Clinical trial results:
A multicenter, pilot study evaluating immune impact and safety of nivolumab in combination with ipilimumab (immune combination) before initial RT-CT treatment for cervix cancer. COLIBRI Study

Summary

EudraCT number	2019-002271-34
Trial protocol	FR
Global end of trial date	04 August 2024

Results information

Result version number	v1 (current)
This version publication date	12 February 2026
First version publication date	12 February 2026

Trial information

Trial identification

Sponsor protocol code	GINECO-CE108b

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04256213
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ARCAGY-GINECO
Sponsor organisation address	8 Rue Lamennais, Paris, France, 75008
Public contact	Project Manager, Sidonie ADAM, ARCAGY-GINECO, 33 184 85 20 18, reglementaire@arcagy.org
Scientific contact	Project Manager, Sidonie ADAM, ARCAGY-GINECO, 33 184 85 20 18, reglementaire@arcagy.org

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	19 February 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the evolution of the CD8+/FOXP3+ ratio of lymphocytes in pre- versus post-treatment biopsies in patients treated with a combination of Nivolumab and Ipilimumab in a window study, just before starting standard RT-CT.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements.

Only patients who signed the written informed consent (including updated versions and addenda) were included in the study.

Before the enrollment of any patient, the final study protocol and informed consent were approved by the the comptent authority, the French National Agency for Medicines and Health Products Safety (ANSM), on 23/10/2019 and the assigned Etthics committte (Comité de Protection des Personnes, CPP) on 04/12/2019.

Before the implementation of any modifications to the approved study protocol, informed consent and / or any other study documents, the approval of the Ethics committee and the comptente authority were acquired.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	01 December 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	40 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	32
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period:
Country: France

Pre-assignment

Screening details:

Screening assessments conducted within 28 days before treatment initiation include a complete physical and gynecological examination, ECOG performance status, vital signs, and evaluation of clinical signs and symptoms, with particular focus on enterocolitis, dermatitis, neuropathy, and endocrinopathy.

Period 1

Period 1 title	Screening
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Nivolumab + Ipilimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab, 3mg/kg, administered as a 30 minutes IV infusion on day 1 and day 15 of the induction period (Cycle 1).

Nivolumab injection is to be administered as an IV infusion through a 0.2-micron to 1.2-micron pore size, low-protein binding (polyethersulfone membrane) in-line filter at the protocol-specified doses and infusion times. It is not to be administered as an IV push or bolus injection. When the dose is based on patient weight (ie, mg/kg), nivolumab injection can be infused undiluted (10 mg/mL) or diluted with 0.9% Sodium Chloride Injection or 5% Dextrose Injection to protein concentrations as low as 0.35 mg/mL.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab, 1mg/kg, is to be administered as a 30 minutes IV infusion on Day 1 of the induction period (Cycle 1).
Ipilimumab injection (5 mg/mL) is to be administered as an intravenous (IV) infusion without dilution after transferring to a polyvinyl chloride (PVC), non PVC/non di (2 ethylhexyl) phthalate (DEHP), or glass container and is stable for 24 hours at 2°C to 8°C or room temperature/room light. Ipilimumab injection must not be administered as an IV push or bolus injection.
Ipilimumab injection may be diluted in 0.9% Sodium Chloride Injection or 5% Dextrose Injection to concentrations between 1 mg/mL and 4 mg/mL and store
On Day 1 of Cycle 1, both nivolumab and ipilimumab are administered. Separate infusion bags and filters must be used for each infusion. Nivolumab is to be administered first and then promptly followed by a saline flush to clear the line before starting the ipilimumab infusion. The second infusion will always be ipilimumab, and will start at least 30 minutes.

Number of subjects in period 1	Nivolumab + Ipilimumab
Started	40
Completed	40

Period 2	
Period 2 title	Induction
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Nivolumab + Ipilimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab, 3mg/kg, administered as a 30 minutes IV infusion on day 1 and day 15 of the induction period (Cycle 1).

Nivolumab injection is to be administered as an IV infusion through a 0.2-micron to 1.2-micron pore size, low-protein binding (polyethersulfone membrane) in-line filter at the protocol-specified doses and infusion times. It is not to be administered as an IV push or bolus injection. When the dose is based on patient weight (ie, mg/kg), nivolumab injection can be infused undiluted (10 mg/mL) or diluted with 0.9% Sodium Chloride Injection or 5% Dextrose Injection to protein concentrations as low as 0.35 mg/mL.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab, 1mg/kg, is to be administered as a 30 minutes IV infusion on Day 1 of the induction period (Cycle 1).
Ipilimumab injection (5 mg/mL) is to be administered as an intravenous (IV) infusion without dilution after transferring to a polyvinyl chloride (PVC), non PVC/non di (2 ethylhexyl) phthalate (DEHP), or glass container and is stable for 24 hours at 2°C to 8°C or room temperature/room light. Ipilimumab injection must not be administered as an IV push or bolus injection.
Ipilimumab injection may be diluted in 0.9% Sodium Chloride Injection or 5% Dextrose Injection to concentrations between 1 mg/mL and 4 mg/mL and store

On Day 1 of Cycle 1, both nivolumab and ipilimumab are administered. Separate infusion bags and filters must be used for each infusion. Nivolumab is to be administered first and then promptly followed by a saline flush to clear the line before starting the ipilimumab infusion. The second infusion will always be ipilimumab, and will start at least 30 minutes.

Number of subjects in period 2	Nivolumab + Ipilimumab
Started	40
Completed	40

Period 3	
Period 3 title	RT-CT
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nivolumab + Ipilimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab, 3mg/kg, administered as a 30 minutes IV infusion on day 1 and day 15 of the induction period (Cycle 1).

Nivolumab injection is to be administered as an IV infusion through a 0.2-micron to 1.2-micron pore size, low-protein binding (polyethersulfone membrane) in-line filter at the protocol-specified doses and infusion times. It is not to be administered as an IV push or bolus injection. When the dose is based on patient weight (ie, mg/kg), nivolumab injection can be infused undiluted (10 mg/mL) or diluted with 0.9% Sodium Chloride Injection or 5% Dextrose Injection to protein concentrations as low as 0.35 mg/mL.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab, 1mg/kg, is to be administered as a 30 minutes IV infusion on Day 1 of the induction period (Cycle 1).

Ipilimumab injection (5 mg/mL) is to be administered as an intravenous (IV) infusion without dilution after transferring to a polyvinyl chloride (PVC), non PVC/non di (2 ethylhexyl) phthalate (DEHP), or glass container and is stable for 24 hours at 2°C to 8°C or room temperature/room light. Ipilimumab injection must not be administered as an IV push or bolus injection.
Ipilimumab injection may be diluted in 0.9% Sodium Chloride Injection or 5% Dextrose Injection to concentrations between 1 mg/mL and 4 mg/mL and store
On Day 1 of Cycle 1, both nivolumab and ipilimumab are administered. Separate infusion bags and filters must be used for each infusion. Nivolumab is to be administered first and then promptly followed by a saline flush to clear the line before starting the ipilimumab infusion. The second infusion will always be ipilimumab, and will start at least 30 minutes.

Number of subjects in period 3	Nivolumab + Ipilimumab
Started	40
Completed	40

Period 4

Period 4 title	Delay of 4-6 weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Nivolumab + Ipilimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab, 3mg/kg, administered as a 30 minutes IV infusion on day 1 and day 15 of the induction period (Cycle 1).

Nivolumab injection is to be administered as an IV infusion through a 0.2-micron to 1.2-micron pore size, low-protein binding (polyethersulfone membrane) in-line filter at the protocol-specified doses and infusion times. It is not to be administered as an IV push or bolus injection. When the dose is based on patient weight (ie, mg/kg), nivolumab injection can be infused undiluted (10 mg/mL) or diluted with 0.9% Sodium Chloride Injection or 5% Dextrose Injection to protein concentrations as low as 0.35 mg/mL.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab, 1mg/kg, is to be administered as a 30 minutes IV infusion on Day 1 of the induction period (Cycle 1).
Ipilimumab injection (5 mg/mL) is to be administered as an intravenous (IV) infusion without dilution after transferring to a polyvinyl chloride (PVC), non PVC/non di (2 ethylhexyl) phthalate (DEHP), or glass container and is stable for 24 hours at 2°C to 8°C or room temperature/room light. Ipilimumab injection must not be administered as an IV push or bolus injection.
Ipilimumab injection may be diluted in 0.9% Sodium Chloride Injection or 5% Dextrose Injection to concentrations between 1 mg/mL and 4 mg/mL and store
On Day 1 of Cycle 1, both nivolumab and ipilimumab are administered. Separate infusion bags and filters must be used for each infusion. Nivolumab is to be administered first and then promptly followed by a saline flush to clear the line before starting the ipilimumab infusion. The second infusion will always be ipilimumab, and will start at least 30 minutes.

Number of subjects in period 4	Nivolumab + Ipilimumab
Started	40
Completed	40

Period 5

Period 5 title	Maintenance
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	Nivolumab + Ipilimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

During the maintenance phase, nivolumab 480 mg will be administered Q4W for 6 months
At day 1 of the maintenance phase, Nivolumab 480 mg should be administered as a 60 minutes IV infusion. At the next administrations (C3D1 to C7D1), Nivolumab may be administered as a 30 minutes IV infusion if there was no infusion-related reaction during the previous infusion.

Number of subjects in period 5	Nivolumab + Ipilimumab
Started	40
Completed	40

Period 6	
Period 6 title	Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: N/A	

Arms	
Arm title	Nivolumab + Ipilimumab
Arm description: -	
Arm type	Follow-up
No investigational medicinal product assigned in this arm	

Number of subjects in period 6	Nivolumab + Ipilimumab
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	Screening

Reporting group description: -

Reporting group values	Screening	Total	
Number of subjects	40	40	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	20	20	
85 years and over	0	0	
Age continuous Units: years			
median	55		
full range (min-max)	31 to 77	-	
Gender categorical Units: Subjects			
Female	40	40	
Male	0	0	
ECOG Units: Subjects			
Zero	26	26	
One	14	14	
Two	0	0	
Three	0	0	
Four	0	0	
Five	0	0	
Aspect of the cervix Units: Subjects			
Normal	4	4	
Ulcered	9	9	
Infilterating	10	10	
Vegetating	6	6	
Missing data	11	11	
Aspect of the vaginal fornix Units: Subjects			
Normal	12	12	
Infiltrating	15	15	
Missing data	13	13	

Cervix maximal diameter Units: Subjects			
40	4	4	
45	3	3	
50	6	6	
51	1	1	
55	1	1	
60	3	3	
70	1	1	
80	2	2	
Missing data	19	19	
Parametrial infilteration Units: Subjects			
No	5	5	
Yes	18	18	
Missing data	17	17	
Adnexa Units: Subjects			
Missing data	23	23	
Normal	17	17	
Lymph nodes Units: Subjects			
Normal	37	37	
Not done	2	2	
Missing data	1	1	
Abdomen Units: Subjects			
Abnormal (Sensible and Pain)	1	1	
Normal	37	37	
Not done	1	1	
Missing data	1	1	
Lumbar fossa Units: Subjects			
Abnormal (Pain left lumbar)	1	1	
Normal	31	31	
Not done	7	7	
Missing data	1	1	
HIV antibody Units: Subjects			
Negative	38	38	
Unknown	2	2	
HIV Antigen Units: Subjects			
Negative	37	37	
Unknown	3	3	
HBs antigen Units: Subjects			
Negative	40	40	
HBc antibody Units: Subjects			
Negative	37	37	

Positive	3	3	
HCV antibody Units: Subjects			
Negative	37	37	
Positive	2	2	
Unknown	1	1	
HCV RNA Units: Subjects			
Not detected	18	18	
Unknown	22	22	
Medical history - Cardiac disorders Units: Subjects			
Mitral valve incompetence	1	1	
Rest	39	39	
Medical history - Congenital, familial and genetic disorders Units: Subjects			
Syringomyelia	1	1	
Rest	39	39	
Medical history - Ear and labyrinth disorders Units: Subjects			
Deafness	1	1	
Rest	39	39	
Medical history - Eye disorders Units: Subjects			
Eye disorder	1	1	
Rest	39	39	
Medical History - Eye disorders Units: Subjects			
Glaucoma	3	3	
Rest	37	37	
Medical History - Eye disorders Units: Subjects			
Ocular hypertension	1	1	
rest	39	39	
Medical History - Eye disorders Units: Subjects			
Retinal vascular disorders	1	1	
Rest	39	39	
Medical History - Gastrointestinal disorders Units: Subjects			
Abdominal pain	1	1	
Rest	39	39	
Medical History - Gastrointestinal disorders Units: Subjects			
Constipation	1	1	
Rest	39	39	
Medical History - Gastrointestinal disorders Units: Subjects			

Diarrhea	1	1	
Rest	39	39	
Medical history - Gastrointestinal disorders Units: Subjects			
Gastroesophageal reflux disease	1	1	
Rest	39	39	
Medical history - Gastrointestinal disorders Units: Subjects			
Inguinal hernia	1	1	
Rest	39	39	
Medical history - Gastrointestinal disorders Units: Subjects			
Volvulus	1	1	
Rest	39	39	
Medical history - Hepatobiliary diosrders Units: Subjects			
Cholelithiasis	1	1	
Rest	39	39	
Medical history - Hepatobiliary diosrders Units: Subjects			
Hepatitis	1	1	
Rest	39	39	
Medical history - Immune system diosrders Units: Subjects			
Drug hypersensitivity	1	1	
Rest	39	39	
Medical history - Immune system disorders Units: Subjects			
Hypersensitivity	2	2	
Rest	38	38	
Medical history - Infections and infestations Units: Subjects			
Bronchitis	1	1	
Rest	39	39	
Medical history - Infections and infestations Units: Subjects			
Hepatitis C	1	1	
Rest	39	39	
Medical history - Infections and infestations Units: Subjects			
Pilonidal cyst	1	1	
Rest	39	39	
Medical histoy - Infections and infestations Units: Subjects			
Pyelonephritis	1	1	

Rest	39	39	
Medical history - Infections and infestations Units: Subjects			
Syphilis	1	1	
Rest	39	39	
Medical history - Infections and infestations Units: Subjects			
Urinary tract infection	1	1	
Rest	39	39	
Medical History - Injury, poisoning and procedural complications Units: Subjects			
Spinal compression fracture	1	1	
Rest	39	39	
Medical history - Investigations Units: Subjects			
Lipase increased	1	1	
Rest	39	39	
Medical history - Metabolism and Nutrition disorders Units: Subjects			
Diabetes Mellitus	2	2	
Rest	38	38	
Medical history - Metabolism and nutrition disorders Units: Subjects			
Dyslipidemia	3	3	
Rest	37	37	
Medical history - Metabolism and nutrition disorders Units: Subjects			
Hypercholesterolemia	1	1	
Rest	39	39	
Medical history - Metabolism and nutrition disorders Units: Subjects			
Obesity	1	1	
Rest	39	39	
Medical history - Metabolism and nutrition disorders Units: Subjects			
Type 2 Diabetes Mellitus	1	1	
Rest	39	39	
Medical history - Mucoskeletal and connective tissue disorders Units: Subjects			
Arthralgia	1	1	
Rest	39	39	
Medical history - Mucoskeletal and connective tissue disorders Units: Subjects			
Back pain	2	2	

Rest	38	38	
Medical history - Mucoskeletal and connective tissue disorders Units: Subjects			
Fibromyalgia	1	1	
Rest	39	39	
Medical history - Musculoskeletal and connective tissue disorders Units: Subjects			
Osteoarthritis	2	2	
Rest	38	38	
Medical history - Musculoskeletal and connective tissue disorders Units: Subjects			
Osteoporosis	3	3	
Rest	37	37	
Medical history - Musculoskeletal and connective tissue disorders Units: Subjects			
Rheumatoid arthritis	1	1	
Rest	39	39	
Medical history - Musculoskeletal and connective tissue disorders Units: Subjects			
Scoliosis	1	1	
Rest	39	39	
Medical History - NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) Units: Subjects			
ANOGENITAL WARTS	1	1	
Rest	39	39	
Medical HIstory - NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) Units: Subjects			
MALIGNANT MELANOMA	1	1	
Rest	39	39	
Medical History - PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS Units: Subjects			
ECTOPIC PREGNANCY	1	1	
Rest	39	39	
Medical History - PSYCHIATRIC DISORDERS Units: Subjects			
ANXIETY	1	1	
Rest	39	39	
Medical HIstory - PSYCHIATRIC DISORDERS Units: Subjects			
BIPOLAR DISORDER	1	1	
Rest	39	39	
Medical History - PSYCHIATRIC			

DISORDERS Units: Subjects			
DEPRESSION	2	2	
Rest	38	38	
Medical History - PSYCHIATRIC DISORDERS Units: Subjects			
DEPRESSION	2	2	
Rest	38	38	
Medical History - PSYCHIATRIC DISORDERS Units: Subjects			
DRUG DEPENDENCE	1	1	
Rest	39	39	
Medical History - PSYCHIATRIC DISORDERS Units: Subjects			
INSOMNIA	1	1	
Rest	39	39	
Medical History - PSYCHIATRIC DISORDERS Units: Subjects			
NICOTINE DEPENDENCE	1	1	
Rest	39	39	
Medical History - RENAL AND URINARY DISORDERS Units: Subjects			
HYDRONEPHROSIS	1	1	
Rest	39	39	
Medical History - RENAL AND URINARY DISORDERS Units: Subjects			
NEPHROLITHIASIS	1	1	
Rest	39	39	
Medical History - RENAL AND URINARY DISORDERS Units: Subjects			
POLLAKIURIA	1	1	
Rest	39	39	
Medical History - RENAL AND URINARY DISORDERS Units: Subjects			
RENAL FAILURE	1	1	
Rest	39	39	
Medical Hiistory - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
BREAST CYST	1	1	
Rest	39	39	
Medical History - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
CERVIX HAEMORRHAGE UTERINE	1	1	
Rest	39	39	

Medical History - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
ENDOMETRIOSIS	2	2	
Rest	38	38	
Medical History - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
OVARIAN CYST	1	1	
Rest	39	39	
Medical History - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
PELVIC PAIN	5	5	
Rest	35	35	
Medical HIstory - REPRODUCTIVE SYSTEM AND BREAST DISORDERS Units: Subjects			
PERINEAL DISORDER	1	1	
Rest	39	39	
Medical History - RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS Units: Subjects			
ASTHMA	1	1	
Rest	39	39	
Medical History - RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS Units: Subjects			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	3	3	
Rest	37	37	
Medical History - RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS Units: Subjects			
EMPHYSEMA	1	1	
Rest	39	39	
Medical History - SOCIAL CIRCUMSTANCES Units: Subjects			
TOBACCO USER	11	11	
Rest	29	29	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
APPENDICECTOMY	8	8	
Rest	32	32	
Medical History - Units: Subjects			
BONE OPERATION	1	1	
Rest	39	39	
Medical History - SURGICAL AND MEDICAL PROCEDURES			

Units: Subjects			
CERVICAL CONISATION	5	5	
Rest	35	35	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
CHOLECYSTECTOMY	4	4	
Rest	36	36	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
HIP ARTHROPLASTY	1	1	
Rest	39	39	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
MAMMOPLASTY	2	2	
Rest	38	38	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
MYOPIA CORRECTION	1	1	
Rest	39	39	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
NASAL POLYPECTOMY	1	1	
Rest	39	39	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
PLASTIC SURGERY	1	1	
Rest	39	39	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
THYROIDECTOMY	3	3	
Rest	37	37	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
TONSILLECTOMY	3	3	
Rest	37	37	
Medical History - SURGICAL AND MEDICAL PROCEDURES Units: Subjects			
VARICOSE VEIN OPERATION	1	1	
Rest	39	39	
Medical History - VASCULAR DISORDERS Units: Subjects			
HYPERTENSION	9	9	
Rest	31	31	
Medical History - VASCULAR DISORDERS			

Units: Subjects			
VARICOSE VEIN	1	1	
Rest	39	39	
Medical History - NERVOUS SYSTEM DISORDERS Units: Subjects			
CARPAL TUNNEL SYNDROME	1	1	
Rest	39	39	
Medical History - NERVOUS SYSTEM DISORDERS Units: Subjects			
EPILEPSY	1	1	
Rest	39	39	
Medical History - NERVOUS SYSTEM DISORDERS Units: Subjects			
MIGRAINE	1	1	
Rest	39	39	
Medical History - NERVOUS SYSTEM DISORDERS Units: Subjects			
SCIATICA	1	1	
Rest	39	39	
Weight Units: kilogram(s)			
arithmetic mean	62.7		
standard deviation	± 11.4	-	
Systolic blood pressure Units: millimetre(s) of mercury			
arithmetic mean	133.9		
standard deviation	± 19.4	-	
Diastolic blood pressure Units: Millimetres(s) of mercury			
arithmetic mean	78.5		
standard deviation	± 11.8	-	
Cardiac frequency Units: Beats per minute			
arithmetic mean	85.2		
standard deviation	± 16.4	-	

End points

End points reporting groups

Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	
Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	
Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	
Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	
Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	
Reporting group title	Nivolumab + Ipilimumab
Reporting group description: -	

Primary: CD8+/FOXP3+ relative change of lymphocytes before and after the induction

End point title	CD8+/FOXP3+ relative change of lymphocytes before and after the induction[1]

End point description:

End point type	Primary

End point timeframe:

Induction

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: The statistical analysis of the primary endpoint was only descriptive.

End point values	Nivolumab + Ipilimumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: N/A				
arithmetic mean (standard deviation)	2.57 (± 6.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall disease response evaluated based on RECIST 1.1 criteria

End point title	Overall disease response evaluated based on RECIST 1.1 criteria

End point description:

End point type	Secondary

End point timeframe:

Induction (1 week before RT-CT)
4 weeks after RT-CT
End of treatment visit (At the end of the maintenance phase)

End point values	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	40	40	
Units: Participants				
Partial response	5	0	7	
Stable disease	33	1	0	
Progressive disease	2	15	4	
Complete response	0	24	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate evaluated based on RECIST 1.1 stratified by patient’s FIGO stage (Figo I and II)

End point title	Overall response rate evaluated based on RECIST 1.1 stratified by patient’s FIGO stage (Figo I and II)

End point description:

End point type	Secondary

End point timeframe:

Induction (1 week before RT-CT)
Maintenance
End of treatment visit

End point values	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: Participants				
Complete response	0	10	11	
Partial response	1	4	3	
Stable disease	11	0	0	
Progressive disease	2	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate evaluated based on RECIST 1.1 stratified by patient's FIGO stage (III and IV)

End point title	Overall response rate evaluated based on RECIST 1.1 stratified by patient's FIGO stage (III and IV)

End point description:

End point type	Secondary

End point timeframe:

Induction
4 weeks after RT-CT
End of treatment of visit

End point values	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	Nivolumab + Ipilimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	26	
Units: Participants				
Complete response	0	14	18	
Partial response	4	11	4	
Stable disease	22	1	0	
Progressive disease	0	0	4	

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year progression free survival

End point title	1-year progression free survival

End point description:

End point type	Secondary

End point timeframe:

Follow-up (1 year from inclusion)

End point values	Nivolumab + Ipilimumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Participants				
Progression	4			
No progression	36			

Statistical analyses

No statistical analyses for this end point

Secondary: 3-year overall survival

End point title	3-year overall survival

End point description:

End point type	Secondary

End point timeframe:

Follow-up (3 years from inclusion)

End point values	Nivolumab + Ipilimumab			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Participants				
Alive	36			
Dead	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported during the induction, RT-CT, and maintenance phases.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Nivolumab + Ipilimumab

