Clinical Study Report Synopsis	
Drug Substance	Osimertinib (AZD9291)
Study Code	D5164C00001
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A Phase III, Double-blind, Randomized, Placebo-Controlled Multi-centre, Study to Assess the Efficacy and Safety of AZD9291 versus Placebo, in Patients with Epidermal Growth Factor Receptor Mutation Positive Stage IB-IIIA Non-small Cell Lung Carcinoma, following Complete Tumour Resection With or Without Adjuvant Chemotherapy (ADAURA)

Study dates:
First subject enrolled: 21 October 2015
Last subject last visit: Not applicable
The analyses presented in this report are based on a data cut-off date of 17 January 2020 and database lock date of 24 June 2020.

Phase of development:
Therapeutic confirmatory (III)

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

Study centre(s)

Patients were enrolled in the study globally at 185 study centres in 24 countries across Europe, Asia-Pacific, North America, and South America.

Publications

Roy S. Herbst, Masahiro Tsuboi, Thomas John, Christian Grohé, Margarita Majem, Jonathan Wade Goldman, Sang-We Kim, Dominika Marmol, Yuri Rukazenkov, and Yi-Long Wu Journal of Clinical Oncology 2020 38:18 suppl, LBA5-LBA5.

Objectives and criteria for evaluation

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Presented in the CSR			
Primary	Efficacy	To assess the efficacy of osimertinib compared to placebo as measured by disease-free survival (DFS)	• DFS by investigator assessment A sensitivity analysis of DFS and subgroup analyses are also conducted comparing DFS between the treatments in specific subgroups of patient demographics, patient/disease characteristics, and mutation status.
Secondary	Efficacy	To further assess the efficacy of osimertinib compared with placebo	• DFS rate at 2, 3, 4, and 5 years (*) • Overall survival (OS) • OS rate at 2, 3, 4 and 5 years (*)
Secondary	HRQoL	To assess the effect of osimertinib compared with placebo on health-related quality of life (HRQoL)	• Changes in generic HRQoL as measured by the SF-36 (version 2, standard) The primary HRQoL outcome measures of interest are time to deterioration of the 2 aggregated summary scores (Mental Component Score [MCS] and Physical Component Score [PCS]).
Secondary	PK	To characterise the pharmacokinetics (PK) of osimertinib and its metabolites (AZ5104 and AZ7550)	• Plasma concentrations of osimertinib, and metabolites AZ5104 and AZ7550; and ratio of metabolite to osimertinib for each PK sample collected • Ratio of metabolite to osimertinib are calculated at pre-dose, and at 0.5-1.5 and 2-4 hours post-dose (**)
Safety	Safety	To assess the safety and tolerability profile of osimertinib compared with placebo	• Adverse events (graded by CTCAE v4.03) • Clinical chemistry, haematology and urinalysis • Vital signs, Physical Examination, Weight • Digital ECG • Left ventricular ejection fraction (LVEF) • WHO Performance Status • Ophthalmologic assessment • These safety data are assessed for all patients who received at least 1 dose of study drug.
Exploratory	Health resource use	To compare health resource use associated with osimertinib treatment versus placebo	• Health Resource Use Module

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Exploratory	Efficacy	To compare the effects of osimertinib with placebo on post recurrence outcomes.	• Time to next treatment(s) • Type of recurrence (local/regional or distant) • Site(s) of relapse • Type of next treatment(s) (including procedures, radiotherapy, and anticancer agents) • Progression-free survival (PFS), as determined by investigator assessment
To be reported separately at a later date (if relevant)			
Exploratory	Efficacy	To further assess the efficacy of osimertinib compared with placebo (***)	• OS • OS rate at 2, 3, 4, and 5 years These endpoints are to be evaluated approximately 1 year post-primary analysis data cut-off date.
Exploratory	Efficacy	To assess the efficacy of osimertinib in patients with confirmed baseline T790M status (positive / negative) using a high sensitivity method yet to be determined (retrospective)	• DFS by investigator assessment • OS
Exploratory	Pharmaco-genetics	To collect and store biopsy material (multiple cores where possible) from all screened patients for exploratory analysis of molecular mechanisms associated with development of NSCLC and response to treatment	• Key genetic and proteomic markers to include, but not limited to, EGFR mutations, human epidermal growth factor receptor 2 (HER2), and protooncogene encoding Hepatocyte Growth Factor Receptor (cMET) expression and/or amplification. • Data generated may be reported separately and may also form part of a pooled analysis with other osimertinib studies.
Exploratory	Biomarker research	To collect and store tumour and plasma samples for potential exploratory research into factors that may influence susceptibility to development of NSCLC and/or response to osimertinib (where response is broadly defined to include efficacy, tolerability or safety) and to assess the relationship between bloodborne biomarkers and selected efficacy endpoints. Tissue and plasma samples may be used to support diagnostic development. (****)	• Evaluate the feasibility of using circulating DNA, RNA, and/or protein (including but not limited to ctDNA) profiling approaches for detection of minimal residual disease (MRD) in early-stage NSCLC patients after completion of surgery (and chemotherapy in eligible patients). Investigate whether detection of MRD is impacted by tumour staging or adjuvant chemotherapy. • Assess dynamics of circulating DNA, RNA, and/or protein as a proof of principle for early prediction of disease recurrence in the adjuvant setting. Investigate how circulating DNA, RNA, and/or protein relates with other efficacy endpoints, including DFS based on detection of tumour recurrence using imaging approaches. • Investigate the prognostic value of DNA, RNA, and/or protein features in predicting response to osimertinib in the adjuvant setting using baseline tumour tissue samples.
Exploratory	Biomarker research	To compare the baseline tumour EGFR mutation status in all randomized patients with evaluable results from baseline plasma.	• Comparison of EGFR mutation status between tumour deoxyribonucleic acid (DNA) and plasma derived ctDNA.

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Exploratory	Biomarker research	To compare plasma-derived ctDNA EGFR mutation status at baseline and at disease recurrence.	• Comparison of EGFR mutation status in plasma samples at baseline and at disease recurrence.
Exploratory	Biomarker research	To assess any changes in EGFR mutation status (including T790M) using the mandated serial plasma samples coupled with a high sensitivity method yet to be determined (retrospective).	• Assessment of EGFR mutation status in serial plasma samples.
Exploratory	PK	To explore the relationship between PK and selected endpoints (which may include efficacy, safety, and/or PRO), where deemed appropriate.	• Correlation of PK with other primary/ secondary/ exploratory endpoints in patients treated with osimertinib.

(*) Note: This endpoint reflects the latest description in CSP Version 3.0, which was updated at the time of CSP Amendment 2 (see Appendix 16.1.1). Changes from the original endpoints described in CSP Version 1.0 were to include an additional pre-planned DFS rate analysis at a 4 year timepoint, and additional pre-planned OS rate analyses at 2, 3, and 4 year timepoints. However, given the IDMC recommendation to complete a full analysis of efficacy and safety earlier than scheduled, only the DFS and OS rates at timepoints up to 3 years are included in this CSR.

(**) This analysis was pre-planned; however, based on a comprehensive evaluation of all available data from completed clinical studies in March 2019, it was decided to discontinue further bioanalysis of metabolite AZ7550 in all osimertinib studies; hence, for samples analysed after March 2019 (including in the current study) this metabolite was not measured, and is therefore the ratio of AZ7550 to osimertinib is summarised only for subjects who had available data.

(***) This objective and corresponding endpoints was introduced in CSP Amendment 2 (reflected in CSP Version 3.0; see Appendix 16.1.1).

(****) Note: This objective reflects the latest description in CSP Version 3.0, which was updated at the time of CSP Amendment 2 (see Appendix 16.1.1). Changes from the original objective described in CSP Version 1.0 were to specify the biological material to be collected (tumour and plasma samples), and to include the definition of 'response'. It was also specified that these data may contribute to future diagnostics development. The corresponding endpoints were also updated to provide details of more specific analyses to be performed in support of the objective.

Study design

ADAURA is an ongoing, phase 3, double-blind, randomised, placebo-controlled study, designed to assess the efficacy and safety of osimertinib versus placebo in patients with stage IB-IIIA epidermal growth factor receptor mutation positive (EGFRm) non-small cell lung cancer (NSCLC) who have undergone complete tumour resection, with or without postoperative adjuvant chemotherapy.

Approximately 700 patients were planned to be randomised, under the assumption that approximately 60% of patients will be recruited from Asia and 40% from non-Asian countries. The proportion of patients randomised with stage IB cancer and stages II-IIIA cancer was to be 30% and 70%, respectively. Patients were stratified by disease stage (IB vs. II vs. IIIA), mutation type status (Ex19del or L858R), and race (Asian or non-Asian).

Patients were randomised 1:1 (using an interactive voice response system [IVRS]) to receive either osimertinib (80 mg, oral, once daily) or matching placebo. Patients must have sufficiently recovered from surgery and completed any standard-of-care adjuvant chemotherapy (if applicable) prior to randomisation; and must have been randomised within 10 weeks of complete surgical resection (if adjuvant chemotherapy was not administered), or within 26 weeks if adjuvant chemotherapy (comprising platinum-based doublet treatment, for a maximum of 4 cycles) was administered.

