Clinical trial results:
A prospective phase II study of nivolumab alone, or in combination with vinblastin in patients aged 61 years and older, with classical Hodgkin Lymphoma and coexisting medical conditions

Summary

EudraCT number	2017-001939-38
Trial protocol	FR BE
Global end of trial date	12 August 2021

Results information

Result version number	v1 (current)
This version publication date	09 March 2023
First version publication date	09 March 2023
Summary attachment (see zip file)	NIVINIHO_Summary Clinical Study Report (Synopsis_CSR NIVINIHO_Final version_LYSARC.pdf)

Trial information

Trial identification

Sponsor protocol code	NIVINIHO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03580408
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	CH LYON SUD BAT 2D, PIERRE BENITE, France, 69495
Public contact	Project Management, LYSARC, +33 (0)472669333, niviniho@lysarc.org
Scientific contact	Pr Hervé Tilly, LYSA, +33 (0)472669333, niviniho@lysarc.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	12 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the Complete Metabolic Response (CMR) rate by the Lugano classification 2014 based on central review at the end of treatment.

Protection of trial subjects:

No specific measures.

Background therapy:

All drugs composing the regimens of the study were registered and were available at the hospital pharmacy.
Vinblastine was used according to the protocol and Nivolumab was provided by the sponsor for this study.

Evidence for comparator: -

Actual start date of recruitment	02 May 2018
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	Belgium: 4
Country: Number of subjects enrolled	France: 60
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	6
From 65 to 84 years	51

85 years and over	7

Subject disposition

Recruitment

Recruitment details:

Date of first recrutement : France : 30/08/2018 // BELGIQUE : 26/02/2019
Date of last recrutement : France : 28/04/2020 // BELGIQUE : 16/01/2020
Date of last visit : France : 25/05/2021 // BELGIQUE : 05/03/2021

Pre-assignment

Screening details:

Screening set : 67 patients
Enrolled set : 64 patients

Period 1

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

Arms

Arm title	Overall
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction : Nivolumab was given alone at 240mg flat dose as a 30 minute IV infusion every 2 weeks.
Consolidation : Nivolumab was given alone or with Vinblastin (6mg/m2 IV) at 240mg flat dose as a 30 minute IV infusion every 2 weeks.

Investigational medicinal product name	Vinblastin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Consolidation : Vinblastin was given at 6mg/m2 IV in addition of Nivolumab (240mg) a 30 minute IV infusion every 2 weeks.

Number of subjects in period 1	Overall
Started	64
Completed	19
Not completed	45
FORTUITE DISCOVERY NEUROENDOCRINE TUMOR DISEASE DU	1

Consent withdrawn by subject	2
Adverse event, non-fatal	15
Death	2
Pogression	22
patient decision	1
Protocol deviation	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	64	64	
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)	6	6	
From 65-84 years	51	51	
85 years and over	7	7	
Age continuous Units: years			
median	75		
inter-quartile range (Q1-Q3)	69 to 81	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	39	39	

Subject analysis sets

Subject analysis set title	Evaluable Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Efficacy Set includes all patients enrolled in the study and having signed the informed consent, and who received at least one dose of Nivolumab and :
- with an available PET response evaluation at end of treatment or at treatment discontinuation
- or who died from lymphoma before end of treatment or treatment discontinuation
- or who withdrew for progression before end of treatment or treatment discontinuation.

Reporting group values	Evaluable Set		
Number of subjects	56		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	5		
From 65-84 years	45		
85 years and over	6		
Age continuous			
Units: years			
median	75		
inter-quartile range (Q1-Q3)	70 to 81		
Gender categorical			
Units: Subjects			
Female	24		
Male	32		

End points

End points reporting groups

Reporting group title	Overall
Reporting group description: -	
Subject analysis set title	Evaluable Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Efficacy Set includes all patients enrolled in the study and having signed the informed consent, and who received at least one dose of Nivolumab and :
- with an available PET response evaluation at end of treatment or at treatment discontinuation
- or who died from lymphoma before end of treatment or treatment discontinuation
- or who withdrew for progression before end of treatment or treatment discontinuation.

Primary: Complete metabolic response rate at the end of study treatment on central review

End point title	Complete metabolic response rate at the end of study treatment on central review[1]

End point description:

Metabolic response rate at the end of study treatment on central review

End point type	Primary

End point timeframe:

At the end of study treatment or at permanent treatment discontinuation

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 comparaison has been done because it is a Phase 2 non comparative study.

