



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Amsterdam, 29 January 2026
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Committee for Medicinal Products for Human Use (CHMP)

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006, as amended

COMIRNATY

International non-proprietary name: COVID-19 mRNA vaccine

Procedure no.: EMA/PAM/0000309529

Marketing authorisation holder (MAH): BioNTech Manufacturing GmbH

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment

Current step	Description	Planned date	Actual Date
<input type="checkbox"/>	Start of Procedure	1 December 2025	1 December 2025
<input type="checkbox"/>	CHMP Rapporteur AR	5 January 2026	23 December 2025
<input type="checkbox"/>	CHMP comments	19 January 2026	19 January 2026
<input type="checkbox"/>	Updated CHMP Rapporteur AR	22 January 2026	n/a
<input checked="" type="checkbox"/>	CHMP outcome	29 January 2026	29 January 2026

List of Abbreviations

Abbreviation	Term
ARI	acute respiratory illness
CHMP	Committee for Medicinal Products for Human Use
COVID-19	coronavirus disease 2019
ED	Emergency department
EHR	Electronic health record
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
KP.2	Omicron KP.2
KPSC	Kaiser Permanente Southern California
MHRA	Medicines and Healthcare products Regulatory Agency
PAC	Post Authorization Commitments
PCR	polymerase chain reaction
SARS-CoV-2	severe acute respiratory syndrome coronavirus - 2
SD	standard deviation
TND	test-negative design
UC	urgent care
US	United States
VE	vaccine effectiveness
WHO	World Health Organization
WT	Wild type
XBB.1.5	Omicron XBB.1.5

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1. Introduction

On 30 October 2025, the MAH submitted a completed paediatric study for COMIRNATY, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that "A non-interventional study (test-negative design) of individuals presenting with symptoms of potential COVID-19 illness in a real-world setting to determine the effectiveness of COVID-19 mRNA variant-adapted vaccines when administered outside of the clinical setting, to estimate the effectiveness of COVID-19 mRNA vaccine against hospitalisation and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection and to assess the effectiveness of COVID-19 mRNA variant-adapted vaccines following their introduction in all authorized age groups (Study nr. C4591014)" is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

BNT162b2 (Comirnaty) is a modified RNA vaccine that encodes the full-length, membrane-anchored S glycoprotein of SARS-CoV-2 with two introduced proline mutations to lock it in the prefusion conformation. Commercially available are Comirnaty Omi XBB. 1.5 and Omi KP.2 in strength 30 µg (for 12 years and older), 10 µg (5-11 years), 3 µg (6 months- 4 years).

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted final reports for "A non-interventional study (test-negative design) of individuals presenting with symptoms of potential COVID-19 illness in a real-world setting to determine the effectiveness of COVID-19 mRNA variant-adapted vaccines when administered outside of the clinical setting, to estimate the effectiveness of COVID-19 mRNA vaccine against hospitalisation and emergency department admission for acute respiratory illness due to SARS-CoV-2 infection and to assess the effectiveness of COVID-19 mRNA variant-adapted vaccines following their introduction in all authorized age groups (Study nr. C4591014)" for two Comirnaty variant adapted vaccines:

- Omi XBB.1.5;
- Omi KP.2

The observational effectiveness study C4591014 evaluates Comirnaty variant vaccines in real world settings in the USA. Earlier, the MAH submitted the final report for BA.4-5 variant-adapted vaccine on 30 June 2023 which was evaluated via procedure EMEA/H/C/005735/P46/067 and approved by the CHMP on 14 September 2023. As the methodology for entire C4591014 is very similar, we only describe the methodology in current report very briefly and refer to the earlier report.

2.3.2. Clinical study

C4591014: Pfizer-BioNTech COVID-19 BNT162b2 (Omi XBB 1.5 and KP.2) Vaccine Effectiveness Study – Kaiser Permanente Southern California

Description

Study C4591014 was conducted in collaboration with Kaiser Permanente Southern California (KPSC) as a real-world evidence study to evaluate the effectiveness of BNT162b2 (Omi XBB.1.5 and Omi KP.2 formulations) against ARI requiring hospitalization due to severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2) infection. The study utilized a Test Negative Design (TND), analyzing existing healthcare data from a large, diverse population. Paediatric age groups included children 6 months to 17 years of age, with analyses stratified by age and vaccination status.

Evaluation of Pfizer-BioNTech's BNT162b2 effectiveness outside of the clinical trial setting was requested as PAC following introduction into the general population. As such, real-world evidence studies were proposed to evaluate Pfizer BioNTech's BNT162b2 effectiveness against ARI requiring hospitalization due to SARS-CoV-2 infection among large and diverse populations. Study C4591014, described in this Critical Expert Overview, was conducted in collaboration with KPSC. The submission of final results of study C4591014 is in fulfilment of Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation').

