



Clinical trial results:

Phase I/IIa, first-in-human, open-label, dose escalation trial with expansion cohorts to evaluate safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of BNT141 as a monotherapy and in combination with other anti-cancer agents in patients with CLDN18.2-positive solid tumors

Summary

EudraCT number	2022-001843-25
Trial protocol	DK ES NL
Global end of trial date	24 July 2023

Results information

Result version number	v1 (current)
This version publication date	03 August 2024
First version publication date	03 August 2024

Trial information

Trial identification

Sponsor protocol code	BNT141-01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04683939
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioNTech SE
Sponsor organisation address	An der Goldgrube 12, Mainz, Germany, 55131
Public contact	BioNTech clinical trials patient information, BioNTech SE, +49 613190840, patients@biontech.de
Scientific contact	BioNTech clinical trials patient information, BioNTech SE, +49 613190840, patients@biontech.de

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	13 October 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of BNT141 at different dose levels and identify the maximum tolerated dose (MTD) or maximally administered dose (MAD) /recommended Phase II dose (RP2D) of BNT141 based on the occurrence of dose-limiting toxicities (DLTs) using the following definitions:

- The MTD defined as the highest tolerated dose, where less than one-third of the patients experience a DLT.
- The MAD defined as the highest dose administered, where all dose levels were tolerated during dose escalation.
- The RP2D defined based on integrated evaluation of safety, tolerability, clinical benefit, pharmacokinetic (PK), and pharmacodynamic data, for all dose levels tested.

However, the sponsor decided to stop the development of BNT141. The study was terminated early and only Part 1A (dose escalation of BNT141 as monotherapy) was conducted. The dose of BNT141 was not fully escalated as planned per protocol (i.e., only four doses were tested).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed. A Safety Review Committee was established to review safety, clinical, and available PK and pharmacodynamic data on an ongoing basis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2022
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	Canada: 5
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	13
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 15 patients (6 from Canada and 9 from the USA) were screened while 13 patients (5 patients and 8 patients respectively from two countries) were enrolled in this study and 2 patients failed screening (primary reason inclusion/exclusion criteria not met). All patients were enrolled into Part 1A of this study and received BNT141.

Pre-assignment

Screening details:

Adult patients with Claudin 18.2 (CLDN18.2)-positive tumors. CLDN18.2 positivity was determined by a central laboratory during the pre-screening phase using a validated immunohistochemistry assay and was defined as moderate (50-75%)-to-strong (more than 75%) CLDN18.2 expression.

Period 1

Period 1 title	Part 1A (dose escalation of BNT141) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	BNT141 monotherapy - Total
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Arm description:

The total number of patients from Part 1A of this study included in four tested dose cohorts.

Arm type	Experimental
Investigational medicinal product name	BNT141
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

BNT141 was administered intravenously (IV) as monotherapy once every three weeks (Q3W) at four dose levels.

Number of subjects in period 1	BNT141 monotherapy - Total
Started	13
Completed	0
Not completed	13
Consent withdrawn by subject	1
Physician decision	1
Deaths	5
Study termination by the sponsor	5
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	BNT141 monotherapy - Total
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Reporting group description:

The total number of patients from Part 1A of this study included in four tested dose cohorts.

Reporting group values	BNT141 monotherapy - Total	Total	
Number of subjects	13	13	
Age categorical			
Units: Subjects			
Adults (18-64 years)	4	4	
From 65-84 years	9	9	
Age continuous			
Age at the time of informed consent			
Units: years			
arithmetic mean	64.9		
standard deviation	± 12.71	-	
Gender categorical			
Units: Subjects			
Female	3	3	
Male	10	10	
Eastern Cooperative Oncology Group performance score (ECOG PS)			
ECOG PS grading defined as follows: Grade 0 - Fully active, able to carry on all pre-disease performance without restriction Grade 1 - Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work Grade 2 - Ambulatory and capable of all self-care, but unable to carry out any work activities, up and about more than 50% of waking hours			
Units: Subjects			
ECOG PS 0	4	4	
ECOG PS 1	9	9	
ECOG PS 2	0	0	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	12	12	
More than one race	0	0	
Unknown or Not Reported	0	0	
Body Mass Index (BMI)			
BMI is the patient's body weight in kilograms divided by the square of the patient's height in meters.			
Units: kg/m ²			
arithmetic mean	25.14		
standard deviation	± 6.42	-	
Number of prior systemic cancer therapies per patient			

Units: Number			
arithmetic mean	3.2		
standard deviation	± 1.46	-	

End points

End points reporting groups

Reporting group title	BNT141 monotherapy - Total
Reporting group description:	
The total number of patients from Part 1A of this study included in four tested dose cohorts.	

