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"SPANISH REAL WORLD DATA ON UNRESECTABLE STAGE III NSCLC PATIENTS TREATED WITH DURVALUMAB AFTER CHEMORADIOTHERAPY"

S-REAL STUDY

Sponsor: Fundación GECP
Protocol Code: GECP 19/02
[redacted]

Version 1.0, 09th January 2020

SPONSOR AND COORDINATING INVESTIGATOR'S SIGNATURE PAGE

Title: "Spanish Real World Data on unresectable stage III NSCLC patients treated with durvalumab after chemoradiotherapy" S-REAL Study

Protocol code: GECP 19/02

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Sponsor: Fundación GECP

Version (number and date): v.1.0, 9th January 2020

Coordinating investigator's signature	Date (dd-mmm-yyyy)

Dr. Pilar Garrido

Coordinating investigator's name

Sponsor's signature	Date (dd-mmm-yyyy)

Dr. Mariano Provencio

Sponsor representative's name

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A. Title

"Spanish Real World Data on unresectable stage III NSCLC patients treated with durvalumab after chemoradiotherapy" S-REAL study

Protocol code: GECP 19/02; [redacted]

Version: 1.0 dated on 09/January/2020

B. Responsible parties

1. Sponsor

Fundación GECP

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2. Principal investigator and coordinator

Dr. Pilar Garrido

Hospital Universitario Ramón y Cajal

M-607, km. 9

28034 Madrid

[redacted]

3. Participating Laboratories

Not applicable

4. CRO

Not applicable. The sponsor of the study, the Fundación GECP will be in charge of managing and monitoring the study.

C. Abstract

1. Study title

"Spanish Real World Data on unresectable stage III NSCLC patients treated with durvalumab after chemoradiotherapy" S-REAL study

2. Protocol code

Study code: GECP 19/02

[redacted]

[redacted]

3. Principal investigator and address

Dr. Pilar Garrido

Hospital Universitario Ramón y Cajal

M-607, km. 9

28034 Madrid

[redacted]

4. Ethics Committee evaluating the study

CEIm Hospital Puerta de Hierro, Majadahonda, Madrid

5. Objectives

5.1. Primary Objective:

To assess effectiveness of durvalumab in patients treated in real-life settings by evaluating PFS defined as time from the index date (date of the first dose of durvalumab received within the EAP) to the date of investigator-determined disease progression or death (if no progression) or the end of follow-up.

5.2. Secondary Objectives:

- To assess effectiveness of durvalumab in patients treated in real-life settings by evaluating 1-year survival rate (1ySr).
- To describe adverse events of special interest (AESIs) leading to treatment temporary interruption or permanent discontinuation of durvalumab, or which require interventions of concomitant use of corticosteroids, immunosuppressants and/or endocrine therapies

- To evaluate efficacy outcome (PFS and 1ySr) in patient subset populations which may include (subgroup definitions will be presented in detail in the final SAP, once patient enrolment has been completed and feasibility has been determined):
    - PACIFIC-LIKE population: unresectable stage III NSCLC patients with performance status (0, 1) who have not progressed following a concurrent platinum-based chemoradiotherapy (cCRT) and who are treated with durvalumab within 42 days after end of chemoradiotherapy , as the real-world population of patients treated in the EAP maybe actually different
    - Elderly patients (< 75 years, ≥ 75 years, as well as < 70 years, 70 – < 75 years, ≥ 75 years as determined by age at EAP inclusion)
    - Frail patients (ECOG/WHO-PS < 2, ECOG/WHO-PS ≥ 2, as determined by PS assessment at Stage III diagnosis date)
    - Disease stage at Stage III diagnosis (IIIA, stage IIIB/C)
    - Initiation of durvalumab relative to end of RT (< 14 days, ≥ 14 days, 14 - ≤ 42 days, as well as ≤ 42 days, > 42 days)
    - Previous RT total dose (≤ 60 Gy, >60 Gy)
    - Type of histology at Stage III diagnosis (squamous and non-squamous)
    - Medical condition and/or history of another cancer (No, Yes)
    - Longest dimension of primary tumour and lymph nodes involvement at Stage III diagnosis (<30 mm, 30 - <50 mm, >50 - 70 mm, >70 mm)
    - PD-L1 expression status (≥ 1%, < 1%, Unknown)
    - Previous type of CRT (Concurrent, Sequential, as well as Concurrent – following induction, Concurrent – without induction, Sequential – no overlap, Sequential – 1 cycle overlap (if sufficient sample size)). As SAP will be centrally written up, this information will not be registered in the case report form. The codification of these variables will the done centrally.
    - Smoking status (current, former, never)

- To estimate time and sites of disease progression or relapse in metastatic setting
- To describe details on durvalumab treatment including: duration of treatment, time to start durvalumab after completion of CRT, temporary treatment interruptions for AESIs, reasons for treatment discontinuation, concomitant use of corticosteroids, immunosuppressants, endocrine therapies and antibiotics
- To describe demographic (age, sex, smoking status) and clinical (stage, PS, histology, RECIST response to CRT, PDL1 status) characteristics of stage III unresectable NSCLC patients treated with durvalumab
- To describe previous CRT strategy including duration of chemotherapy, number of cycles and type of chemotherapy, and details of RT (total dose, number of fractions, type of RT, chest organ doses)
- To describe the baseline staging status ('de novo' versus 'relapse' patients), diagnostic Tumour Node Metastasis (TNM) classification edition used, staging, testing characteristics of these patients in this setting and physicians' and hospitals' characteristics
- To further assess subsequent treatments pattern at the time of disease progression including duration of therapy, type of therapy (targeted therapy, chemotherapy, immunotherapy) when available
- To explore healthcare resource utilization while on durvalumab treatment.

5.3 Exploratory objectives:

- To assess the impact of previous RT on occurrence of pneumonitis and cardiac events where applicable
- To explore the influence of corticosteroids and antibiotics on efficacy parameters (time to progression).
- To compare healthcare resources utilization and toxicity parameters based on duration of durvalumab treatment 1 year vs. > 1 year)

6. Study design

Non-PAS, non-interventional, observational, multicentre, one-arm, non-comparative, retrospective study.

7. Study disease or disorder

Unresectable stage III non-small cell lung cancer patients treated with durvalumab after chemoradiotherapy.

8. Other Analysis

For patients with no prior PD-L1 available, a PD-L1 testing will be done using archived tissue samples from diagnosis, when available. More details on the tumor tissue shipment will be detailed in the Samples Management Manual that will be provided to the participant sites.

9. Details of the study drugs

The study is based on the collection of data about the patients treated with Durvalumab after chemoradiotherapy in the real world. The patients participating in this non-interventional study will not receive treatment in relation to the study. Prospective information about treatments will not be collected.

10. Study population and total number of subjects

The sample of patients identified for the current study will be based on a portion of patients enrolled into the durvalumab EAP and no hypothesis and power analysis will be conducted. The study will include all patients who have participated in the EAP between 1 September 2017 up to 21 December 2018 and have received at least 1 dose of durvalumab. It is estimated that around 80 Spanish sites are enrolling patients in the EAP. Any physicians and their affiliated sites who previously participated in the EAP, will be invited to participate in the S-Real study. Based on the current recruitment, 547 patients were enrolled in the EAP during the patients' selection period. A 50% attrition rate from the EAP has been used to estimate the sample size for this study, meaning 50% of patients from the EAP may not enter in the S-Real study. Based on this, a reasonable sample size would be 250 patients enrolled in the study (40 sites).

11. Data analysis

PFS is calculated from the index date (date of the first dose of durvalumab received within the EAP) to the date of investigator-determined disease progression or death (if no progression) or the end

of follow-up for censored patients. PFS S will be estimated and plotted using the Kaplan-Meier method. The median and associated 95% confidence interval will be estimated. The percentage of patients remaining event free at specific timepoints will be displayed: PFS at 12, 18 months. Clinical characteristics, previous and subsequent treatment patterns will be displayed descriptively.

Progression will be measured preferably by RECIST v 1.1. As RECIST is not always used in routine; the Spanish Case report form will include a drop-down menu to choice between RECIST and clinical judgement.

-Patients with unknown progression status at the time of data collection will be censored at the date they were last known not to have radiologically and/or clinically progressed.
Patients will be followed from the index date (date of the first dose of durvalumab received within the EAP) to the end of follow-up (date of death for patient, withdrawal from study drug, loss to follow-up, or end of study period).
Safety of the Durvalumab administration will be described according to the information provided by the physician in the patient chart and could be done if possible by tabulation of the CTCAE version 5.0.
For the use of resources, the average number of resources per patient and for the full period, standard deviation and 95% CI. The median of hospitalizations per patient and the median of time of these hospitalizations will be collected for all the patients.

12. Schedule

AEMPS classification: January 2020

Ethics Committee submission: January-February 2020

Start of data collection: March 2020

End of data collection: September 2020

Cleaned data: November 2020

13. Financial source

AstraZeneca will provide financing support to conduct the study.

D. Study plan

Once the study has obtained classification from the AEMPS, approval by the Local Ethics Committee and the other administrative procedures have been completed, the study will start at the participating sites.

This is a non-PAS, non-interventional, observational, multicenter and retrospective study that will not under any circumstances interfere in the physician's normal clinical practice. Being limited to the collection of patient data, it does not entail any diagnostic or therapeutic procedure outside of normal clinical practice.

The investigator will be responsible for ensuring the correct completion of all sections of the Case Report Form.

Description of the visits

No additional follow up visits will be done for the purposes of this study, different from the clinical practice schedule. Study data will be collected retrospectively and during one routine visit.

The following information will be collected during the study visit:

- Date when the data of a patient is collected
- Confirmation of the informed consent signature.
- Inclusion date in the project
- Date of diagnosis
- Demographic data (e.g., age, sex, race, ECOG/PS, stage IIIA, IIIB or IIIC)
- Biomarker data: PDL1 status (≥1%, <10%, Unknown)
- Smoking History, and comorbidities including information about previous malignancies
- Characteristics of the tumor (e.g., histological type, TNM and edition used, size of the primary tumor…), metastasis localization at progression).
- Previous treatment and lines received, including radiotherapy (dates, dose, fractions, type of radiotherapy) and current treatment, Type of CRT (concurrent, sequential, concurrent + induction, concurrent without induction)

- Data relating to the treatment with Durvalumab: Start date of the treatment, response to the Durvalumab treatment, reason for discontinuation, AESIs observed, use of corticosteroids, immunosuppressants, endocrine therapies and antibiotics.
- Vital Status (alive /progression/ death) and last follow up date
- Date of death and cause of death (if applicable)
- Date of progression (if applicable)
- Data about tumor progressions during the treatment (details on metastasic sites) and further treatment lines (when available)
- Toxicity/Safety of Durvalumab treatment
- Consumption of hospital and primary care resources (from the first Durvalumab dose)

E. Rationale and background

Lung cancer represent approximately 13% of total cancer diagnoses worldwide and continues to be the leading cause of cancer-related mortality (Siegel, Miller et al. 2015), with approximately 1.8 million patients per year and caused an estimated 1.6 million deaths.

Non Small Cell Lung Cancer (NSCLC) represents approximately 85% of all lung cancer. Of these, approximately 80% are non-squamous (non-Sq) and 20% are squamous (Sq) histology.

In Spain[1] occur about 18,800 new cases per year and has been responsible for 19,513 deaths in 2006, twice the mortality of colon cancer (the most common tumor in absolute terms in Spain). Most patients are diagnosed with unresectable disease and around 40% advanced disease. Progress has been made in the clinical management of early stage NSCLC by establishing comprehensive, multi-modality treatment regimens; however, the prognosis for advanced disease has not improved substantially. With an overall 5-year survival rate of 9% to 13%.

Stage III represents between 25-30% of NSCLCs and the majority of them are unresectable. The standard treatment in unresectable patients was chemoradiotherapy concurrently if possible (cCRT) but the long-term results were disappointing.

The PACIFIC study is a randomised, double-blind, placebo-controlled, multi-centre, Phase III study to evaluate the efficacy and safety of durvalumab compared with placebo, as sequential therapy in

patients with locally advanced, unresectable stage III NSCLC who have not progressed following definitive, concurrent platinum-based chemotherapy and thoracic RT. The study was positive for both primary endpoints progression- free survival (PFS) and overall survival (OS). Following the presentation of PACIFIC results, AstraZeneca decided to open an early access programme (EAP) to provide access to durvalumab for patients with locally advanced, unresectable NSCLC (stage III) who have not progressed following chemoradiation.

The purpose of this study is to enroll patients who have received durvalumab as part of the Spanish EAP to provide the first real-world data on the use of durvalumab in this NSCLC patient population treated outside a clinical trial in Spain.

F. Research question and objectives

1. Primary objective

- To assess effectiveness of durvalumab in patients treated in real-life settings by evaluating PFS defined as time from the index date (date of the first dose of durvalumab) to the date of investigator-determined disease progression or death (if no progression) or the end of follow-up.

2. Secondary objectives

- To assess effectiveness of durvalumab in patients treated in real-life settings by evaluating 1-year survival rate (1ySr).
- To describe adverse events of special interest (AESIs) leading to treatment temporary interruption or permanent discontinuation of durvalumab, or which require interventions of concomitant use of corticosteroids, immunosuppressants and/or endocrine therapies
- To evaluate efficacy outcome (PFS and 1ySr) in patient subset populations which may include (subgroup definitions will be presented in detail in the final SAP, once patient enrolment has been completed and feasibility has been determined):
    - PACIFIC-LIKE population: unresectable stage III NSCLC patients with performance status (0, 1) who have not progressed following a concurrent platinum-based chemoradiotherapy (cCRT) and who are treated with durvalumab within 42 days after end of chemoradiotherapy , as the real-world population of patients treated in the EAP maybe actually different

- Elderly patients (< 75 years, ≥ 75 years, as well as < 70 years, 70 – < 75 years, ≥ 75 years as determined by age at EAP inclusion)
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- To describe previous CRT strategy including duration of chemotherapy, number of cycles and type of chemotherapy, and details of RT (total dose, number of fractions, type of RT, chest organ doses)
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- To further assess subsequent treatments pattern at the time of disease progression including duration of therapy, type of therapy (targeted therapy, chemotherapy, immunotherapy) when available
- To explore healthcare resource utilization while on durvalumab treatment.

Exploratory Objectives:

- To assess the impact of previous RT on occurrence of pneumonitis and cardiac events where applicable
- To explore the influence of corticosteroids and antibiotics on efficacy parameters (time to progression).
- To compare healthcare resources utilization and toxicity parameters based on duration of durvalumab treatment 1 year vs. > 1 year)

G. Research methods

1. Study design

Non-PAS, non-interventional, observational, multicentre, one-arm, non-comparative, retrospective study.

2. Setting

2.1. Inclusion criteria

1. Patients must have histologically or cytologically documented diagnosis of NSCLC with a locally advanced, or locally recurrent, unresectable (stage III) disease (according to American Joint Committee on Cancer [AJCC] lung cancer edition 7 or 8).
2. Age ≥ 18 years at time of study Entry

3. Patients must have been treated with chemotherapy and radiotherapy concurrently or sequentially and shown no progressive disease following chemoradiation
4. Patients must have been enrolled in durvalumab EAPs between 1 September 2017 and 21 December 2018.
5. Patients must have been treated with at least one dose of durvalumab within the EAP
6. Alive patients must have signed, dated and IRB/EC-approved written informed consent* form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol-related procedures that are not part of normal subject care.

**Only for patients who are alive on the date of chart review and a follow-up visit is scheduled for date within 3 months after the chart review date. Also, the data can be collected, in case patients are still alive but the principal investigator (PI) of a site considers that:*

- The study represents a minimum risk or do not represent a risk for the patients
- The study is retrospective and covers a long period of time so, it will be impossible to collect all the informed consents in time (in the time foreseen for the data collection) and this would make the carrying out of the study impracticable
- The anonymization of data is guaranteed

The sponsor will accept that this consent will not be collected and will guarantee that the data will be collected always respecting the general regulation of data protection (see section 5.).

For all the stated above, in relation to deceased patients and given the importance of collecting as many cases as possible to achieve the main objective of the study, the sponsor considers that anonymized data can be collected from the patients if the PI of the center is willing to participate and has been duly informed that the data will be collected anonimized.

2.2. Exclusion criteria

1. Alive patients who do not want to sign and date an IRB/IEC-approved written informed consent form.
2. Patients who were accepted in the EAP, but did not receive treatment.

3. Patients treated with durvalumab in clinical studies prior to the index date (first dose of durvalumab received within the EAP

3. Variables

3.1. Demographics/ baseline characteristics

Date of birth, sex, race, smoking history, ECOG/PS, date of stage IIIA, b or C diagnosis, histology, TNM, Stage, comorbidities, previous treatments, previous history of other malignancies, PDL1 status.

3.2. Efficacy

Date of progression PFS will be defined from the date of starting Durvalumab treatment until the date of radiological and/or clinical progression or the date of death for any reason, whichever occurred first.

3.3. Safety

Toxicity/Safety data:

Adverse events referred by the patients related to the durvalumab treatment received within the EAP program will be filled in a Remote Data Capture system (RDC)/Case Report Form (CRF).

The type of AE and the severity will be classified according to the NCI CTCAE Version 5.0. The causal relationship to study drug is determined by the physician and should be used to assess all AEs. The casual relationship can be one of the following: related or not related.

3.4. Use of resources

For each resource will be collected the number consumed by each patient in the study period; from 1st September 2017 (beginning of the treatment with Durvalumab in the EAP) to December 2018 or before depending on when the treatment was stopped. In the case of supportive treatments (medicines, transfusions, enteral nutrition), they will only be indicated if they were used or not.

- PRIMARY CARE health resources:
  - Visits
  - Primary care Physician
  - Primary care Nurse
  - Tests

- Chest x-ray
- Complete blood count
- Other (free field)

- HOSPITAL CARE health resources:
  - Visits
  - Medical Oncologist
  - Other hospital Physician (free field)
  - Hospital Nurse
  - Hospital visits / admissions
  - Emergency room visits (without admission)
  - Days of hospitalization in the Emergency room
  - Days of hospitalization in plant
- Imaging tests:
  - Chest x-ray
  - CT scan
  - Magnetic resonance
  - Endobronchial ultrasound
  - Esophageal Endoscopic Ultrasound
  - Other (free field)
- Other complementary tests:
  - Bone scintigraphy
  - Sputum cytology
  - Thoracentesis
  - Biopsy
  - Bronchoscopy
  - Mediastinoscopy
  - Mediastinotomy
  - Thoracoscopy
  - Spirometry
  - Plethysmography
  - Electrocardiogram
  - Other (free field)

- Laboratory tests
  - Immunohistochemistry
  - Molecular tests (EGFR, ALK, ROS1, BRAF)
  - Complete blood count
  - Blood chemistry
  - Proteins in urine
  - Other (free field)
- Surgery
  - Pneumectomy
  - Lobectomy
  - Segmentation or wedge resection
  - Sleeve resection
  - Other (free field)
- Other resources / support
  - Radiofrequency ablation
  - Radiotherapy palliative (number of sessions)
  - Pleurodesis
  - Corticosteroids (yes / no)
  - Bisphosphonates (yes / no)
  - Stimulants of erythropoietin (yes / no)
  - Blood transfusions (yes / no)
  - Enteral nutrition (yes / no)
  - Others (free field)
- Management and concomitant drug treatment due to AE: type, dosage and duration of treatment.
- Drug treatment (dosage, duration).

a. Data sources

The source of information will be, the medical history of the patient regarding the treatments received before and within the Expanded Access Program (EAP) of Durvalumab.

b. Study size

The sample of patients identified for the current study will be based on a portion of patients enrolled into the durvalumab EAP and no hypothesis and power analysis will be conducted. The study will include all patients who have participated in the EAP between 1 September 2017 up to 21 December 2018 and have received at least 1 dose of durvalumab. It is estimated that around 80 Spanish sites are enrolling patients in the EAP. Any physicians and their affiliated sites who previously participated in the EAP, will be invited to participate in the S-Real study. Based on the current recruitment, 547 patients were enrolled in the EAP during the patients' selection period. A 50% attrition rate from the EAP has been used to estimate the sample size for this study, meaning 50% of patients from the EAP may not enter in the S-Real study.

Based on this, a reasonable sample size would be 250 patients enrolled in the study (40 sites).

c. Data management

All the patient information required will be filled in a Remote Data Capture system (RDC)/Case Report Form (CRF). Only the investigator and his/her staff can access to this system and enter patient data. A username and password will be done to the staff in order to allow them to register patients in the study.

The investigator will be responsible for ensuring the correct completion of all sections of the Case Report Form and for signing them. The staff of each site will be trained by the Fundación GECP staff on the electronic Case Report Form management.

In order to guarantee the confidentiality of the study data, only the following persons and entities will have access thereto: the investigator and his/her staff, the sponsor or a person designated by the sponsor, the IEC, the relevant healthcare authorities and the persons responsible for analyzing the data.

The content of the CRFs, as well as any documents generated during the study, will be protected against non-permitted use by persons not involved in the investigation and will therefore be considered strictly confidential and will not be revealed to third parties.

Only the PI and research collaborators of the project will handle the data that can identify patients. The patient will be identified by a numerical code in order to respect the confidentiality of patients' personal data, according to the Regulation (EU) 2016/679 of the European Parliament and the Council of April 27th, 2016 on Data Protection (GDPR). In Spain, it is regulated by the Organic Law 3/2018, 5th of December, on Personal data protection and digital rights guarantee.

The investigator must make sure to maintain patients' anonymity and protect their identity from unauthorized parties. Patients will not be identified by name or initials on the CRFs, but by an identification code. The investigator must keep a record of patient recruitment, including the codes assigned for participation in the study.

The investigator will organize the safeguarding of the study documentation until the end of the study. He/she must also comply with the local standards/recommendations regarding the safeguarding of patients' records.

The processing of data of a personal nature required for this study is subject to the Regulation (EU) 2016/679 of the European Parliament and the Council of April 27th, 2016 on Data Protection (GDPR). In Spain, it is regulated by the Organic Law 3/2018, 5th of December, on Personal data protection and digital rights guarantee.

d. Data analysis

The following descriptive statistics will be used:

- Frequency statistics for categorical variables: number and percentage.
- Mean, standard deviation, median (interquartile range) and categorical distribution for quantitative variables (e.g. number of: exacerbations, hospital admissions, emergency units' attendances, prescriptions, visits).
- In addition, two-sided 95% confidence intervals will be presented for the study outcomes presented.

PFS will be defined from the date of starting Durvalumab treatment until the date of radiological and/or clinical progression or the date of death for any reason, whichever occurred first. Progression will be measured preferably by RECIST v 1.1; patients with unknown progression status at the time of data collection will be censored at the date they were last known not to have radiologically and/or clinically progressed.

PFS will be estimated using Kaplan–Meier analysis.

Safety of the Durvalumab administration will be described by tabulation of the CTCAE version 5.0.

No inferential analyses are foreseen. No interim analyses are predefined. All the results of this study will be considered exploratory and descriptive by design.

e. Quality control

The application used for the collection of the data will have safety margins and internal coherence rules to avoid the entry of incorrect data or anomalous or incoherent values. Quality of data and queries will be revised and attended by Fundación GECP Data Management department. In the event that data are incorrect, incomplete or have not been collected in accordance with the protocol, the Fundación GECP Data Management team will issue queries and inform the investigator who will be asked to review and make corrections.

f. Limitations of the research methods

This is an exploratory study. The results obtained will provide some insight about the treatment of Durvaumab in the real world outside clinical trials.

2. Protection of human subjects

a. Risk–benefit analysis for research subjects

Due to its observational nature, there is no possibility of the study generating any risk whatsoever for the subjects studied as it does not entail any change in patient care with respect to normal clinical follow-up. The patient will not receive any benefit as a result of his/her participation in the study and will be treated in accordance with the participating physician's normal clinical practice. Nevertheless, this study may help to enable improvements to be made in the care of such patients in normal clinical practice.

b. Considerations regarding patient information and informed consent

This study will follow standards of good pharmaco-epidemiology practice (GPP) and applicable regulatory requirements, thereby ensuring that its design and conduct and the communication of the data are reliable and protect the rights and integrity of the participating subjects and the confidentiality of their data.

Before starting the study, the protocol, patient information sheet and informed consent form for the study will be submitted for approval to the Ethics Committee (EC).

This study follows the Spanish law SAS/3470/2009 of 16th December 2009, which states the guidelines on post-authorization observational studies for medicinal products for human use.

The sponsor will keep the EC's favorable opinion, together with the versions of the documents approved and the list of members of the committee that have issued the approval.

Patients who meet the inclusion criteria and sign the informed consent will be recruited in the project until the indicated sample size is reached. Each subject invited to participate in the project will be informed by an investigator and will receive a "Patient Information Sheet" containing the relevant and necessary information to enable him/her to decide whether to participate in the project. (see exceptions for the obtention of the informed consent in section 2.1. Inclusion criteria.

The investigator must inform the patient as fully as possible, using language and terms that the latter can understand, about the voluntary nature of participation and that this will not entail any change to his/her treatment or medical care with regard to what he/she would receive if not participating. The investigator will respond to the patient's doubts and questions and, in accordance with current legislation, obtain the subject's written informed consent which must be signed by the subject (in his/her own hand with name and date) or the witness written informed consent can be obtained if necessary. The patient will receive a signed and dated hard copy of the informed consent form.

Subjects participating in the study may at any time withdraw their consent to the use of their data in the analysis, without giving a reason and without incurring any liability or loss.

c. Data confidentiality

In order to guarantee the confidentiality of the study data, only the following persons and entities will have access to the study data: the investigator and his/her staff, the sponsor or a person designated by the sponsor, the IRB/EC, the relevant healthcare authorities and the persons responsible for analyzing the data.

Only the PI and research collaborators of the project will handle the data that can identify patients.

The patient will be identified by a numerical code in order to respect the confidentiality of patients' personal data, according to the Regulation (EU) 2016/679 of the European Parliament and the Council of April 27th, 2016 on Data Protection (GDPR). In Spain, it is regulated by the Organic Law 3/2018, 5th of December, on Personal data protection and digital rights guarantee.

The investigator must make sure to maintain patients' anonymity and protect their identity from unauthorized parties. Patients will not be identified by name or initials on the CRFs, but by an

identification code. The investigator must keep a record of patient recruitment, including the codes assigned for participation in the study.

In all cases, the database will respect the data protection law according to the Regulation (EU) 2016/679 of the European Parliament and the Council of April 27th, 2016 on Data Protection (GDPR). In Spain, it is regulated by the Organic Law 3/2018, 5th of December, on Personal data protection and digital rights guarantee.

Materials and information used in this project will be coded in order to respect the confidentiality of patients' personal data.

d. Interference with the physician's prescription habits

This study is observational, therefore it will not under any circumstances interfere in the physician's normal clinical practice, as it is limited to the collection of patient data and does not entail any diagnostic or therapeutic procedure outside of normal clinical practice.

For this reason, each physician will have to select those individuals eligible to participate in the study from among the population he/she treats. Whether the investigator decides to use a treatment or not will be independent of the study, and treatments may be altered based on normal clinical practice regardless of the patient's participation.

Before accepting and signing the investigator's commitment, the participating professionals must ensure that their participation in the study does not interfere with their prescribing habits or their healthcare duties.

3. Management and reporting of adverse events/adverse reactions

Management and reporting of adverse events are not applicable. The study is based on retrospectively collection of data. The patients participating in this non-interventional study will not receive treatment in relation to the study.