Reporting group description: -

Serious adverse events	Nivolumab + Ipilimumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 40 (15.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
UROSTOMY COMPLICATION			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nivolumab + Ipilimumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Vascular disorders			
LYMPHOEDEMA			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Hypertension			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Lymphocele			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	2		
Hot flush			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	25 / 40 (62.50%)		
occurrences (all)	46		
PYREXIA			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
FATIGUE			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	8		
Oedema			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Hyperthermia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	2		
Vaccination site reaction			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Reproductive system and breast disorders			
GENITAL HAEMORRHAGE			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
VULVOVAGINAL PAIN			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
METRORRHAGIA			

subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	10		
VAGINAL DISCHARGE			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
PELVIC PAIN			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	7		
Vulvovaginal inflammation			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Vulvovaginal discomfort			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Uterine adhesions			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Vulval eczema			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
COUGH			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Dysphonia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Psychiatric disorders			

Affective disorder subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2 2 / 40 (5.00%) 2		
Investigations GAMMA-GLUTAMYLTRANSFERASE INCREASED subjects affected / exposed occurrences (all) Blood thyroid stimulating hormone decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	 3 / 40 (7.50%) 4 2 / 40 (5.00%) 2 5 / 40 (12.50%) 6 2 / 40 (5.00%) 3		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Radiation vulvovaginitis subjects affected / exposed occurrences (all) Radiation skin injury subjects affected / exposed occurrences (all)	 2 / 40 (5.00%) 2 1 / 40 (2.50%) 1 2 / 40 (5.00%) 2		
Cardiac disorders TACHYCARDIA subjects affected / exposed occurrences (all)	 1 / 40 (2.50%) 1		
Nervous system disorders			

HEADACHE subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
PARAESTHESIA subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
SCIATICA subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Dizziness subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Dysgeusia subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Neuropathy peripheral subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Presyncope subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Dysaesthesia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Blood and lymphatic system disorders IRON DEFICIENCY ANAEMIA subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
ANAEMIA subjects affected / exposed occurrences (all)	22 / 40 (55.00%) 27		
Lymphopenia			

subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	13		
Neutropenia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Thrombocytopenia			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	13		
Leukopenia			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	10		
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Hypoacusis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Eye disorders			
XEROPHTHALMIA			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Eyelid oedema			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	28 / 40 (70.00%)		
occurrences (all)	35		
CONSTIPATION			
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	15		
Nausea			
subjects affected / exposed	23 / 40 (57.50%)		
occurrences (all)	25		
Abdominal pain			

subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 10		
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 40 (12.50%) 5		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Proctalgia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Vomiting subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6		
Gastrointestinal motility disorder subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Abdominal rigidity subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Haematochezia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Rectal tenesmus subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Mouth ulceration subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Hepatobiliary disorders Hepatocellular injury subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Skin and subcutaneous tissue disorders RASH			

subjects affected / exposed	4 / 40 (10.00%)			
occurrences (all)	6			
PRURITUS				
subjects affected / exposed	10 / 40 (25.00%)			
occurrences (all)	10			
URTICARIA				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
XERODERMA				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
RASH ERYTHEMATOUS				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
Hyperhidrosis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
ERYTHEMA				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
Onycholysis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
Rash pruritic				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	2			
Alopecia				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
Dermatitis				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences (all)	2			
Dermatitis exfoliative generalised				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences (all)	1			
Eczema				

subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Renal and urinary disorders			
RENAL IMPAIRMENT			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Pollakiuria			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	9		
Stress urinary incontinence			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Urinary tract disorder			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Renal failure			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Urinary tract discomfort			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	7		
Hypothyroidism			
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	14		
Anorectal discomfort			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	7		
MUSCLE SPASMS			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Flank pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Oral fungal infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Oral candidiasis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Acinetobacter infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Vaginal infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	10		
Hyperkalaemia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Cell death			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Hyperglycaemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	2		
Hypercreatininaemia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2020	- Modification or correction of selection criteria, - Modification of the description of secondary endpoints analyses and efficacy assessments - Corrections to typographical errors and discrepancies between the summary and the protocol and/or the Investigator's brochure - Modification of the composition of the steering committee - Administrative update
26 January 2021	- Modification of the infusion duration for Nivolumab 480 mg at C2D1 and subsequent administrations if necessary
20 August 2021	Appendix 3 and 4 updated according to the Nivolumab IB v20 and Ipilimumab IB v24 - Administrative update: change of biostatistician
04 July 2022	Modification of the patient participation and the definition of the end of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported