------------|
| 1 | Female | 21 | - | +/+ | 57 | 3 | >500 | 9886 |
| 2 | Female | 68 | HTN, HD, CD | +/+ | 60 | 5 | >500 | 5372 |
| 3 | Female | 42 | DM | +/+ | 26 | 9 | >500 | 8657 |
| 4 | Female | 51 | - | +/+ | 58 | 28 | >500 | 5389 |
| 5 | Female | 39 | - | +/+ | 58 | 50 | >500 | 8853 |

Median [Inter Quartile] or number (percentage) are shown for continuous or categorical variables. AR adverse reaction, HTN hypertension, HD heart disease CD collagen disease, DM diabetes mellitus. Of note, we observed one participant with a nonreactive T-SPOT.COVID result, one with a borderline result, and three with reactive results. These findings align with the cohort without a history of COVID-19 infection (n =1,084), in which 249 (22.9%) individuals had nonreactive results, 138 (12.7%) had borderline results, and 697 (64.3%) had reactive results. In humoral immune response, all individuals with a history of COVID-19 infection showed strong reactivity of neutralizing antibody titer > 500 AU/ml and anti-SARS-CoV-2 IgG >5,000 AU/mL.

**Table S4. Descriptive data of reactive interpretation of T-SPOT.*COVID***

| Variables | | N=1089 | Reactive Interpretation | | |
|---|---|---|---|---|---|
| | | | Non-Reactive (n =250) | Reactive (n =700) | Borderline (n =139) |
| Age | | 56 [42–68] | | | |
| | <40 years | 215 (19.7) | 19 (7.6) | 177 (25.3) | 19 (13.7) |
| | 40–65 years | 543 (49.7) | 93 (37.2) | 388 (55.4) | 62 (44.6) |
| | >65 years | 331 (30.3) | 138 (55.2) | 135 (19.3) | 58 (41.7) |
| Sex - Female | | 737 (67.5) | 151 (60.4) | 487 (69.6) | 99 (71.2) |
| Blood type | | | | | |
| | A | 392 (35.9) | 87 (40.1) | 257 (38.2) | 48 (35.3) |
| | B | 223 (20.4) | 49 (22.6) | 139 (20.7) | 35 (25.7) |
| | O | 316 (28.9) | 66 (30.4) | 211 (31.4) | 39 (28.7) |
| | AB | 95 (8.7) | 15 (6.9) | 66 (9.8) | 14 (10.3) |
| Days from booster vaccination | | 53 [29–65] | 54 [30–65] | 52 [29–65] | 54 [29–64] |
| | <30 days | 332 (30.4) | 77 (30.8) | 212 (30.3) | 43 (30.9) |
| | 30–60 days | 367 (33.6) | 83 (33.2) | 237 (33.9) | 47 (33.8) |
| | >60 days | 390 (35.7) | 90 (36.0) | 251 (35.9) | 49 (35.3) |
| Vaccine type | | | | | |
| | BNT162b2 (Pfizer–BioNTech) | 682 (62.5) | 131 (52.4) | 459 (65.6) | 92 (66.2) |
| | mRNA-1273 (Moderna) | 407 (37.3) | 119 (47.6) | 241 (34.4) | 47 (33.8) |
| Previous infection- IgN≧10.0 | | 11 (1.0) | 1 (0.0) | 9 (0.8) | 1 (0.0) |
| anti-SARS-COV-2 IgG titter (AU/ml) | | 2221 [1376–3966] | 1593 [977.5–2603] | 2674 [1608–4418] | 1853 [1202–3606] |
| Smoking | | 194 (17.8) | 38 (15.7) | 132 (19.2) | 24 (17.8) |
| Drinking Habits | | 406 (37.2) | 83 (34.7) | 276 (40.6) | 47 (35.9) |
| Comorbidities - At least one | | 616 (56.4) | 182 (72.8) | 355 (50.7) | 79 (56.8) |
| Drug - At least one | | 180 (16.5) | 62 (24.8) | 87 (12.4) | 31 (22.3) |
| Adverse reaction after 2nd and 3rd dose vaccination | | | | | |
| | At least once | 930 (85.2) | 175 (71.1) | 636 (91.9) | 119 (87.5) |
| Adverse reaction after 2nd dose vaccination | | | | | |
| | At least once | 825 (75.5) | 137 (54.8) | 587 (84.0) | 101 (73.2) |
| Adverse reaction after 3rd dose vaccination | | | | | |
| | At least once | 876 (80.2) | 153 (62.2) | 612 (88.3) | 111 (81.0) |

Median [Inter Quartile] or number (percentage) are shown for continuous or categorical variables. Of note, a significant difference in age groups was observed between those receiving BNT162b2 and mRNA-1273 vaccines for booster administration. (p with Pearson's chi-square test <0.001; the numbers (percentages) in <40 years, 40–65 years, and >65 years old were 150 (22.0), 391 (57.3), and 141 (20.7) in BNT162b2, and 65 (16.0), 152 (37.3), 190 (46.7) in mRNA-1273 group, respectively.

**Figure S1. Difference in anti-SARS-COV-2 IgG titer between non-reactive & borderline and reactive group of T-SPOT.*COVID***



Box-and-whisker plots show the difference in anti-SARS-COV-2 IgG titer between non-reactive & borderline and reactive group of T-SPOT.*COVID*. In each box-and-whisker plot, the horizontal line represents the median, the top and bottom of the boxes the interquartile range, and the I bar the minimum and maximum values. Spots≧50 is scored as 50. Spots ≦4, 5–7, and ≧8 were considered as non-reactive, borderline and reactive respectively.