End point values	Evaluable Set			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: percentage				
RESPONDEUR	16			
NO RESPONDER	40			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete metabolic response rate at the end of induction on central review

End point title	Complete metabolic response rate at the end of induction on central review

End point description:

End point type	Secondary

End point timeframe:

At the end of induction

End point values	Evaluable Set			
Subject group type	Subject analysis set			
Number of subjects analysed	56			
Units: rate				
CMR	8			
PMR	23			
NMR	8			
PMD	9			
Not evaluated	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Median PFS

End point title	Median PFS

End point description:

End point type	Secondary

End point timeframe:

From inclusion until progression, death or lost of follow-up

End point values	Overall			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: Months				
median (full range (min-max))	9.8 (0.9 to 32.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median EFS

End point title	Median EFS

End point description:

End point type	Secondary

End point timeframe:

From inclusion until progression death initiation of a new lymphoma therapy or lost to follow-up

End point values	Overall			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: month				
median (full range (min-max))	9.8 (0.9 to 32.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival at 2 years

End point title	Overall Survival at 2 years

End point description:

End point type	Secondary

End point timeframe:

From inclusion until death or lost to follow-up

End point values	Overall			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: percent				
number (confidence interval 74.1%)	74.1 (58.9 to 84.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the first drug administration and up to 100 days after last drug administration of the study will be recorded

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Adverse event

Reporting group description: -

Serious adverse events	Adverse event		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 64 (43.75%)		
number of deaths (all causes)	18		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine tumour			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonitis				
subjects affected / exposed	4 / 64 (6.25%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	1 / 1			
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood electrolytes abnormal				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accidental overdose				

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Pericarditis				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Immune-mediated myocarditis				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Paralysis				
subjects affected / exposed	4 / 64 (6.25%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Encephalitis autoimmune				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Autoimmune colitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal ischaemia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic disorder			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatobiliary disease			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Toxic skin eruption			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphocytic hypophysitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thyroid disorder			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		
Viral infection			

subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neurological infection			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 64 (1.56%)		
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	Adverse event		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 64 (76.56%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Lung neoplasm malignant			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Neuroendocrine tumour			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Venous thrombosis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Surgical and medical procedures			

Cataract operation subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) General physical health deterioration subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	 3 / 64 (4.69%) 3 2 / 64 (3.13%) 2 2 / 64 (3.13%) 2 1 / 64 (1.56%) 1		
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	 1 / 64 (1.56%) 1		
Respiratory, thoracic and mediastinal disorders Pneumonitis subjects affected / exposed occurrences (all) Acute respiratory distress syndrome subjects affected / exposed occurrences (all) Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all) Lung disorder subjects affected / exposed occurrences (all)	 4 / 64 (6.25%) 4 1 / 64 (1.56%) 1 1 / 64 (1.56%) 1 1 / 64 (1.56%) 1		
Psychiatric disorders			

Confusional state subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 2		
Investigations Blood electrolytes abnormal subjects affected / exposed occurrences (all) Eosinophil count increased subjects affected / exposed occurrences (all)	 2 / 64 (3.13%) 2 1 / 64 (1.56%) 1		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Accidental overdose subjects affected / exposed occurrences (all)	 4 / 64 (6.25%) 4 1 / 64 (1.56%) 1		
Cardiac disorders Pericarditis subjects affected / exposed occurrences (all) Cardio-respiratory arrest subjects affected / exposed occurrences (all) Immune-mediated myocarditis subjects affected / exposed occurrences (all)	 2 / 64 (3.13%) 2 1 / 64 (1.56%) 2 1 / 64 (1.56%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all) Paralysis	 2 / 64 (3.13%) 2 2 / 64 (3.13%) 2 		

subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Aphasia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Encephalitis autoimmune			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Ischaemic stroke			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Loss of consciousness			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Neuromuscular toxicity			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	17		
Lymphopenia			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Anaemia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	7		
Pancreatic disorder			

subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Autoimmune colitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Intestinal ischaemia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Oral lichenoid reaction			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatobiliary disease			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Toxic skin eruption			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Pruritus			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	4		
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	3		
Proteinuria			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Endocrine disorders			
Thyroid disorder			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	6		
Diabetes mellitus			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Adrenal insufficiency			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Immune-mediated endocrinopathy			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Lymphocytic hypophysitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Polymyalgia rheumatica			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Trismus			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	10 / 64 (15.63%)		
occurrences (all)	13		

Urinary tract infection subjects affected / exposed occurrences (all)	9 / 64 (14.06%) 11		
Sepsis subjects affected / exposed occurrences (all)	7 / 64 (10.94%) 7		
Viral infection subjects affected / exposed occurrences (all)	3 / 64 (4.69%) 3		
Gastrointestinal infection subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 2		
Neurological infection subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 2		
Device related infection subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Oral infection subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		
Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2018	Protocol v2.0 dated 5 Nov 2018: - Modification of definition of evaluable patients - Sample size calculation method corrected - Vinblastine confirmed IMP - Vinblastine dose adapted to grade of neutropenia - Death not due to lymphome is not to be reported as an adverse event - Hepatitis B serology at C6, C12 and EoT - Bilirubine dosage includes conjugated and total bilirubine - After C6, evaluation period goes from 2 months to 1 month +/- 14 days Investigator Brochure Nivolumab v17 dated 23/06/2017 with modification of expected adverse events impacting patients' safety. Study documents updated including a complementary information note.
23 December 2019	Protocol v3.0 dated 08 Nov 2019: - Primary endpoint based on central review - Modification of estimated timelines - After C6, evaluation period goes between 14 and 42 days after C6D1 - No obligation of social security for Belgium - Stable patients at C6 eval can continue treatment, only patients in progression will stop the study - Administration of vinblastine and nivolumab adapted - New procedure to handle myocarditis Investigator Brochure v18 dated 25 Jun 2019 with modification of expected adverse events impacting patients' safety. Study documents updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported