### Supplementary Material

### Table S1. Severity grading scale for local reactions and systemic events.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Mild** | **Moderate** | **Severe** |
| Local reaction |  |  |  |
| Pain | Does not interfere with activity | Interferes with activity | Prevents daily activity |
| Redness | >2.0–5.0 cm | >5.0–10.0 cm | >10 cm |
| Swelling | >2.0–5.0 cm | >5.0–10.0 cm | >10 cm |
| Systemic event |  |  |  |
| Vomiting | 1–2 × in 24 h | >2 × in 24 h | Requires IV hydration |
| Diarrhea | 2–3 loose stools in 24 h | 4–5 loose stools in 24 h | ≥6 loose stools in 24 h |
| Headache | Does not interfere with activity | Some interference with activity | Prevents daily routine activity |
| Fatigue | Does not interfere with activity | Some interference with activity | Prevents daily routine activity |
| Chills | Does not interfere with activity | Some interference with activity | Prevents daily routine activity |
| Muscle pain | Does not interfere with activity | Some interference with activity | Prevents daily routine activity |
| Joint pain | Does not interfere with activity | Some interference with activity | Prevents daily routine activity |

IV=intravenous.

For the fever scale, refer to the key of **Figure 3**.

### Table S2. Participant demographics of the variant neutralization subset

|  |  |  |
| --- | --- | --- |
|  | **Current study:** **XBB.1.5-adapted BNT162b2 30 μg**  | **Comparator group:** **BA.4/BA.5-adapted BNT162b2 30 μg** |
|  | **18–55 years old****(Na=20)** | **>55 years old****(Na=20)** | **Total(Na=40)** | **18–55 years old****(Na=20)** | **>55 years old****(Na=20)** | **Total(Na=40)** |
| Sex, nb (%) |  |  |  |  |  |  |
|  Male | 12 (60.0)  | 7 (35.0)  | 19 (47.5)  | 12 (60.0)  | 7 (35.0)  | 19 (47.5)  |
|  Female | 8 (40.0)  | 13 (65.0)  | 21 (52.5)  | 8 (40.0)  | 13 (65.0)  | 21 (52.5)  |
| Race, nb (%) |  |  |  |  |  |  |
|  White | 18 (90.0)  | 16 (80.0)  | 34 (85.0)  | 17 (85.0)  | 16 (80.0)  | 33 (82.5)  |
|  Black or African American | 2 (10.0)  | 2 (10.0)  | 4 (10.0)  | 1 (5.0)  | 3 (15.0)  | 4 (10.0)  |
|  Other | 0 | 2 (10.0)  | 2 (5.0)  | 1 (5.0) | 1 (5.0)  | 2 (5.0)  |
| Ethnicity, nb (%) |  |  |  |  |  |  |
|  Hispanic/Latino  | 9 (45.0)  | 4 (20.0)  | 13 (32.5)  | 3 (15.0)  | 4 (20.0)  | 7 (17.5)  |
| Age at vaccination (years)  |  |  |  |  |  |  |
|  Mean (SD)  | 38.0 (10.04)  | 70.1 (6.51)  | 54.0 (18.30)  | 37.9 (9.97)  | 69.7 (5.95)  | 53.8 (18.00)  |
|  Median (range) | 35.5 (25–55) | 69.5 (56–82) | 55.5 (25–82) | 36.0 (25–54) | 69.5 (56–81) | 55.0 (25–81) |
| Baseline SARS-CoV-2 status, nb (%) |  |  |  |  |  |  |
|  Positivec | 20 (100.0)  | 20 (100.0)  | 40 (100.0)  | 20 (100.0)  | 20 (100.0)  | 40 (100.0)  |
| Time from last dose of mRNA COVID-19 vaccined to the study vaccination (monthse) |  |  |  |  |  |  |
|  Mean (SD)  | 8.8 (1.98)  | 9.6 (2.04)  | 9.2 (2.03)  | 11.0 (1.41)  | 11.4 (1.16)  | 11.2 (1.29)  |
|  Median (range) | 8.3 (5.8–12.0) | 10.2 (5.8–11.9) | 9.5 (5.8–12.0) | 11.3 (7.4–12.8) | 11.9 (8.5–12.6) | 11.4 (7.4–12.8) |
|  ≥5 to <7 months, nb (%) | 4 (20.0)  | 4 (20.0)  | 8 (20.0)  | 0 | 0 | 0 |
|  ≥7 to <9 months, nb (%)  | 7 (35.0)  | 2 (10.0)  | 9 (22.5)  | 3 (15.0)  | 1 (5.0)  | 4 (10.0)  |
|  ≥9 to ≤12 months, nb (%)  | 9 (45.0)  | 14 (70.0)  | 23 (57.5)  | 13 (65.0)  | 10 (50.0)  | 23 (57.5)  |
|  >12 months, nb (%) | 0  | 0  | 0  | 4 (20.0)  | 9 (45.0)  | 13 (32.5)  |
| Time from last dose of mRNA COVID-19 vaccine to study vaccination (days)  |  |  |  |  |  |  |
|  Mean (SD)  | 245.7 (55.35)  | 269.5 (57.01)  | 257.6 (56.75)  | 306.7 (39.39)  | 318.8 (32.39)  | 312.7 (36.12)  |
|  Median (range) | 233.5 (162–336) | 285.0 (162–333) | 265.5 (162–336) | 317.0 (207–359) | 334.5 (239–354) | 320.5 (207–359) |
| BMI, nb (%) |  |  |  |  |  |  |
|  Underweight (<18.5 kg/m2)  | 0  | 1 (5.0)  | 1 (2.5)  | 0 | 0 | 0 |
|  Normal weight (≥18.5–24.9 kg/m2)  | 6 (30.0) | 6 (30.0) | 12 (30.0)  | 5 (25.0) | 3 (15.0) | 8 (20.0) |
|  Overweight (≥25.0–29.9 kg/m2)  | 9 (45.0)  | 7 (35.0)  | 16 (40.0)  | 8 (40.0)  | 12 (60.0)  | 20 (50.0)  |
|  Obese (≥30.0 kg/m2) | 5 (25.0)  | 6 (30.0)  | 11 (27.5)  | 7 (35.0)  | 5 (25.0)  | 12 (30.0)  |

Data are for the all-available immunogenicity population. Data for BA.4/BA.5-adapted BNT162b2 are in a comparator group of participants from another study (NCT05472038) who were matched by age, and baseline SARS-CoV-2 status.

BMI=body mass index; NAAT=nucleic acid amplification test; N-binding=SARS-CoV-2 nucleoprotein–binding; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SD=standard deviation.

aN was the number of participants in the specified group, or the total sample; this value was the denominator for the percentage calculations.

bn was the number of participants with the specified characteristic.

cPositive N-binding antibody result at baseline, positive NAAT result at baseline, or medical history of COVID-19.

d The inclusion criteria required the participant to have received: ≥3 prior doses of a US-authorized mRNA COVID-19 vaccine with the most recent dose being a US-authorized Omicron BA.4/BA.5–adapted vaccine ≥150 days before study vaccination (current study); 3 or 4 prior doses of 30 μg BNT162b2 with the last dose being 150–365 days before study vaccination (comparator group).

eMonth was calculated as 28 days.

**Figure S1.** Serum neutralizingGMTs (95% CIs) before and 7 days after vaccination with XBB.1.5-adapted BNT162b2 30 μg or BA.4/BA.5-adapted BNT162b2 30 μg and GMFRs (95% CIs) from before to 1 week after vaccination to Omicron XBB.1.5 (**a**), EG.5.1 (**b**), and BA.2.86 (**c**). Data for BA.4/BA.5-adapted BNT162b2 are in participants from another study (NCT05472038) who were matched by age, sex, and baseline SARS-CoV-2 status. Data are for the all-available immunogenicity population. Assay results <LLOQ were set to 0.5 × LLOQ. Numbers within the bars are the GMTs. 7d=7 days after vaccination; FFRNT=fluorescent focus reduction neutralization test; GMFR=geometric mean fold rise; GMT=geometric mean titer; LLOQ=lower limit of quantitation; Pre=before vaccination.



**Figure S2.** Percentage of participants achieving seroresponse (95% CIs) 1 week after vaccination with XBB.1.5-adapted BNT162b2 30 μg or BA.4/BA.5-adapted BNT162b2 30 μg to Omicron XBB.1.5 (**a**), EG.5.1 (**b**), and BA.2.86 (**c**). Data for BA.4/BA.5-adapted BNT162b2 are in participants from another study (NCT05472038) who were matched by age, sex, and baseline SARS-CoV-2 status. Data are for the all-available immunogenicity population. Seroresponse was defined as achieving a ≥4-fold rise from before study vaccination in FFRNT 50% serum neutralizing titers. If the baseline measurement was <LLOQ, a postvaccination assay result ≥4 × LLOQ was considered a seroresponse. Numbers above the bars are percentages rounded to the nearest full number. FFRNT=fluorescent focus reduction neutralization test; LLOQ=lower limit of quantitation.