Methods

Study Periods and Populations included:

- 2023 – 2024 Formulation -XBB.1.5-adapted: 10 October 2023 – 31 July 2024
- 2024 – 2025 Formulation - KP.2-adapted: 17 September 2024 – 30 April 2025

Study participants

Eligible participants included children aged 6 months to 17 years who were KPSC members and had an ARI diagnosis with a SARS-CoV-2 PCR test during the study periods. The study included the following age groups:

2023 – 2024 Formulation (Omi XBB.1.5-adapted)

- Adolescents 12 to 17 years of age
- Children 5 to 11 years of age
- Children 6 months to 4 years of age

2024 – 2025 Formulation (Omi KP.2-adapted)

- Children and adolescents 5 to 17 years of age
- Children 6 months to 4 years of age

Treatments

In this non-interventional retrospective study, the study participants had received either zero, single or multiple doses of different commercially available Comirnaty original or variant vaccines.

Objectives and Outcomes and endpoints relevant to current P46

The primary objective was to estimate the VE of each BNT162b2 formulation against COVID-19-associated hospitalization, ED, and UC visits in paediatric populations.

Secondary objectives included effectiveness analyses stratified by vaccine type, time since vaccination, and prior infection status.

Objectives	Endpoints
To estimate the effectiveness of the BNT162b2 (Omi XBB.1.5 or Omi KP.2) booster against hospitalization for ARI due to SARS-CoV-2 infection.	VE calculated as 1 minus the odds ratio (OR) comparing the odds of being vaccinated with BNT162b2 (Omi XBB.1.5) booster for hospitalized cases and controls, multiplied by 100%.
To estimate the effectiveness of the BNT162b2 (Omi XBB.1.5 or Omi KP.2) booster against emergency room admissions/urgent care visits for ARI due to SARS-CoV-2 infection.	VE calculated as 1 minus the odds ratio (OR) comparing the odds of being vaccinated with BNT162b2 Omi (XBB.1.5) for emergency room admissions/urgent care visit cases and controls, multiplied by 100%.

Statistical Methods

This was a database only study of existing healthcare data, no individuals were actively enrolled.

Vaccine exposure was defined as the receipt of a BNT162b2 (Omi XBB.1.5 or KP.2) vaccine \geq 14 days prior to ARI diagnosis compared to not receiving a XBB or KP.2 vaccine of any kind (including unvaccinated persons) regardless of prior COVID-19 vaccination or SARS-CoV-2 infection history.

Additional analyses compared the odds of receipt of a BNT162b2 adapted vaccine vs the odds of (1) receipt of 1 or more doses of a another earlier adapted vaccine, (2) receipt of 3 or more or 2 or more doses of an original WT mRNA vaccine but no variant-adapted vaccines of any kind (eg, KP.2, XBB or BA.4/5 bivalent doses), and (3) being unvaccinated across cases and controls. Among those who did not receive an XBB vaccine of any kind, we also compared the odds of receiving 1 or more doses of a BA.4/5 bivalent vaccine or receiving 3 or more or 2 or more original WT COVID-19 vaccine doses without a bivalent vaccine of any kind with the odds of being unvaccinated across cases and controls. These comparisons were used to estimate remaining protection from prior non-XBB vaccines (ie, either BA.4/5 or WT doses) during the study period.

Test Negative Case-Control Design

A TND study design was used to evaluate the objectives in this study. It included all KPSC patients eligible for vaccination admitted to the hospital with ARI 10 October 2023 through 31 July 2024, and who received a PCR test for SARS-CoV-2. For objectives estimating VE against ED/UC admission, the TND included KPSC patients eligible for vaccination who presented to the ED or UC with ARI without a subsequent hospital admission and among in-person outpatient visits without a subsequent higher acuity visit (i.e., UC, ED or hospitalization)

The index date was defined as the date of hospitalization or ED/UC admission. Patients could contribute more than one ARI event to the study if a subsequent ARI event for the same patient occurred >30 days after the previous event.

Per KPSC clinical protocol, it was expected all patients with ARI diagnoses were tested for COVID-19. VE was estimated separately for prevention of hospitalization and for prevention of ED/UC presentation without hospitalization

For the main analysis, vaccine exposure was defined as receipt of Pfizer-BioNTech XBB.1.5-adapted monovalent vaccine with ≥ 14 days between receipt of vaccine and the event date (e.g., admission). The unexposed included individuals who have not received Pfizer- BioNTech XBB.1.5-adapted monovalent vaccine or any other manufacturer's XBB-adapted formulation.

Cases: Cases were defined as those with any SARS-COV-2 positive KPSC laboratory-confirmed PCR test from a sample collected within 14 days prior to the index event through 3 days after an index event with an ARI code.

Controls: Controls were defined as those with laboratory confirmed negative SARS-COV-2 (negative SARS-COV-2 test collected within 14 days prior to index event through 3 days after index event with an ARI code) and no positive SARS-CoV-2 tests within 14 days prior to encounter).

Exposure Definition: The exposure of interest was vaccination with BNT162b2 (Omi XBB.1.5 or KP.2). Individuals were considered vaccinated if they had documented evidence of receiving BNT162b2 (Omi XBB.1.5 or KP.2) ≥ 14 days before index date

Relative VE comparisons were made comparing BNT162b2 (Omi XBB.1.5 or KP.2) and previous vaccination schedules.

Results

Year 2023 – 2024 Formulation: BNT162b2 (Omi XBB.1.5)

Participant flow, baseline characteristics

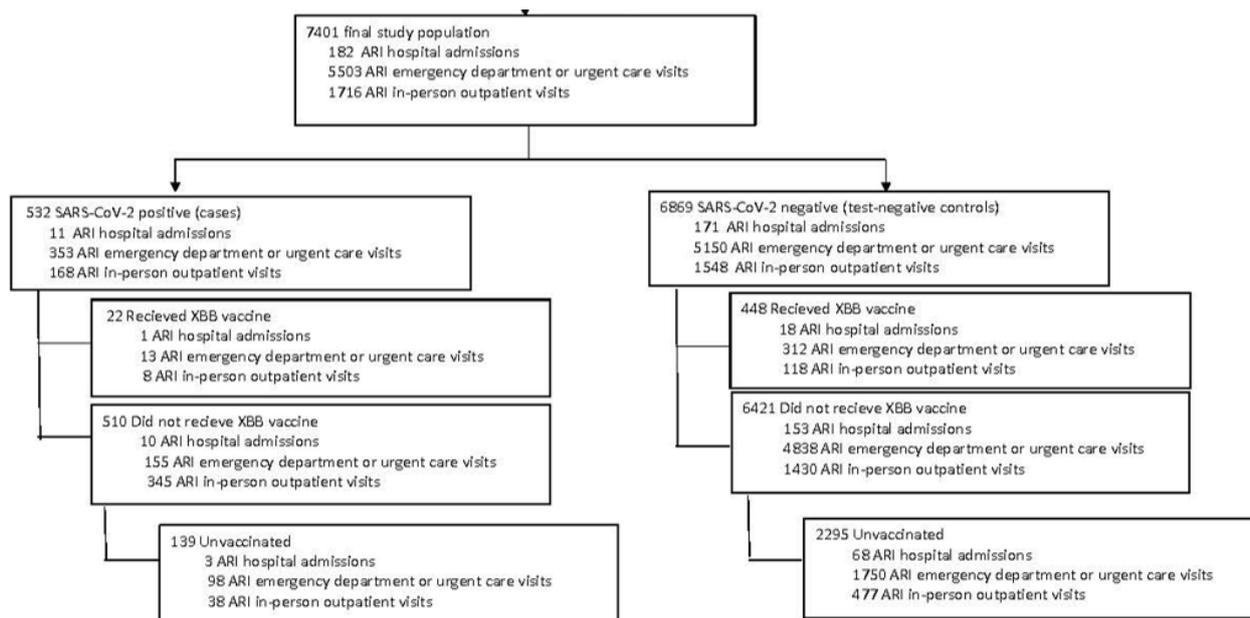
Adolescents 12 to 17 Years of Age

There were 7,401 KPSC individuals 12-17 years of age with ARI and SARS-CoV-2 PCR test included in the analysis. The mean age was 14.4 years (SD 1.69 years) and median was 14 years. More than half (55.3%) were Hispanic and 20.0% were White.

Most individuals received ≥ 2 original WT doses and no BA.4/BA.5 bivalent dose or XBB.1.5 (47.4%), followed by 32.9% unvaccinated, 11.4% received ≥ 1 BA.4/BA.5 bivalent doses and no XBB.1.5, 6.4% received ≥ 1 BNT162b2 (Omi XBB.1.5), and 2.0% received 1 original WT dose and no BA.4/BA.5 bivalent doses or XBB.1.5.

- Approximately 22 percent of individuals (21.5%) had a prior history of Omicron SARS-CoV-2 infection.
- 6.7% of individuals had prior pre-Delta SARS-CoV-2 infection.
- 3.6% of individuals had prior Delta SARS-CoV-2 infection.