Despite of this, adverse events referred by the patients related to the durvalumab treatment received within the Expanded Access Program (EAP) in Spain will be filled in a Remote Data Capture system (RDC)/Case Report Form (CRF). See section 3.3.

4. Resources for conducting the study and assigning tasks. Supply method for the medicinal product. Funding

This study will be financed by AstraZeneca in accordance with the directions given in this protocol. This funding includes the cost of submitting the study for approval to an accredited IRB/EC, submitting the study for classification to the AEMPS, the design, maintenance and management of the database, monitoring activities, the statistical analysis and corresponding statistical report.

Only a collection of patient data will be carried out. No intervention outside of normal clinical practice will be performed. No supplies of medication are needed.

The study does not entail any extraordinary expenses for the investigator or the site beyond the time spent by the investigator filling in the case report form with the required information.

All information relating to this project is considered confidential and the property of the sponsor until its publication. It may not be revealed to others without the prior written consent of the sponsor and may not be used for any reason other than for the execution of this project.

The results of this project will be published in scientific journals and/or presented at conferences.

The final decision to publish any article/abstract/presentation shall be made by the sponsor.

5. References

1. López-Abente G, Pollán M, Aragonés N et al. Situación del cáncer en España: incidencia. An Sist Sanit Navar 2004; 27 (2): 165-173.
2. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2017;28(suppl_4):iv1-iv21.
3. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, et al, for the PACIFIC Investigators. Durvalumab after chemoradiotherapy in stage III non-small cell lung cancer. New England Journal of Medicine 2017; 377:1919-1929.
4. Antonia SJ, Villegas A, Daniel D, et al. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. N Engl J Med. 2018 Dec 13;379(24):2342-2350.
5. Collen C, Schallier D, De Ridd M. Concurrent chemoradiation in inoperable, locally advanced non-small cell lung cancer comparison of efficacy and toxicity in the elderly. Lung Cancer 2012;8(1):39–41.

6. De Ruysscher D, Botterweck A, Dirx M, Pijls-Johannesma M, Wanders R, Hochstenbag M, Dingemans AM, Bootsma G, Geraedts W, Simons J, Pitz C, Lambin P. Eligibility for concurrent chemotherapy and radiotherapy of locally advanced lung cancer patients: a prospective, population-based study. Annals of Oncology 2009;20(1):98-102.

7. Protocol amendments

All changes made to the protocol must be the subject to a written amendment that shall be signed by the coordinating investigator and the sponsor and filed together with the protocol. In some cases, the amendment may require that changes be made to the informed consent document too. Any changes made to this protocol shall be reported to the IRB/EC that performed its review. In the case of substantial amendments, those that affect the objectives, methods or ethical considerations shall be subject to a new evaluation by the IRB/EC that approved it, and administrative authorization shall be sought for the amendment. For amendments that do not affect these aspects, the IRB/EC will be notified, giving the reasons why the amendment is not considered substantial.

6. Practical considerations

a. Follow-up and final reports

The definitive closure of this study will occur once all the data of the last patient included in the study has been collected. After closing the database, the statistical analysis shall be carried out and a report submitted, that will be reviewed and approved by the study sponsor and coordinating investigator.

b. Publication and results

The results of this study will be published in scientific journals and/or presented at conferences.

The final decision to publish any manuscript/abstract/presentation shall be made by the sponsor and allowing an internal review and comments to be made. All manuscripts/abstracts/presentations must be sent for internal review by the sponsor at least forty-five calendar days prior to submission.

The sponsor may delay the publication or presentation for a limited period in order to protect the confidentiality or protected nature of any of the information contained therein.

C. Trial Master File and Investigator's Site File

The documentation related to the post-authorization study constitutes the trial master file that contains the essential documents that allow the evaluation of the realization of a post-authorization study and the quality of the data obtained. These documents must demonstrate the compliance by

the researcher and the sponsor of the established requirements for post-authorization studies. The sponsor and the principal investigator (researcher) will keep the essential documents and material of each study for at least five years after its completion, or during a longer period if necessary, by other applicable requirements.

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