Spanish Real World Data on unresectable stage III NSCLC patients treated with durvalumab after chemoradiotherapy (S-REAL Study)

First published: 11/01/2021

Last updated: 02/07/2025

Study Finalised

Administrative details

EU PAS number

EUPAS38961

Study ID

38962

DARWIN EU® study

No

Study countries

- Spain

Study description

Lung Cancer represent approximately 13% of total cancer diagnoses worldwide. Stage III represents between 25-30% of NSCLC and the majority of them are unresectable. The SOC in unresectable patients was chemoradiotherapy consurrently if possible. The PACIFIC study is a phase III study to evaluate the efficacy and safety of durvalumab as a sequential therapy concurrent platinum-based chemo and thoracic RT. The study was positive for both primary endpoints PFS and OS. After that, it was decided to open an early acces program to provide acces to durvalumab for patients with locally advanced, unresectable NSCLC (stage III) who have not progressed following chemoradiation. S-Real study is a non-interventional, observational, multicentre, one-arm, non-comparative, and retrospective study.This observational study is based on the collection of data about the patients treated with Durvalumab after chemoradiotherapy in the real world. The study will include all patients who have participated in the Pacific study between 1 September 2017 up to 21 December 2018 and have received at least 1 dose of durvalumab. The primary objective is to assess affectiveness of durvalumab in patients treated in real-life settings by evaluating Progression Free Survival. Secondary objectives are:To assess effectiveness of durvalumab in patients treated in real-life settings by evaluating 1-year survival rate, to describe adverse events of special interests, to stimate time and sites of disease progression or relapse in metastatic setting, to describe details on durvalumab treatment, to describe demographic and clinical characteristics of stage III unresectable NSCLC patients treated with Durvalumab, to describe previous chemoradiotherapy strategy, to describe the baseline staging status, to further assess subsequent treatments pattern at the time of disease progression including duration and type of therapy, and to explore healthcare resource utilization while on durvalumab treatment.

Study status

Finalised

Research institutions and networks

Institutions

Fundación Grupo Español de Cáncer de Pulmón (GECP)

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Pilar Garrido

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 14/02/2020

Study start date

Actual: 25/05/2020

Data analysis start date

Actual: 31/12/2020

Date of final study report

Planned: 31/12/2021

Actual: 20/09/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AstraZeneca

Study protocol

Protocol_S-REAL_ENG_v.1.0_09Jan2020_FP.pdf (527.93 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

GEC-DUR-2020-01

ClinicalTrials.gov NCT04285866

Link to Clinicaltrials.gov

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Primary data collection

Study design:

The S-REAL study was a Spanish multicentre, observational, retrospective study on patients with unresectable stage III LA-NSCLC treated in 39 participating centres who were enrolled in Spanish early access program for durvalumab (10 mg/kg every 2 weeks) between 1 September 2017 and 21 December 2018

Main study objective:

Primary Objective of S-REAL study: 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 Spanish early access program) to the date of investigator-determined disease progression or death (if no progression) or the end of follow-up.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

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

Study drug and medical condition

Medicinal product name

IMFINZI

Study drug International non-proprietary name (INN) or common name

DURVALUMAB

Anatomical Therapeutic Chemical (ATC) code

(L01XC28) durvalumab

durvalumab

Medical condition to be studied

Non-small cell lung cancer stage III

Population studied

Short description of the study population

The study population are unresectable stage III non-small cell lung cancer patients treated with durvalumab after chemoradiotherapy. For patients with no prior PD-L1 available, a PD-L1 testing will be done using archived tissue samples from diagnosis, when available.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. The S-REAL study was a Spanish multicentre, observational, retrospective study on patients with unresectable stage III locally advanced non-small cell lung cancer treated in 39 participating centres who were enrolled in an Spanish early access program for durvalumab between 1 September 2017 and 21 December 2018. A total of 251 patients were screened; 244 met the study criteria and were included in data analyses.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)

- Adults (85 years and over)

Estimated number of subjects

250

Study design details

Setting

The heterogeneity of unresectable stage III NSCLC and the diversity of multidisciplinary treatment approaches used in the real-world setting justify the need to collect data from independent cohorts of patients to obtain a more detailed characterization. To achieve this goal, we performed this study to assess the real-world effectiveness and tolerability of durvalumab in a cohort of 244 patients with unresectable stage III NSCLC enrolled in a Spanish early access program. The S-REAL study was a Spanish multicentre, observational, retrospective study on patients with unresectable stage III LA-NSCLC treated in 39 participating centres who were enrolled in an EAP for durvalumab between 1 September 2017 and 21 December2018. A total of 251 patients were screened; 244 met thestudy criteria and were included in data analyses. In April2021, data collected in this study were integrated into the global analyses performed in the international real-world PACIFIC-R study .