Regular Independent Data Monitoring Committee (IDMC) meetings took place during the study to monitor safety data, and a scheduled event-based futility analysis took place to support the 6th IDMC meeting in February 2019. AstraZeneca remained blinded to the data at this time, and did not see the results of this analysis. After ruling out futility, the IDMC made an ad hoc request to re-evaluate key efficacy data (Kaplan-Meier [KM] curves for disease-free survival [DFS] and key recurrence data tables) at their 7th meeting (IDMC-7), which was conducted on 07 April 2020 with a DCO date of 17 January 2020. Following IDMC-7, the IDMC made a recommendation that due to the overwhelming benefit observed in osimertinib-treated patients in the primary (stage II-IIIA disease) and overall populations, a full analysis of efficacy and safety should be performed by Sponsor as soon as possible for public disclosure. Of note, patients and investigators remain blinded to individual treatment allocations, and the study is continuing as originally planned.

Target subject population and sample size

The target population was male or female adult patients with stage IB-IIIA NSCLC with a centrally confirmed common sensitising EGFR mutation (Ex19del and/or L858R, either alone or in combination with other EGFR mutations), who have undergone complete tumour resection, with or without postoperative adjuvant chemotherapy.

This study was sized to characterise DFS (based on investigator assessment), assessed primarily in a subset of patients with stage II-IIIA cancer, and additionally in the overall population (additional comprising patients with stage IB disease).

The study was event-driven, with approximately 247 disease recurrence events required in approximately 490 stage II-IIIA patients (ie, non-IB) in the FAS at the planned time of the primary analysis (50% maturity). The original sample size calculation was based on the assumption that if the true DFS hazard ratio (HR) for the comparison of osimertinib versus placebo in this patient population was 0.70, then 247 disease recurrence events at the time of the primary analysis would provide 80% power to demonstrate a statistically significant difference in DFS at a 5% 2-sided significance level, which could translate to an improvement in median DFS from 40 months to 57 months, assuming DFS is exponentially distributed. Under these conditions, the minimum DFS HR that would be statistically significant ($p < 0.05$, 2-sided) was 0.78.

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

	Osimertinib	Placebo
Study treatment name:	AZD9291	AZD9291-matching placebo
Dosage formulation:	80 mg tablets 40 mg tablets	N/A
Batch numbers:	Blinded 80 mg tablets: CCI Blinded 40 mg tablets: CCI	Placebo 80 mg matching tablets: CCI Placebo 40 mg matching tablets: CCI
Provider:	AstraZeneca	AstraZeneca
Route of administration:	Oral	Oral
Dosing instructions:	Patients were instructed to swallow 1 tablet daily. Tablets should be taken whole with approximately 240 mL water, with or without food. Doses are to be taken approximately 24 hours apart, at the same time point each day. Doses should not be missed. If a patient misses a scheduled dose, within a window of 12 hours, it is acceptable to take the dose. If it is more than 12 hours after the scheduled dose time, the missed dose should not have been be taken, and patients are instructed to take the next dose at the next scheduled time. If a patient vomits after taking their study drug, they are not to make up for this dose, but should take the next scheduled dose. Any changes from the dosing schedule, dose interruption or dose reduction are recorded in the eCRF. On site visit days on which PK samples were scheduled, dosing was delayed until arrival at the site. Patients were not to take their dose until instructed to do so by the site personnel.	
Packaging and labelling:	Tablets are packed in high-density polyethylene (HDPE) bottles, with child-resistant closures. Bottles are dispensed to patients in the AstraZeneca packing provided. The packaging included bottles, caps, and a label. Bottle tampers should not have been broken prior to dispensing the study drug to a patient. Labels are in accordance with Good Manufacturing Practice (GMP) and local regulatory guidelines. Label text is translated into local language, as applicable. The label includes the Name of the Sponsor, Study Code, 'For Clinical Trial use only', and/or any other market specific requirements.	

Duration of treatment

All patients receive randomised treatment until recurrence of disease, a treatment discontinuation criterion was met, or the 3-year (156 weeks) treatment period was completed.

Statistical methods

The primary endpoint of DFS and secondary endpoint of overall survival (OS) were to be tested in a subset of patients with stage II-IIIA disease at the time of diagnosis, as well as in the overall population. In order to strongly control the type I error at the 5% 2-sided level, a hierarchical testing procedure was employed across these endpoints. The hierarchical testing procedure was ordered such that DFS in stage II-IIIA patients was tested first using the full alpha. DFS in the overall population was subsequently only to be tested if statistical significance was shown for DFS in patients with stage II-IIIA disease at the time of diagnosis. Overall survival (in both populations) was only to be tested if statistical significance was shown for DFS in the overall population.