Primary: Occurrence of treatment-emergent adverse events (TEAEs) within a patient including Grade ≥ 3 , serious, fatal TEAE by relationship

End point title	Occurrence of treatment-emergent adverse events (TEAEs) within a patient including Grade ≥ 3 , serious, fatal TEAE by relationship ^[1]
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End point description:

All adverse events (AEs) are included with an onset date on or after the first dose of BNT141 (if the AE was absent before the first dose) or worsened after the first dose of BNT141 (if the AE was present before the first dose). AEs with an onset date >60 days after the last dose of BNT141 are included only if assessed as related to BNT141 by the investigator.

Intensity of AEs was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0, i.e.,:

Grade 1 - Mild

Grade 2 - Moderate

Grade 3 - Severe

Grade 4 - Life-threatening consequences; urgent intervention indicated

Grade 5 - Death related to AE

Safety Set - All patients who received investigational medicinal product (IMP) (i.e., at least one dose of BNT141).

End point type	Primary
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End point timeframe:

From start of BNT141 treatment until the second Safety Follow-up Visit (60 \pm 7 days after last dose)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As per protocol, no formal statistical analysis was planned for this endpoint.

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Number of patients with TEAEs				
Any TEAE	13			
Related TEAE	13			
Grade ≥ 3 TEAE	5			
Related Grade ≥ 3 TEAE	1			
Any serious TEAE	5			
Related serious TEAE	2			
TEAE of special interest	1			
TEAE leading to death	0			

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of dose reductions and discontinuation of BNT141 due to TEAEs

End point title	Occurrence of dose reductions and discontinuation of BNT141 due to TEAEs ^[2]
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End point description:

All AEs are included with an onset date on or after the first dose of BNT141 (if the AE was absent before the first dose) or worsened after the first dose of BNT141 (if the AE was present before the first dose). AEs with an onset date >60 days after the last dose of BNT141 are included only if assessed as related to BNT141 by the investigator.

Safety Set - All patients who received IMP (i.e., at least one dose of BNT141).

End point type	Primary
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End point timeframe:

From start of BNT141 treatment until the second Safety Follow-up Visit (60 ± 7 days after last dose)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As per protocol, no formal statistical analysis was planned for this endpoint.

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Number of patients				
TEAE leading to treatment discontinuation	0			
Related TEAEs leading to treatment discontinuation	0			
TEAE leading to study drug interruption	4			
Related TEAE leading to study drug interruption	3			
TEAE leading to dose reduction	0			
Related TEAE leading to dose reduction	0			
TEAE leading to dose rate reduction	0			
Related TEAE leading to dose rate reduction	0			

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence of dose-limiting toxicities (DLTs) within a patient during the DLT evaluation period

End point title	Occurrence of dose-limiting toxicities (DLTs) within a patient during the DLT evaluation period ^[3]
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End point description:

Serious AEs, non-serious Grade ≥ 3 non-hematological and hematological AEs as defined per DLT criteria and clinically significant abnormal laboratory values Grade ≥ 3 were collected and considered a DLT if assessed by the investigator to be at least possibly related to BNT141. Toxicities clearly not related to BNT141 (e.g., progressive disease, comorbidity, etc.) were not considered a DLT. The NCI-CTCAE v.5.0 was used to grade the intensity of AEs.

Safety Set - All patients who received IMP (i.e., at least one dose of BNT141).

End point type	Primary
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End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As per protocol, no formal statistical analysis was planned for this endpoint.

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Number of patients				
Number of patients with DLTs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Area under the concentration time curve (AUC)

End point title	RiboMab PK parameter - Area under the concentration time curve (AUC)
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End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

AUC (0-tau), AUC (0-inf) and AUC (0-504) were estimated from serum concentration data from Cycle 1 using non-compartmental analysis.

AUC (0-inf): Area under the drug concentration-time curve, from time zero to infinity.

AUC (0-504): Area under the drug concentration-time curve, from time zero to 504 hours after the start of the infusion.

AUC (0-tau): Area under the drug concentration-time curve, from time zero over the dosing interval at steady-state (Tau = 504 hours corresponding to 3-weeks administration) after the start of the infusion.

PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type	Secondary
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End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13 ^[4]			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
AUC (0-tau)	4149170.5191 (± 0.7)			
AUC (0-inf)	6017645.7202 (± 0.9)			
AUC (0-504)	4183178.1280 (± 0.8)			

Notes:

[4] - The number of patients included in the analysis of AUC (0-inf) & AUC (0-504) is 12 patients only.

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Clearance

End point title RiboMab PK parameter - Clearance

End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

Clearance was estimated from serum concentration from Cycle 1 data using non-compartmental analysis.

PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type Secondary

End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: L/h				
geometric mean (geometric coefficient of variation)				
Clearance	0.0042 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Volume of distribution at steady state (Vss)

End point title RiboMab PK parameter - Volume of distribution at steady state (Vss)

End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

Volume of distribution at steady state (Vss) was estimated as mean residence time calculated using last measured concentration (MRT inf) * CL.

PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type Secondary

End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: L				
geometric mean (geometric coefficient of variation)				
V _{ss}	1.6718 (± 0.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Maximum serum drug concentration (C_{max})

End point title	RiboMab PK parameter - Maximum serum drug concentration (C _{max})
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End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

C_{max} was estimated from serum concentration from Cycle 1 data using non-compartmental analysis. PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type	Secondary
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End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C _{max}	15473.7738 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Time to reach C_{max} (T_{max})

End point title	RiboMab PK parameter - Time to reach C _{max} (T _{max})
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End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

Tmax was estimated from serum concentration from Cycle 1 data using non-compartmental analysis.
PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type Secondary

End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: hours				
median (full range (min-max))				
Tmax	65.8000090 (45.517 to 95.417)			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Concentration at the end of a dosing interval (taken directly before next administration) (Ctough)

End point title RiboMab PK parameter - Concentration at the end of a dosing interval (taken directly before next administration) (Ctough)

End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

Ctough was estimated from serum concentration from Cycle 1 data using non-compartmental analysis.
PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type Secondary

End point timeframe:

Before start of Cycle 3 (plasma sample taken directly before BNT141 Cycle 3 administration)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Ctough	3660.2117 (± 0.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: RiboMab PK parameter - Half-time (t_{1/2})

End point title	RiboMab PK parameter - Half-time (t _{1/2})
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End point description:

Intact RiboMab (full-length and fully assembled antibody) PK serum samples were collected and analyzed.

T_{1/2} was estimated from serum concentration from Cycle 1 data using non-compartmental analysis.

PK Set - All patients with baseline and at least one valid on-treatment/post-treatment PK assessment.

End point type	Secondary
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End point timeframe:

First treatment cycle (From first dose up to 21 days after first dose)

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: hours				
geometric mean (geometric coefficient of variation)				
t _{1/2}	274.6523 (± 0.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)
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End point description:

ORR was defined as the number of patients in whom a complete response (CR) or partial response (PR), per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 is confirmed as best overall response. Data were not available for this endpoint due to early termination of the study meaning ORR could not be determined.

End point type	Secondary
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End point timeframe:

From start of first dose of BNT141 until end of trial or start of a new anti-cancer therapy.

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[5]			
Units: Number of patients				
ORR				

Notes:

[5] - Data were not available for this endpoint due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)
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End point description:

DCR was defined as the number of patients in whom a CR or PR or stable disease ([SD], per RECIST 1.1, SD assessed at least 6 weeks after first dose) is observed as best overall response. Data were not available for this endpoint due to early termination of the study meaning DCR could not be determined.

End point type	Secondary
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End point timeframe:

From start of first dose of BNT141 until end of trial or start of a new anti-cancer therapy

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: Number of patients				
DCR				

Notes:

[6] - Data were not available for this endpoint due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DoR)

End point title	Duration of response (DoR)
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End point description:

DoR was defined as the time from first objective response (CR or PR per RECIST 1.1) to first occurrence of objective tumor progression (progressive disease per RECIST 1.1) or death from any cause, whichever occurs first. Data were not available for this endpoint due to early termination of the study meaning DoR could not be determined.

