Clinical trial results:
A Phase 3, Open Label, Randomized, Non-Inferiority Pharmacokinetic Study of Nivolumab Subcutaneous (Nivo SC) Versus Intravenous (Nivo IV) Administration in Participants with Stage IIIA/B/C/D or Stage IV Adjuvant Melanoma Following Complete Resection

Summary

EudraCT number	2021-003208-42
Trial protocol	ES BE PL DE IT
Global end of trial date	08 February 2024

Results information

Result version number	v1 (current)
This version publication date	22 February 2025
First version publication date	22 February 2025

Trial information

Trial identification

Sponsor protocol code	CA209-6GE

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

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	08 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of nivolumab SC co-formulated with rHuPH20 and nivolumab IV

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 Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	14
EEA total number of subjects	12

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

14 participants were randomized and treated

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Nivo SC (BMS-986298) 600 mg with 8,000 U of rHuPH20 administered via 2 sequential injections Q2W. Nivo SC will be administered in-clinic through cycle 5, Day 1.

Arm type	Experimental
Investigational medicinal product name	nivolumab/rHuPH20
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg/mL/2,000 U/mL Nivolumab/rHuPH20

Arm title	Arm B

Arm description:

-Nivo IV (BMS-936558) 240 mg Q2W for Cycles 1 through 4. -Nivo IV 480 mg Q4W Cycle 5 onwards for up to total of 52 weeks. -All dosing will be performed in-clinic.

Arm type	Experimental
Investigational medicinal product name	nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

10mg/mL

Number of subjects in period 1	Arm A	Arm B
Started	6	8
Completed	5	6
Not completed	1	2
Physician decision	-	1
Disease recurrence	1	-

other reasons	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Nivo SC (BMS-986298) 600 mg with 8,000 U of rHuPH20 administered via 2 sequential injections Q2W. Nivo SC will be administered in-clinic through cycle 5, Day 1.	
Reporting group title	Arm B
Reporting group description:	
-Nivo IV (BMS-936558) 240 mg Q2W for Cycles 1 through 4. -Nivo IV 480 mg Q4W Cycle 5 onwards for up to total of 52 weeks. -All dosing will be performed in-clinic.	

Reporting group values	Arm A	Arm B	Total
Number of subjects	6	8	14
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	5	7	12
>=65 years	1	1	2
Age continuous Units: years			
arithmetic mean	55.2	55.4	
standard deviation	± 11.51	± 11.11	-
Sex: Female, Male Units: Participants			
Female	3	5	8
Male	3	3	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	8	14
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	8	14
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Nivo SC (BMS-986298) 600 mg with 8,000 U of rHuPH20 administered via 2 sequential injections Q2W. Nivo SC will be administered in-clinic through cycle 5, Day 1.	
Reporting group title	Arm B
Reporting group description:	
-Nivo IV (BMS-936558) 240 mg Q2W for Cycles 1 through 4. -Nivo IV 480 mg Q4W Cycle 5 onwards for up to total of 52 weeks. -All dosing will be performed in-clinic.	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]
End point description:	
An adverse event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation participant administered study treatment that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.	
End point type	Primary
End point timeframe:	
From first dose to 100 days post last dose (Approximately up to 14 Months)	

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: No statistical analysis done for this endpoint

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: Participants				
Any Grade	6	8		
Grade 3 to 4	0	2		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events

End point title	Number of Participants with Serious Adverse Events[2]
End point description:	
A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: - Results in death. - Is life-threatening (defined as an event in which the participant was at risk of death at the time of the	

event; it does not refer to an event which hypothetically might have caused death if it were more severe).
- Requires inpatient hospitalization or causes prolongation of existing hospitalization.

End point type	Primary

End point timeframe:

From first dose to 100 days post last dose (Approximately up to 14 Months)

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: No statistical analysis done for this endpoint

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: Participants				
Any Grade	0	0		
Grade 3 to 4	0	0		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Treatment Related Adverse Events

End point title	Number of Participants with Treatment Related Adverse

End point description:

An adverse event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation participant administered study treatment.

An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom or disease.

End point type	Primary

End point timeframe:

From first dose to 100 days post last dose (Approximately up to 14 Months)

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: No statistical analysis done for this endpoint

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: Participants				
Any Grade	6	8		
Grade 3 to 4	0	2		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Treatment Related Serious Adverse Events

End point title	Number of Participants with Treatment Related Serious Adverse Events[4]

End point description:

A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose:

- Results in death.
- Is life-threatening (defined as an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe).
- Requires inpatient hospitalization or causes prolongation of existing hospitalization.

End point type	Primary

End point timeframe:

From first dose to 100 days post last dose (Approximately up to 14 Months)

Notes:

[4] - 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: No statistical analysis done for this endpoint

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	8		
Units: Participants				
Any Grade	0	0		
Grade 3 to 4	0	0		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events: (From first dose to last dose + 100 days): Approximately 14 Months

All-Cause mortality (From randomization to end of study): Approximately 14 Months

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Arm A

Reporting group description:

Nivo SC (BMS-986298) 600 mg with 8,000 U of rHuPH20 administered via 2 sequential injections Q2W. Nivo SC will be administered in-clinic through cycle 5, Day 1.

Reporting group title	Arm B

Reporting group description:

-Nivo IV (BMS-936558) 240 mg Q2W for Cycles 1 through 4. -Nivo IV 480 mg Q4W Cycle 5 onwards for up to total of 52 weeks. -All dosing will be performed in-clinic.

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	8 / 8 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	4 / 8 (50.00%)	
occurrences (all)	0	4	
Lymphoedema			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Puncture site erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Administration site reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Asthenia			
subjects affected / exposed	4 / 6 (66.67%)	1 / 8 (12.50%)	
occurrences (all)	6	1	
Device related thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Impaired healing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Puncture site inflammation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Puncture site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Puncture site pruritus			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
Menstrual disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	3 / 6 (50.00%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	3 / 8 (37.50%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Skin laceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Colitis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)	1 / 8 (12.50%)	
occurrences (all)	4	1	
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	
occurrences (all)	1	2	
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal toxicity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	15	1	
Tongue pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	3	
Drug eruption			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Ecchymosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Eczema nummular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	2	1	

Pruritus			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	
occurrences (all)	4	2	
Rash			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Groin pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Muscle contracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Body tinea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Bronchiolitis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2023	Bristol-Myers Squibb has made a strategic decision to terminate the CA2096GE trial. This decision was not related to any safety concerns. Study recruitment has closed and treatment of ongoing, active participants will continue per Protocol Amendment 01. Changes implemented in this amendment aim to alleviate participant and site burden and include updates to sample collection, study procedures, and study design. Pharmacokinetic (PK) co-primary endpoints, and secondary endpoints have been removed. Efficacy, patient-reported outcomes (PROs), and biomarker analyses will not be completed. Samples already collected for PK and immunogenicity assessments will be analyzed bioanalytically for nivolumab concentrations and anti-drug antibodies (ADAs) and reported as listings. Further collections for PK, ADAs, biomarkers, and PROs will be discontinued. Only safety assessments will be conducted. Part 2 was removed (Part 2 was scheduled to start when 90% of participants in Part 1 were enrolled). Balanced the frequency of clinic visits between treatment arms.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported