Clinical trial results:
Prospective monitoring of immune response following COVID-19 vaccination in children with cancer

Summary

EudraCT number	2021-003388-90
Trial protocol	NL
Global end of trial date	31 May 2023

Results information

Result version number	v1 (current)
This version publication date	08 May 2024
First version publication date	08 May 2024

Trial information

Trial identification

Sponsor protocol code	PB21VAC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Princess Máxima Center for pediatric oncology
Sponsor organisation address	Heidelberglaan 25, Utrecht, Netherlands, 3584 CS
Public contact	Prof. Dr. W.J.E. Tissing, Princess Máxima Center for Pediatric Oncology, 0031 88972 72 72, trialmanagement@prinsesmaximacentrum.nl
Scientific contact	Prof. Dr. W.J.E. Tissing, Princess Máxima Center for Pediatric Oncology, 0031 88972 72 72, trialmanagement@prinsesmaximacentrum.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2023
Global end of trial reached?	Yes
Global end of trial date	31 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the antibody response after mRNA (Pfizer, Moderna) SARS-CoV-2 vaccination in children with cancer as compared to healthy children

Protection of trial subjects:

Patients were vaccinated according to the Dutch national vaccination program.
Standard of Care, no additional protection.

Background therapy:

Patients were vaccinated according to the Dutch national vaccination program.
They received a 2-dose series of 10 µg (5–11 years) or 30 µg (12–17 years) BNT162b2 (Pfizer/BioNTech) mRNA COVID-19
Vaccine. Later on, immunocompromised children aged 12 and above, were also offered an additional third vaccination.

Evidence for comparator:

Not applicable

Actual start date of recruitment	17 July 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 89
Worldwide total number of subjects	89
EEA total number of subjects	89

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	36

Adolescents (12-17 years)	53
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Dates of recruitment period 17/07/2021 – 16/02/2023.
All participants were patients treated at the Princess Máxima Center.
A letter containing study information was send to their home address to invite them to participate in blood sampling. Written informed consent was obtained from all study participants and parents/legal guardians.

Pre-assignment

Screening details:

Patients treated at the Princess Máxima Center because of hematological, solid or neurological malignancies, or allogenic stem cell transplantation because of non-malignant disease, were identified from electronic medical records.

Period 1

Period 1 title	Recruitment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Entire cohort
Arm description: -	
Arm type	intervention acc to SOC
Investigational medicinal product name	BNT162b2 BioNTech/Pfizer COVID-19 Vaccine
Investigational medicinal product code	
Other name	Cominaty
Pharmaceutical forms	Concentrate for dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

For children aged 12-17 years
- Comirnaty is administered intramuscularly after dilution as a single dose of 0.3 mL for individuals 12 years of age and older regardless of prior COVID-19 vaccination status. For individuals who have previously been vaccinated with a COVID-19 vaccine, Comirnaty should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

For children aged 5-11 years
- Comirnaty 10 micrograms/dose is administered intramuscularly after dilution as a single dose of 0.2 mL for children 5 to 11 years of age regardless of prior COVID-19 vaccination status. For individuals who have previously been vaccinated with a COVID-19 vaccine, Comirnaty should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

Number of subjects in period 1	Entire cohort
Started	89
Completed	89

Baseline characteristics

Reporting groups	
Reporting group title	Recruitment
Reporting group description:	
All patients recruited started and completed treatment	

Reporting group values	Recruitment	Total	
Number of subjects	89	89	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	36	36	
Adolescents (12-17 years)	53	53	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	45	45	
Male	44	44	

Subject analysis sets	
Subject analysis set title	Tx < 6 weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
Children who received chemo or immunotherapy less than 6 weeks before 1st vaccination	
Subject analysis set title	Tx > 6 weeks
Subject analysis set type	Full analysis
Subject analysis set description:	
Children who received chemo or immunotherapy more than 6 weeks before 1 st vaccination	
Subject analysis set title	No Tx
Subject analysis set type	Full analysis
Subject analysis set description:	
Children without a history of chemo or immunotherapy	

Reporting group values	Tx < 6 weeks	Tx > 6 weeks	No Tx
Number of subjects	39	28	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	21	7	0
Adolescents (12-17 years)	18	21	6
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	18	16	3
Male	21	12	3

End points

End points reporting groups

Reporting group title	Entire cohort
Reporting group description: -	
Subject analysis set title	Tx < 6 weeks
Subject analysis set type	Full analysis
Subject analysis set description: Children who received chemo or immunotherapy less than 6 weeks before 1st vaccination	
Subject analysis set title	Tx > 6 weeks
Subject analysis set type	Full analysis
Subject analysis set description: Children who received chemo or immunotherapy more than 6 weeks before 1 st vaccination	
Subject analysis set title	No Tx
Subject analysis set type	Full analysis
Subject analysis set description: Children without a history of chemo or immunotherapy	

Primary: Antibody based immune response to vaccination against SARS-CoV-2 1 month after the 2nd vaccination and 1 month after the 3rd vaccination

End point title	Antibody based immune response to vaccination against SARS-CoV-2 1 month after the 2nd vaccination and 1 month after the 3rd vaccination
End point description: SARS-CoV-2 spike 1-specific antibody concentration at 28 (21–42) days after the 2nd and/or 3rd vaccination. Participants with anti-S1 levels >300 BAU/mL were classified as responders, between 10 and 300 BAU/mL as low responders and <10 BAU/mL as non-responders BAU=Binding antibody units	
End point type	Primary
End point timeframe: Blood was sampled 28 days after the 2nd vaccination and when possible 28 days after the third vaccination	

End point values	Tx < 6 weeks	Tx > 6 weeks	No Tx	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	39	28	6	
Units: BAU/mL				
number (not applicable)				
2 dose vaccination group – 28 days after 2nd vacci	28	18	4	
3 dose vaccination group – 28 days after 3rd vacci	10	6	0	
Hybrid group (2 vaccinations + infection)	9	7	1	
Hybrid group (1 vaccination + infection)	4	4	1	

Statistical analyses

Statistical analysis title	SARS-CoV-2 specific antibody levels

Statistical analysis description:

SARS-CoV-2 specific antibody levels following 2 dose vaccination in patients on treatment (Tx <6 weeks) and off treatment (Tx > 6 weeks)
Mann-Whitney U test comparing SARS-CoV-2 specific antibody levels 1 month after 2-dose vaccination in patients with Tx <6 weeks and in patients with Tx >6 weeks

Comparison groups	Tx < 6 weeks v Tx > 6 weeks
Number of subjects included in analysis	67
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	< 0.0001
Method	Mann-Whitney U test

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Within 7 days after each vaccination (only for cohort I, children aged 12-17 years vaccinated at the Princess Máxima Center)

Adverse event reporting additional description:

No adverse events were reported

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	5

Reporting groups

Reporting group title	Entire cohort

Reporting group description: -

Serious adverse events	Entire cohort		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 89 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Entire cohort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 89 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Reporting criteria were limited and intervention according to standard of care

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not applicable

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37174028