End point type	Secondary
End point timeframe:	
From start of first dose of BNT141 until end of trial or start of a new anti-cancer therapy	

End point values	BNT141 monotherapy - Total			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: years				
median (full range (min-max))				
DoR	(to)			

Notes:

[7] - Data were not available for this endpoint due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of IMP treatment until the second Safety Follow-up Visit (60 ± 7 days after last dose)

Adverse event reporting additional description:

All AEs are presented with an onset date on or after the first dose of BNT141 (if the AE was absent before the first dose) or worsened after the first dose of BNT141 (if the AE was present before the first dose). AEs with an onset date >60 days after the last dose of BNT141 are included only if assessed as related to BNT141 by the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	BNT141 monotherapy
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Reporting group description:

The total number of patients from Part 1A of this study included in four tested dose cohorts, who received IMP (i.e., at least one dose of BNT141).

Serious adverse events	BNT141 monotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Enterococcal bacteraemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bacteraemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	BNT141 monotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Embolism			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	6 / 13 (46.15%)		
occurrences (all)	8		
Drug intolerance			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	3		
Non-cardiac chest pain			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pyrexia			

subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 5		
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	9 / 13 (69.23%) 13		
Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all) Dyspnoea at rest subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 2 1 / 13 (7.69%) 1 3 / 13 (23.08%) 4		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Investigations Weight decreased subjects affected / exposed occurrences (all) Neutrophil count decreased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 2 / 13 (15.38%) 2		

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 3		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Infusion related reaction subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 2 / 13 (15.38%) 5		
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Dizziness postural subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 3 / 13 (23.08%) 5 1 / 13 (7.69%) 1		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Lymphocytosis subjects affected / exposed occurrences (all) Lymph node pain subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 2 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Ear and labyrinth disorders Tinnitus			

subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 6		
Abdominal distension subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Nausea subjects affected / exposed occurrences (all)	5 / 13 (38.46%) 10		
Obstruction gastric subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Vomiting subjects affected / exposed occurrences (all)	8 / 13 (61.54%) 12		
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Faeces discoloured subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Dry mouth subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	5 / 13 (38.46%) 6		
Constipation subjects affected / exposed occurrences (all)	5 / 13 (38.46%) 5		

Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2 1 / 13 (7.69%) 1		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) Micturition disorder subjects affected / exposed occurrences (all) Haemorrhage urinary tract subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2 2 / 13 (15.38%) 2		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) Dehydration	1 / 13 (7.69%) 1		

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Decreased appetite			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2021	Amendment following feedback from the (United States) Food and Drug Administration (FDA) (23 and 25 February 2021). This update was issued before any trial subjects have been enrolled into the trial. This change had no impact on the planned trial objectives or trial conduct.
06 August 2021	Amendment to specify unique identifiers to the inclusion criteria, to correct an error in the implementation of the change to DLT definitions, and minor administrative changes. This update was issued before any trial subjects have been enrolled into the trial. This change had no impact on the planned trial objectives or trial conduct.
13 June 2022	Amendment to include additional eligible indications; clarification of secondary PK endpoints and revisions of exploratory objectives/endpoints; updates of inclusion and exclusion criteria related to AEs, contraception guidance, receipt of live vaccine prior to start of trial, handling of COVID-19 infection, glomerular filtration rate, previous receipt of BNT141; modifications of schedules of activities; inclusion of 48 hour safety window between second and third patient in each dose cohort to account for any acute safety signals in each new dose level; update of end of trial and patient completion definitions; addition of detailed recommendations for premedication and allowed concomitant medications; update of treatment guidelines for injection/infusion-related reactions (IRRs); update of terms under which treatment will be made available after the end of the trial; Revision of definition of AEs of special interest to include IRRs grade ≥ 3 instead of grade ≥ 2 ; inclusion of further information on dissemination of trial data; update of serious AE definition regarding inpatient hospitalization or prolongation of existing hospitalization.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
05 May 2023	The study was temporarily halted on 05 May 2023 due to in-line filter occlusions observed at two doses levels of the drug product BNT141. This affected the treatment schedule of in total three patients in two dose cohorts, who were in continued treatment at that time. Independent from the in-line filter occlusions observed, the sponsor decided to stop the development of BNT141 on 24 July 2023 and the study was terminated early. Due to the early study termination, only Part 1A was conducted and the dose of BNT141 was not fully escalated as planned per protocol (i.e., only four doses were tested). Part 1B (planned to be a dose escalation of BNT141 in combination with nab-paclitaxel and gemcitabine) and Part 2 (predefined 2 expansion cohorts) did not proceed.	-

Notes:

Limitations and caveats

None reported