Clinical trial results:
A phase II exploratory study of durvalumab (MEDI4736) in HIV-1 patients with advanced solid tumors

Summary

EudraCT number	2016-004524-38
Trial protocol	ES
Global end of trial date	29 March 2021

Results information

Result version number	v1 (current)
This version publication date	06 June 2022
First version publication date	06 June 2022
Summary attachment (see zip file)	GECP_DURVAST_summary final report (DURVAST CSR_summary final report_v.1.0_12March2022.pdf)

Trial information

Trial identification

Sponsor protocol code	GECP16/04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03094286
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación GECP
Sponsor organisation address	Avda. Meridiana 358, Barcelona, Spain, 08027
Public contact	Clinical Trial Information section, Fundación GECP (Grupo Español de Cáncer de Pulmón), +34 934302006, epereira@gecp.org
Scientific contact	Clinical Trial Information section, Fundación GECP (Grupo Español de Cáncer de Pulmón), +34 934302006, epereira@gecp.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 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the feasibility of durvalumab (MEDI4736) monotherapy at the recommended dose of 1500mg every 4 weeks in solid tumors in HIV-1-infected patients.

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 (ICH) Good Clinical Practice (GCP) 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 2017
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	Spain: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between May 2017 and July 2018, a total of 33 patients were enrolled in the study from 7 different sites.

Pre-assignment

Screening details:

Histologically advanced/metatasic lung cancer, head and neck cancer, cervical cancer, melanoma, anal cancer, pancreatic cancer, gastrio-esophageal cancer, triple negative breast cancer, bladder or renal cancer, Cholangiocarcinoma, Kaposi sarcoma, lymphomas, ovarian cancer or Merkel cell carcinoma. HIV infection. Undetectable viral load at last test

Period 1

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

Arms

Arm title	Experimental

Arm description:

Durvalumab 1500 mg IV commences on Day 1 following confirmation of eligibility into the study and continues on a Q4W schedule until confirmed PD (unless the investigator considers the subject to continue to receive benefit from treatment), initiation of alternative cancer therapy, unacceptable toxicity, withdrawal of consent, or if other reasons to discontinue study treatment occur.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	Medi4736
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab, 1500 mg intravenous infusion Q4W durvalumab (equivalent to 20 mg/kg Q4W) if> 30 kg. If patient is ≤30 kg, weight-based dosing, equivalent to 20 mg/kg Q4W, should be used.

Number of subjects in period 1	Experimental
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)

Reporting group description: -

Reporting group values	Overall study (overall period)	Total	
Number of subjects	20	20	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	53.50		
standard deviation	± 10.50	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	16	16	
Race Units: Subjects			
Caucasian	19	19	
Other	1	1	
ECOG Units: Subjects			
ECOG 0-1	19	19	
ECOG 2	1	1	
Smoking status Units: Subjects			
Former smoker	9	9	
Never smoker	2	2	
Smoker	9	9	
No of prior systemic therapies Units: Subjects			
None	8	8	
One	4	4	
Equal or major of Two	8	8	
Basal CD4-count cells/mm3 Units: Subjects			

<200	1	1	
200-350	8	8	
>350	11	11	
Type of Cancer Units: Subjects			
Anal	2	2	
Bladder	1	1	
Melanoma	2	2	
NSCLC	14	14	
SCLC	1	1	
LungCancer Units: Subjects			
YES	15	15	
NO	5	5	
Lung cancer type Units: Subjects			
NSCLC EGFR-, ALK-	14	14	
SCLC	1	1	
Other	5	5	
NSCLC histology Units: Subjects			
Adenocarcinoma	8	8	
Squamous	3	3	
NOS/Undifferenciated	3	3	
N/A	6	6	
HIV-1 group transmission Units: Subjects			
Heterosexual individuals	6	6	
MSM	6	6	
IDUs	6	6	
Unknown	2	2	
Metastasis by cancer type Units: Subjects			
Anal	2	2	
Bladder	1	1	
Melanoma	2	2	
NSCLC	14	14	
SCLC	1	1	
Number of metastatic sites Units: Subjects			
One	5	5	
Two	9	9	
Three	4	4	
Five	2	2	
Years since cancer diagnosis Units: Years			
arithmetic mean	1.80		
standard deviation	± 2.80	-	
Years since HIV diagnosis Units: year			
arithmetic mean	17.68		

standard deviation	± 10.18	-	
CD4 at baseline Units: cells/mm3			
arithmetic mean	416.95		
standard deviation	± 181.27	-	
Plasma Viral load at baseline Units: copies/mL			
arithmetic mean	25.39		
standard deviation	± 15.58	-	
Treatment duration Units: month			
arithmetic mean	8.73		
standard deviation	± 11.57	-	
Time on treatment and PD-L1 negative Units: month			
arithmetic mean	5.97		
standard deviation	± 8.57	-	
Time on treatment and PD-L1 positive Units: month			
arithmetic mean	13.18		
standard deviation	± 6.14	-	
Distribution of time on treatment for patients with Integrase Inhibitors Units: month			
arithmetic mean	10.90		
standard deviation	± 13.13	-	
Distribution of time on treatment for patients without Integrase Inhibitors Units: month			
arithmetic mean	3.67		
standard deviation	± 3.99	-	

End points

End points reporting groups

Reporting group title	Experimental

Reporting group description:

Durvalumab 1500 mg IV commences on Day 1 following confirmation of eligibility into the study and continues on a Q4W schedule until confirmed PD (unless the investigator considers the subject to continue to receive benefit from treatment), initiation of alternative cancer therapy, unacceptable toxicity, withdrawal of consent, or if other reasons to discontinue study treatment occur.

Primary: Efficacy: Best response during the treatment period

End point title	Efficacy: Best response during the treatment period[1]

End point description:

Durvalumab treatment is confirmed after a long follow-up as a feasible and active treatment in HIV-1-infected cancer patients under cART. HIV-1-infected subjects on suppressive antiretroviral therapy and advanced cancer had clinical benefit in 45% of cases, including patients with long lasting responses.

End point type	Primary

End point timeframe:

From the first dose until end of study.

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: Kaplan Meier method will be used to estimate the survival function. Secondary measurements will be PFS rate at 6 months and OS rate at 12 months.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Subject				
Complete Response	1			
Partial Response	3			
Stable disease	5			
Progression Disease	7			
Not Evaluated	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response global

End point title	Duration of response global

End point description:

Only patients with best response Stable disease, Partial Response or Complete response during the treatment period are included in the response analysis.

End point type	Secondary

End point timeframe:

Duration of response is the time from response (R) to progression/death (P/D).

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: month				
arithmetic mean (standard deviation)				
Anal	3.78 (± 0)			
Melanoma	7.39 (± 0)			
NSCLC	13.90 (± 16.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response- Dolutegravir/ no Dolutegravir

End point title	Duration of response- Dolutegravir/ no Dolutegravir

End point description:

Only patients with best response Stable disease, Partial Response or Complete response during the treatment period are included in the response analysis.

End point type	Secondary

End point timeframe:

Duration of response is the time from response (R) to progression/death (P/D).

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: month				
median (confidence interval 95%)				
Dolutegravir	27.4 (3.7 to 40)			
No Dolutegravir	2.8 (1.2 to 3.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response by treatment with INSTIs or no INSTIs

End point title	Duration of response by treatment with INSTIs or no INSTIs

End point description:

Only patients with best response Stable disease, Partial Response or Complete response during the treatment period are included in the response analysis.

End point type	Secondary

End point timeframe:

Duration of response is the time from response to progression/death.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: month				
median (confidence interval 95%)				
Integrase Inhibitors	11.32 (3.71 to 27.40)			
No Integrase Inhibitors	2.10 (1.22 to 3.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS analysis by PD-L1

End point title	OS analysis by PD-L1

End point description:

Kaplan Meier method will be used to estimate the survival function. OS will be mesure at 12 months.

End point type	Secondary

End point timeframe:

OS is defined as the time from the inclusion date to the death, due to any cause. A patient who does not dies, is censored at the last contact date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: month				
median (confidence interval 95%)				
PDL-1 negative	7.4 (1.2 to 16.3)			
PDL-1 positive	18.9 (17.0 to 25)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS analysis by Integrase Inhibitors

End point title	OS analysis by Integrase Inhibitors

End point description:

End point type	Secondary

End point timeframe:

OS is defined as the time from the inclusion date to the death, due to any cause. A patient who does not dies, is censored at the last contact date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)				
Integrase Inhibitors	11.5 (4.8 to 18.8)			
No Integrase Inhibitors	6.0 (0.4 to 33.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS analysis by Dolutegravir

End point title	OS analysis by Dolutegravir

End point description:

End point type	Secondary

End point timeframe:

OS is defined as the time from the inclusion date to the death, due to any cause. A patient who does not dies, is censored at the last contact date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)				
Dolutegravir	1.0 (1.0 to 18.8)			
No Dolutegravir	0.4 (0.4 to 19.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival

End point description:

Kaplan Meier method will be used to estimate the survival function. PFS rate will be mesure at 6 months

End point type	Secondary

End point timeframe:

PFS is defined as the time from the inclusion date to the progression or death, due to any cause, date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)	2.5 (1.4 to 5.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS analysis by PD-L1

End point title	PFS analysis by PD-L1

End point description:

End point type	Secondary

End point timeframe:

PFS is defined as the time from the inclusion date to the progression or death, due to any cause, date. A patient who does not progresses neither dies, is censored at the last tumor evaluation where no progression is detected.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: month				
median (confidence interval 95%)				
Negative PDL-1	2.3 (1.2 to 6.2)			
Positivi PDL-1	5.7 (4.1 to 17.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS analysis by Integrase Inhibitors

End point title	PFS analysis by Integrase Inhibitors

End point description:

End point type	Secondary

End point timeframe:

PFS is defined as the time from the inclusion date to the progression or death, due to any cause, date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)				
Integrase Inhibitors	2.5 (1.4 to 9.6)			
No Integrase Inhibitors	2.5 (0.4 to 6.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS analysis by Dolutegravir

End point title	PFS analysis by Dolutegravir

End point description:

End point type	Secondary

End point timeframe:

PFS is defined as the time from the inclusion date to the progression or death, due to any cause, date.

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)				
Dolutegravir	4.2 (1.0 to 17.0)			
No Dolutegravir	2.3 (0.4 to 4.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any adverse event or breakdown occurring during the course of the study.
The investigator will have to collect all adverse events once they have signed informed consent, during treatment and 90 days after the last administration of Durvalumab.

Adverse event reporting additional description:

The severity of AE will be determined using CTCAE version 4.0.3

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Subjects per protocol

Reporting group description: -

Serious adverse events	Subjects per protocol		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	4		
Vascular disorders			
Vascular arterial ischemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	3 / 3		
Pain			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Creatinine increased			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Oral hemorrhage			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thromboembolic event			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Gastric hemorrhage			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory insufficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hemoptysis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Upper respiratory infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic toxicity			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung infection			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Coronavirus infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Subjects per protocol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Thromboembolic event			

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 20 (70.00%)		
occurrences (all)	14		
Pain			
subjects affected / exposed	12 / 20 (60.00%)		
occurrences (all)	12		
Fever			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	6		
Reproductive system and breast disorders			
Dyspnea			
subjects affected / exposed	7 / 20 (35.00%)		
occurrences (all)	7		
Prostate syndrom			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 20 (35.00%)		
occurrences (all)	7		
Upper respiratory infection			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Sore throat			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Respiratory insufficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Hemoptysis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Confusion subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 3 1 / 20 (5.00%) 1		
Investigations Serum amylase increased subjects affected / exposed occurrences (all) Creatinine increased subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 3 3 / 20 (15.00%) 3		
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all) Percardial effusion subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Nervous system disorders Ataxia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1		
Blood and lymphatic system disorders Anemia			

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Neutropenia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	7 / 20 (35.00%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Diarrhea			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Dysphagia			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Mucositis oral			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Pancreatitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hepatic toxicity			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Seborreic dermatitis			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	10		
Infections and infestations			
Lung infection			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Non respiratory infection			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	7 / 20 (35.00%)		
occurrences (all)	7		
Hyperkalemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2017	Updating information regarding the safety of the investigational product and adverse effects in the protocol and in the patient information sheet and inform consent. Correct and expand the inclusion/exclusion criteria.Update management of toxicities.
10 May 2018	Make two changes to the inclusion/exclusion criteria.
19 January 2019	Change of Sponsor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32271353