Fig. Study C4591014 Enrollment Flow Chart – Participants aged 12 - 17 Years of Age - 10 October 2023 – 31 July 2024; Test Negative Design



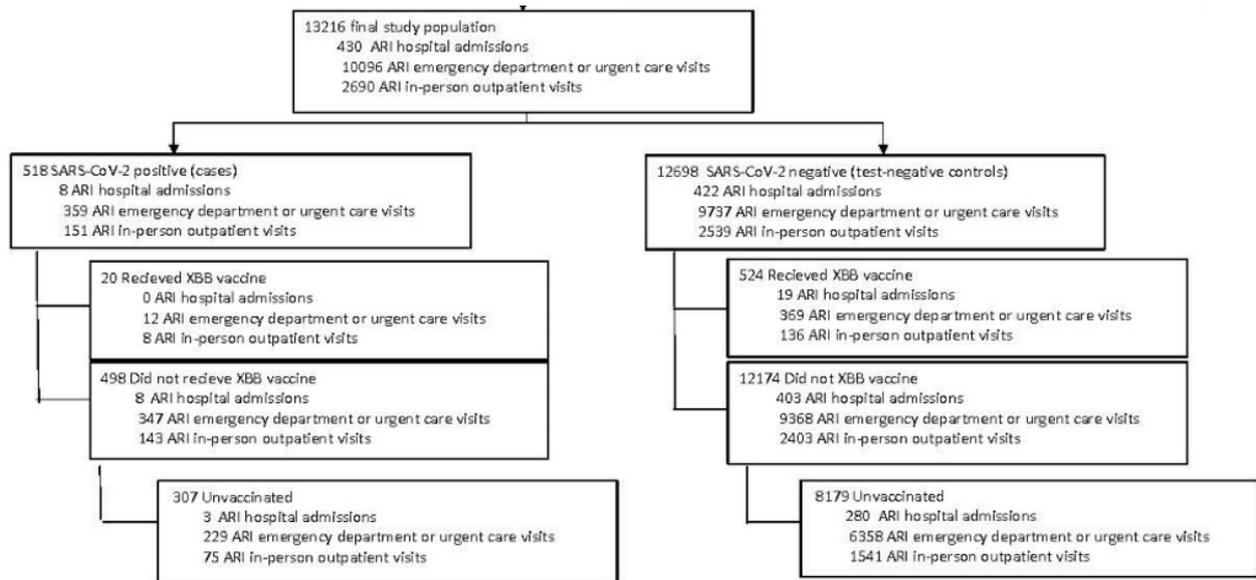
Children 5 - 11 Years of Age

There were 13216 KPSC individuals 5 – 11 years of age with ARI and a SARS-CoV-2 PCR test result included in the analysis. The mean age was 7.6 years (SD 2.0 years) and median was 7 years. More than half (57.8%) were Hispanic and 16.7% were White.

Most individuals were unvaccinated (64.2%), followed by vaccination with ≥ 2 original WT doses and no BA.4/BA.5 bivalent dose or XBB.1.5 (23.2%), 6.1% received ≥ 1 BA.4/BA.5 bivalent doses and no XBB.1.5, 4.1% received ≥ 1 Omi XBB.1.5, and 2.3% received 1 original WT dose and no BA.4/BA.5 bivalent doses or XBB.1.5.

- 20% of individuals had prior Omicron SARS-CoV-2 infection.
- 5.1% of individuals had prior pre-Delta SARS-CoV-2 infection.
- 2.6% of individuals had prior Delta SARS-CoV-2 infection.

Fig. Study C4591014 Enrollment Flow Chart – Participants aged 5 - 11 Years of Age - 10 October 2023 – 31 July 2024; Test Negative Design



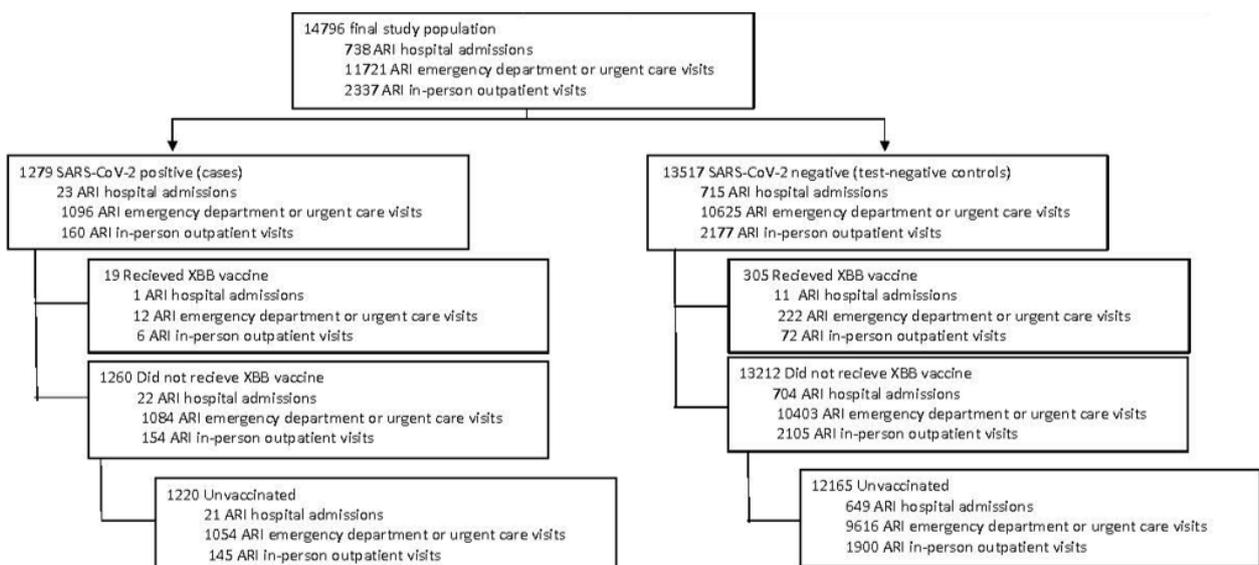
Children 6 Months to 4 Years of Age

There were 14,796 KPSC individuals 6 months to 4 years of age with ARI and SARS-CoV-2 PCR test included in the analysis. The mean age was 1.8 years (SD 1.40 years), and median was 2 years. More than half of individuals (56.5%) were Hispanic and 19.2% were White.

Most individuals were unvaccinated (90.5%), followed by 4.9% of individuals who received ≥ 2 original WT doses and no BA.4/BA.5 bivalent dose or XBB.1.5, 2.2% received ≥ 1 XBB.1.5, 1.3% received 1 original WT dose and no BA.4/BA.5 bivalent doses or XBB.1.5, and 1.2% received ≥ 1 BA.4/BA.5 bivalent doses and no XBB.1.5.

- Approximately 16% (15.5%) of individuals had prior Omicron SARS-CoV-2 infection.
- 1.8% of individuals had prior pre-Delta SARS-CoV-2 infection.
- 1.2% of individuals had prior Delta SARS-CoV-2 infection.

Fig. Study C4591014 Enrollment Flow Chart – Participants aged 6 months - 4 Years of Age - 10 October 2023 – 31 July 2024; Test Negative Design



Efficacy results

Adolescents 12 to 17 Years of Age

Among adolescents 12–17 years who received BNT162b2 (Omi XBB.1.5), adjusted VE for ED/UC visit was 62% (95% CI: 22–82) compared to no XBB.1.5-adapted vaccine.

- Effectiveness was generally similar within three months of vaccination, with adjusted VE for ED/UC visit at 67% (95% CI: 10–88), and for all encounter types at 49% (95% CI: 2–73).
- After more than three months, adjusted VE declined to 55% (95% CI: –26–84) for ED/UC visit and 16% (95% CI: –57–55) for all encounter types.

Children 5 to 11 Years of Age

Among children 5–11 years who received BNT162b2 (Omi XBB.1.5), the adjusted VE for emergency/urgent care was 19% (95% CI: –49–55) compared to no XBB.1.5-adapted vaccine.

- Effectiveness was higher within three months of vaccination, with adjusted VE for ED/UC visit at 41% (95% CI: –61–78), and for all encounter types at 35% (95% CI: –40–70).
- After more than three months, adjusted VE declined to –3% (95% CI: –120–52) for ED/UC visit and –7% (95% CI: –94–41) for all encounter types.

Children ≥6 Months to 4 Years of Age

Among children 6 months through 4 years who received BNT162b2 (Omi XBB.1.5), the adjusted VE for ED/UC visit was 16% (95% CI: –56–55) compared to no XBB.1.5-adapted vaccine.

- Effectiveness was higher within three months of vaccination, with adjusted VE for ED/UC visit at 20% (95% CI: –77–64), and for all encounter types at –2% (95% CI: –89–45).
- After more than three months, adjusted VE declined to 9% (95% CI: –138–66) for ED/UC visit and –2% (95% CI: –130–55) for all encounter types.

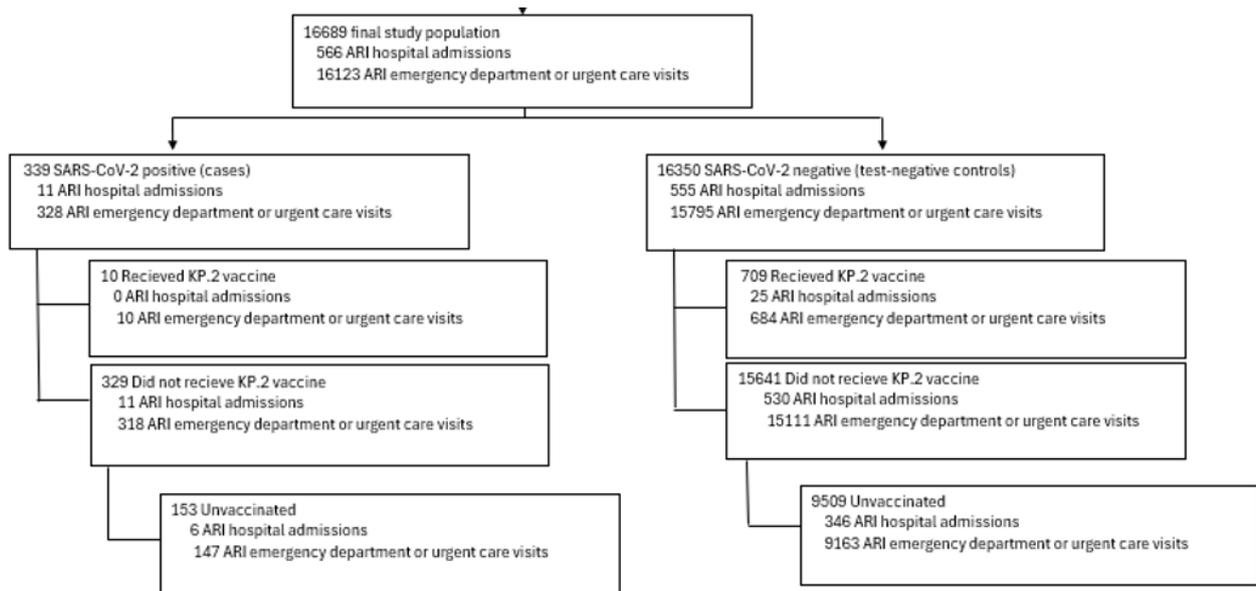
Year 2024 – 2025 Formulation: BNT162b2 (Omi KP.2)

Participant flow, baseline characteristics

Children 5 to 17 Years of Age

Between 17 September 2024 and 30 April 2025, there were 16689 encounters among children 5 to 17 years of age, of which 15970 were among individuals who did not receive a KP.2-adapted vaccine of any kind.

Fig. Study C4591014 Enrollment Flow chart – Individuals Aged 5 Through 17 Years of Age – 17 September 2024 – 30 April 2025; Test Negative Design



Baseline and Clinical Characteristics by Exposure Status and Age

No Receipt of KP.2 Vaccine of Any Kind

The mean age at index was 10.1 years (SD: 3.84). Most participants (52.4%) were male. Fifty-eight percent (57.5%) of individuals were Hispanic and 17.3% were White.

- The most common encounter type was ED/UC visit (96.6%).
- Few individuals had prior pre-Delta SARS-CoV-2 infection (5%) or prior Delta SARS-CoV-2 infection (2.8%), with 19.9% having prior Omicron SARS-CoV-2 infection and 73.6% having no prior documented SARS-CoV-2 test.
- Approximately 28% (28.4%) of individuals received an influenza vaccine in the year prior to admission. Approximately 15% (15.1%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 7.7% had 0 encounters.
- Approximately 7% (7.2%) of individuals had ≥ 2 ED encounters 1 year prior, while 76.0% had 0 encounters. Approximately 1% (0.5%) of individuals had ≥ 2 hospital admissions, while 97.7% had 0 admissions.

Received BNT162b2 (Omi KP.2) Vaccine

The mean age at index was 11.2 years (SD: 3.74). Approximately half of participants (50.9%) were male. Forty-seven percent (46.6%) of individuals were Hispanic and 20.6% were White.

- The most common encounter type was ED/UC visit (96.6%).
- Few individuals had prior pre-Delta SARS-CoV-2 infection (3.2%) or prior Delta SARS-CoV-2 infection (1.7%), with 27.4% having prior Omicron SARS-CoV-2 infection and 68.7% having no prior documented SARS-CoV-2 test.
- Approximately 97% (96.9%) of individuals received an influenza vaccine in the year prior to admission. Approximately 27% (27.4%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 1.3% had 0 encounters.

- Approximately 9% (9.2%) of individuals had ≥ 2 ED encounters 1 year prior, while 77.6% had 0 encounters. Approximately 2% (1.5%) of individuals had ≥ 2 hospital admissions, while 96.1% had 0 admissions.

Children 6 months to 4 years of age

Between 17 September 2024 and 30 April 2025, there were 11878 KPSC encounters.

Baseline and Clinical Characteristics by Exposure Status and Age

No Receipt of KP.2 Vaccine of Any Kind

Overall, the mean age at index was 1.9 (SD: 1.38) years of age. Most participants (55.2%) were male. Approximately 59% (58.8%) of individuals were Hispanic and 18% were White. The most common encounter type was ED/UC visit (94.5%).

- Few individuals had prior pre-Delta SARS-CoV-2 infection (0.8%) or prior Delta SARS-CoV-2 infection (0.7%), with 14.7% having prior Omicron SARS-CoV-2 infection and 84% having no prior documented SARS-CoV-2 test.
- Approximately 37% (36.6%) received an influenza vaccine in the year prior to index event.
- Approximately 30% (29.5%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 1.9% had 0 encounters.
- Approximately 13% (13.1%) of individuals had ≥ 2 ED encounters 1 year prior, while 64.1% had 0 encounters.
- Approximately 2% (1.5%) of individuals had ≥ 2 hospital admissions, while 84% had 0 admissions.

Received BNT162b2 (Omi KP.2) Vaccine

Overall, the mean age at index was 1.5 years (SD: 1.24). Most participants (60.7%) were male. Approximately 39% (39.1%) of individuals were Hispanic and 26.5% were White.

- The most common encounter type was ED/UC visit (88.6%).
- No individuals had prior pre-Delta SARS-CoV-2 infection, few had prior Delta SARS-CoV-2 infection (0.2%), with 13.7% having prior Omicron SARS-CoV-2 infection and 86.1% having no prior documented SARS-CoV-2 test.
- Approximately 98% (98.4%) of individuals received an influenza vaccine in the year prior to admission. Approximately 46% (46.1%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 0.4% had 0 encounters.
- Approximately 13% (12.8%) of individuals had ≥ 2 ED encounters 1 year prior, while 65.3% had 0 encounters.
- Approximately 3% (3.2%) of individuals had ≥ 2 hospital admission encounters, while 72.3% had 0 admissions.

Baseline and Clinical Characteristics by Outcome Status and Age

SARS-CoV-2 Positive

Overall, the mean age at index was 1.0 (SD: 1.25) years of age. Most participants (52.8%) were male. Fifty-four percent (54%) of individuals were Hispanic and 18.2% were White.

- The most common encounter type was ED/UC visit (98.5%).
- Few individuals had prior pre-Delta SARS-CoV-2 infection (0.2%) or prior Delta SARS-CoV-2 infection (0.5%), with 4.4% having prior Omicron SARS-CoV-2 infection and 94.9% having no prior documented SARS-CoV-2 test.
- Approximately 42% (42.1%) received an influenza vaccine in the year prior to index event.
- Approximately 34% (34.1%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 2.2% had 0 encounters.
- Approximately 10% (9.9%) of individuals had ≥ 2 ED encounters 1 year prior, while 66.6% had 0 encounters.
- Approximately 2% (2.2%) of individuals had ≥ 2 hospital admissions, while 56.7% had 0 admissions.

SARS-CoV-2 Negative

Overall, the mean age at index was 1.9 years (SD: 1.38). Most participants (55.6%) were male. Fifty-eight percent (58.0%) of individuals were Hispanic and 18.4% were White.

- The most common encounter type was ED/UC visit (94.1%).
- Few individuals had prior pre-Delta SARS-CoV-2 infection (0.8%) or prior Delta SARS-CoV-2 infection (0.7%), with 15% having prior Omicron SARS-CoV-2 infection and 83.8% having no prior documented SARS-CoV-2 test.
- Approximately 40% (39.5%) of individuals received an influenza vaccine in the year prior to admission. Approximately 30% (30.2%) of individuals had ≥ 10 outpatient encounters within 1 year prior to index date, while 1.8% had 0 encounters.
- Approximately 13% (13.2%) of individuals had ≥ 2 ED encounters 1 year prior, while 64% had 0 encounters.
- Approximately 2% (1.5%) of individuals had ≥ 2 hospital admission encounters, while 80.8% had 0 admissions.

Efficacy results

Children 5 to 17 years of age

Among individuals 5 through 17 years of age who received BNT162b2 (Omi KP.2):

- The adjusted VE for ED/UC visit was 50% (95% CI: 4–74) compared to no KP.2-adapted vaccine.
- 55% (95% CI: 4–78) compared to XBB.1.5-adapted vaccine but no KP.2-adapted vaccine.
- 62% (95% CI: 19–82) compared to BA.4/5-adapted bivalent vaccine but no KP.2-adapted or XBB.1.5-adapted vaccine.
- 53% (95% CI: 7–76) compared to ≥ 2 doses of wild-type vaccine but no variant-adapted vaccines.

- 38% (95% CI: -23-69) compared to unvaccinated.

For all encounter types (ED/UC/hospitalization), adjusted VE was:

- 51% (95% CI: 6-75) compared to no KP.2-adapted vaccine.
- 57% (95% CI: 10-79) compared to XBB.1.5-adapted vaccine but no KP.2-adapted vaccine.
- 62% (95% CI: 19-82) compared to BA.4/5-adapted bivalent vaccine but no KP.2-adapted or XBB.1.5-adapted vaccine.
- 53% (95% CI: 9-76) compared to ≥ 2 doses of wild-type vaccine but no variant-adapted vaccines.
- 39% (95% CI: -21-69) compared to unvaccinated.

Children 6 months to 4 years of age

Among individuals 6 months through 4 years of age who received BNT162b2 (Omi KP.2), the adjusted vaccine effectiveness for all encounters (ED/UC/hospitalization) was:

- 44% (95% CI: 4-68) compared to those who did not receive a KP.2-adapted vaccine, and 46% (95% CI: 6-68) compared to unvaccinated. For ED/UC visits.
- The adjusted vaccine effectiveness was 41% (95% CI: -2-66) compared to those who did not receive a KP.2-adapted vaccine. 42% (95% CI: 0-67) compared to unvaccinated.

2.3.3. MAH Discussion on clinical aspects

Key results

Paediatric adjusted VE against emergency department, urgent care, and hospitalization visits for individuals 12 – 17 years of age, and emergency department and urgent care visits for individuals 5-11 years of age and for >6 months - 4 years demonstrated effectiveness against these COVID-19 outcomes following BNT162b2 (Omi XBB.1.5 and KP.2) vaccination.

TND Limitations

There are several limitations to take into consideration when interpreting the findings. The study was observational, and therefore cannot establish causal relationships between vaccination and COVID-19 outcomes. The test-negative design restricts the study population to those who have a SARS-CoV-2 test, thereby minimizing biases caused by health-seeking behavior, including the propensity to test.

While the company used a test-negative design and statistical methods to control for confounding, there may be unmeasured confounding. They compared cases and test-negative controls from the same time periods to balance testing availability, infection rates, and other inputs that may affect health behaviors and SARS-CoV-2 testing.

Due to the timeframe and the predominant circulating variant, outcomes like UC/ED were combined due to paucity of data. As such, many of the paediatric VE estimates were reported as a combination of outcomes.

Prior infection may be underestimated in this study because data were limited to what was available in the patient's record. There was a systematic mechanism to report SARS-CoV-2 testing that was administered outside the KPSC health system or through at-home tests, but not all may have been

reported. Furthermore, underreporting may have occurred because not all infected individuals are tested for SARS-CoV-2.

Key strata were deemed vital in understanding VE as the pandemic evolved including time since last dose. Unfortunately, there were many instances where VE could not be calculated reliably when stratified by these factors. Any VE estimates that resulted in a 95% confidence interval width greater than 50 percentage points were deemed unstable due to imprecision and need to be interpreted with caution.

The TND study may be subject to selection bias. It is possible that some cases were hospitalized or had ED admissions "with COVID-19" rather than "for COVID-19." This could result in spurious findings of waning VE against severe outcomes if vaccine breakthroughs were only incidental infections among individuals admitted to the hospital for something other than COVID-19. The analysis was also restricted only to individuals admitted with a diagnosis of ARI, however, it is possible that milder cases were included in the analysis and biased the VE downwards.

3. CHMP overall conclusion and recommendation

The MAH has presented the paediatric findings from Study C4591014, which evaluated the real-world effectiveness of the BNT162b2 Omicron XBB.1.5-adapted (Omi XBB.1.5) and KP.2-adapted (Omi KP.2) formulations in paediatric populations. Although the number of hospitalisations were too low to estimate a reliable estimate for these young age cohorts, the real-world data provided in this procedure generally corroborate what has been previously shown. In real-world settings, measurable VE was observed across children 6 months to 17 years of age, with the highest effectiveness seen within three months of vaccination. Both vaccine formulas continue to support a favourable benefit-risk profile for BNT162b2 in the paediatric population. These findings support the continued use of updated BNT162b2 formulations for the prevention of severe COVID-19 outcomes in children and adolescents, in alignment with current regulatory guidance.

Fulfilled:

No regulatory action required.