Clinical Study Report Synopsis

Drug Substance	Osimertinib (AZD9291)/ Durvalumab (MEDI4736)
Study Code	D5165C00001
Edition Number	1
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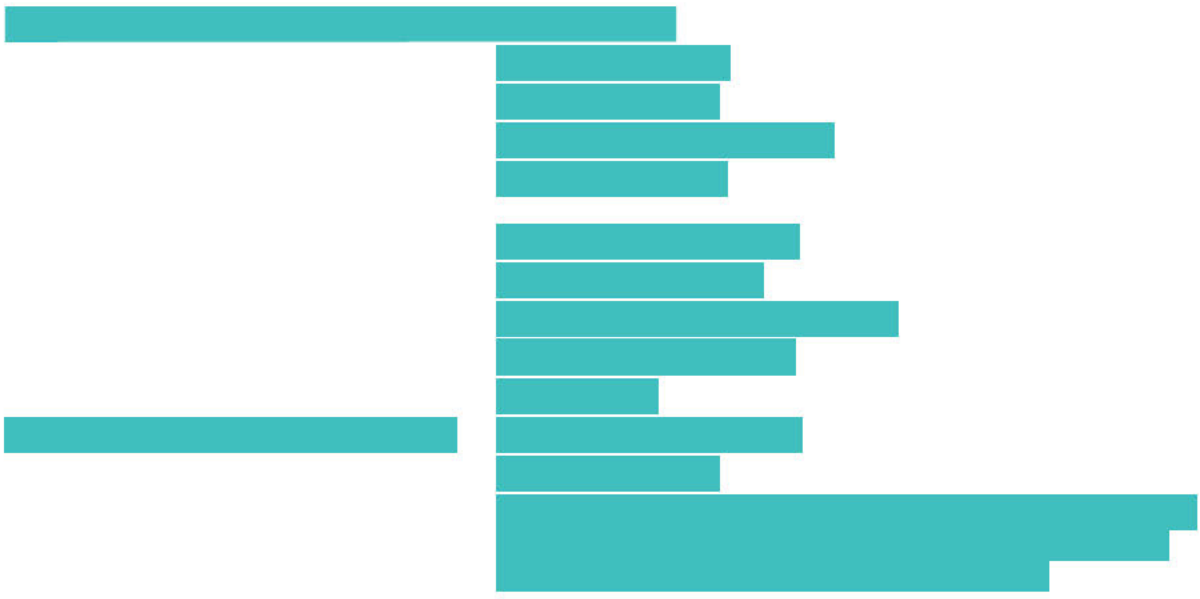
NCT Number	NCT02454933

A Phase III, Multi-Centre, Open-Label, Randomized Study to Assess the Efficacy and Safety of AZD9291 in Combination with MEDI4736 versus AZD9291 Monotherapy in Patients with Locally Advanced or Metastatic Epidermal Growth Factor Receptor T790M mutation-positive Non-Small Cell Lung Cancer who have received Prior Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Therapy (CAURAL)

Study dates: First subject enrolled: 26 August 2015
Last subject last visit: study is ongoing

Date of data cut-off 21 August 2017

Phase of development: Therapeutic confirmatory (III)



This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study design

This trial was initially designed as a Phase III multi-centre, open-label, randomised study to assess the efficacy and safety of osimertinib (80 mg, orally, once daily) in combination with durvalumab (10 mg/kg IV infusion every 2 weeks) versus osimertinib monotherapy (80 mg, orally, once daily) in patients with a confirmed diagnosis of Epidermal Growth Factor Receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC; Stage IIIB-IV), who had progressed following prior therapy with an approved EGFR-Tyrosine Kinase Inhibitor (TKI) agent.

However, due to the results of the osimertinib plus durvalumab combination arm of the D1560C00006 (TATTON) trial, that showed an increased incidence of interstitial lung disease (ILD) in a subset of patients similar to those patients recruited to this study, recruitment was terminated early.

In light of the early recruitment termination, the Clinical Study Protocol was amended and 2 summaries of the study data were planned:

- A primary summary was performed with a data cut-off date representative of when the last country with active patients received ethics and regulatory approval for protocol Version 2.0. This summary is presented in this abbreviated Clinical Study Report (CSR) and reports data according to the randomised or actual treatment groups.

- A final addendum summary to this abbreviated CSR will be produced when the last patient discontinues durvalumab and completes their required safety follow up. All outputs from the primary summary will be repeated, except those relating to change in tumour size at 6 weeks, which have been fully reported in this CSR. As there are ≤3 patients for specific data, listings will be provided in place of summaries. Only data collected between the primary summary data cut-off and the time when last patient receiving durvalumab reaches the end of safety follow up, will be summarised.

Target subject population and sample size

Three hundred and fifty patients were planned to be enrolled in this Phase III, multi-centre, open-label, randomised study. Patient enrolment was to consist of 2 populations:

- Second line cohort: Approximately 100 patients with T790M+ NSCLC who had progressed following an approved first-line EGFR-TKI treatment but who had not received further treatment

- Third line or higher cohort: Approximately 250 patients with T790M + NSCLC who had progressed following prior therapy with an approved EGFR-TKI and an additional anti-cancer treatment. Patients may have also received additional lines of treatment.

However, due to the early recruitment termination, at the time of the data cut-off, a total of 60 patients had been screened and 29 patients were randomised.

Investigational product and comparator(s): dosage and mode of administration

Osimertinib monotherapy arm: osimertinib 80 mg, orally, once daily.

Osimertinib + durvalumab arm: osimertinib (80 mg, orally, once daily) in combination with MEDI4736 (10 mg/kg intravenous infusion every 2 weeks).

Duration of treatment

Patients were able to continue dosing with study treatments as long as they were continuing to show clinical benefit, as judged by the Investigator.

Subject population

Overall, 60 patients were consented for screening and of these 31 were screen failures. Of the 29 patients who received treatment, 13 (44.8%) were ongoing in the study at the data cut-off (9 patients in the osimertinib group and 4 patients in the osimertinib + durvalumab group). Sixteen (55.2%) patients discontinued osimertinib treatment during the study: 12 (41.4%) patients due to progressive disease, 2 (6.9%) patients due to adverse events (AEs) and 2 (6.9%) patients due to withdrawal by subject. Nine (31.0%) patients discontinued durvalumab treatment during the study due to progressive disease, AEs and withdrawal by subject (3 [10.3%] patients each); 8 of these 9 patients also discontinued osimertinib during the study.

Summary of efficacy results

Overall, 21 (72.4%) patients had a confirmed response; 12 (80.0%) patients in the osimertinib group and 9 (64.3%) patients in the osimertinib + durvalumab group.

[redacted]

Summary of safety results

In the safety analysis set, AEs were reported in all 29 patients. The most frequently reported AEs were diarrhoea, dermatitis acneiform, [redacted]

[redacted]

[redacted] With the exception of one SAE of ILD, [redacted] were considered by the Investigator as unrelated to study treatment.

[redacted]

There were no other significant AEs determined for this study.

Conclusion(s)

- Due to the early termination of the study, and thus the limited number of patients included, differences between the treatment groups in terms of safety and efficacy could not be established.

- No new safety findings were observed for osimertinib as monotherapy or in combination with durvalumab.