The aim of the study was to determine the effectivenessof at least 1 dose of durvalumab in unresectable stage III

LA-NSCLC patients after completion of CRT. In addition, we also aimed to characterize this patient population and the routine management and regimen patterns used to treat their disease. Data were obtained retrospectively and during one routine clinical visit from the electronic medical records of the 39 participating hospitals. The index date was defined as the date on which

patients in the EAP received the first dose of durvalumab. Patients were followed from the index date to the end of follow-up.

Outcomes

A total of 244 patients with unresectable stage III NSCLC enrolled in the EAP that received at least one dose of durvalumab after definitive CRT were included for analysis. The median follow-up from the start of durvalumab was 21.9 months [range 1.2–34.7] and only 2 patients (0.8%) were lost to follow-up. Baseline characteristics of patients at the time of EAP inclusion are median age of patients was 67.0 years at the time of EAP inclusion, and 18% were over 75 years. Most patients were men (79.9%), and the majority (97%) were current or former smokers. At the time of initial NSCLC diagnosis, 47.3% of patients presented nonsquamous histology and 92.7% had stage III disease. The most prevalent comorbidity was hypertension (39.3%), followed by chronic obstructive pulmonary disease (23.8%). From the total of patients tested for EGFR mutational status
(n = 98), 2% had an EGFR-sensitizing mutation. From a total of 176 patients (72.1%) tested for PDL1-
expression, 72.2% presented PD-L1 ≥ 1% (PD-L1 positive patients), 19.9% had PD-L1 < 1%, and 8.0% had
unknown PD-L1 levels. In general, baseline characteristics were similar across both PD-L1 subgroups. One hundred seventy patients (69.7%) had received concurrent CRT (cCRT) and 38 patients (15.6%), sequential CRT (sCRT). The median dose of RT received was 66 Gray (Gy) delivered in a median of 33 fractions.
After CRT, most patients achieved a partial response (76.8%) and 18.6% presented stable disease. Overall, 97.6% of patients with available data had not progressed. All patients had received platinum based regimens of CT. Median time to start of durvalumab after CRT was 72 days. Only 5.6% of patients

started treatment within
42 days of CRT completion, and 94.4% were treated outside the 42-day window. Median duration of durvalumab treatment was 10.5 months. Overall, 44.7% of patients completed 12 months of planned durvalumab regimen and received a median of 19 infusions.

Data analysis plan

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. -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).

Summary results

A total of 244 patients were followed up for a median of 21.9 months [range 1.2–34.7]. Median duration of durvalumab was 45.5 weeks (11.4 months) [0–145]. Median PFS was 16.7 months (95% CI 12.2–25). No remarkable differences in PFS were observed between patients with programmed cell death-ligand 1 (PD-L1) expression ≥ 1% or < 1% (16.7 versus 15.6 months, respectively). However, PFS was higher in patients who had received prior concurrent CRT (cCRT) versus sequential CRT (sCRT) (20.6 versus 9.4 months).

AESIs leading to durvalumab discontinuation were registered in 11.1% of patients.
These results are in line with prior published evidence and confirm the benefits of durvalumab in the treatment
of LA-NSCLC patients in a real-world setting. We also observed a lower incidence of important treatment associated toxicities, such as pneumonitis, compared with the pivotal phase III PACIFIC clinical study.

Documents

Study report

CTO_1Febrero2024 (002).pdf (1.08 MB)

Study publications

Clinical and Translational Oncology paper

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Other data source

Data source(s), other

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

Data sources (types)

Other

Data sources (types), other

The sample of patients identified for the current study will be based on a portion of patients enrolled into the durvalumab PACIFIC study and no hypothesis and power analysis will be conducted. The study will include all patients who have participated in the PACIFIC study between 1 September 2017 up to 21 December 2018 and have received at least 1 dose of durvalumab

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction

Data characterisation details

Missing values were not considered when calculating percentages or any other descriptive estimator, meaning
that only valid values are presented. No methods for handling missing data were used. The analysis was performed
using IBM SPSS Statistics software, Version 26.0 (IBM Corp. Armonk, NY).