Following the IDMC recommendation to complete a full analysis of efficacy and safety earlier than scheduled, and in consultation with a major health authority, the SAP was updated following data unblinding. The alpha allocation required revision to control for the type I error to account for this unplanned interim analysis, which is based on a smaller number of disease recurrence events than originally planned for the primary analysis. No changes were made to the order of the hypothesis being tested.

Disease-free survival (as determined by the Investigator) was defined as the time from the date of randomisation until the date of disease recurrence or death (by any cause in the absence of recurrence). DFS in the subset of patients with stage II-IIIA cancer and in the overall population (equivalent to the Full Analysis Set [FAS]) was analysed using a log rank test stratified by stage, mutation type, and race. The effect of osimertinib versus placebo was estimated by the hazard ratio (HR) together with its 95% and (1-alpha) confidence intervals (CIs) and p-value. Kaplan-Meier plots of DFS in both stage II-IIIA patients and the overall population were presented by treatment group. Sensitivity analyses of DFS were performed to assess the presence of quantitative interactions, possible evaluation-time bias, and possible attrition bias.

Subgroup analyses were conducted by comparing DFS between treatments in the following planned groups: Stage (IB, II, IIIA), EGFR mutation type (Ex19del, L858R), Race (Asian, Non-Asian), Adjuvant chemotherapy (Yes, No), Gender (Male, Female), Age at screening (<65, ≥ 65), and Smoking history (Never, Ever). No adjustment to the significance level for testing was made since the subgroup analysis is only supportive of the primary analysis of DFS. For each subgroup level, the HR and 95% CI are calculated from a single Cox PH model that contains a term for treatment, the subgroup covariate of interest, and the treatment by subgroup interaction term. The HR is obtained for each level of the subgroup from this model.

Overall survival was defined as the time from randomisation to the date of death (from any cause). OS data were analysed using the same methodology and model as for the analysis of DFS.

Patient-reported HRQoL was a secondary variable and was assessed using the SF-36 questionnaire.

Safety and tolerability were assessed in terms of adverse events (AEs) (including serious adverse events [SAEs]), deaths, laboratory data, vital signs, LVEF measurements, electrocardiograms, WHO performance status, ophthalmologic assessment, and exposure. Data are summarised descriptively.

All analyses were based on a data cut-off date of 17 January 2020.

Subject population

The overall study population (FAS) comprised a total of 682 patients randomised to treatment in a 1:1 ratio (osimertinib arm: 339 patients; placebo: 343 patients) at 185 study centres in 24 countries, of whom 337 osimertinib arm patients and 343 placebo arm patients received at least 1 dose of study treatment (Safety Analysis Set). Out of the overall study population, 470 patients had stage II-IIIA disease (osimertinib: 233 patients; placebo: 237 patients).

At the DCO of this analysis (17 January 2020), 266 patients had discontinued their randomised study treatment prior to the planned 3-year treatment duration (osimertinib: 92 patients [27.3% of those who received treatment]; placebo: 174 patients [50.7%]). In the osimertinib arm, the most frequently reported reason for study treatment discontinuation was AE (36 patients). In the placebo arm, the most frequently reported reason for study treatment discontinuation was disease recurrence (148 patients).

Overall, 73 patients (10.7% of those who received treatment) had completed study treatment, which comprised similar numbers of patients in each treatment arm (osimertinib: 40 patients [11.9%]; placebo: 33 patients [9.6%]). At the DCO, the majority of patients were ongoing in the study (osimertinib: 309 patients [91.2% of randomised patients]; placebo: 307 patients [89.5%]).

Overall, the demographic and patient characteristics were well balanced between treatment arms and representative of the intended population of patients with stage IB-IIIA, EGFRm NSCLC who had undergone complete tumour resection. The majority of patients randomised in the study were female, and Asian, with a median age of 63.0 years (range 30 to 86 years). Approximately one third of patients randomised in the study had American Joint Committee on Cancer (AJCC; 7th Edition) stage IB disease, approximately one third had stage II disease, and approximately one third had stage IIIA disease at the time of diagnosis.

As expected, and in line with standard-of-care guidelines for the adjuvant treatment of NSCLC, 60.1% of overall population had received platinum-based doublet chemotherapy prior to randomisation.

Summary of efficacy results

The primary endpoint was DFS, with OS as a secondary endpoint. According to the pre-specified multiple testing procedure, the primary analysis of DFS was in the stage II-IIIA population, and analysis in the overall population (FAS) was a multiplicity-controlled secondary analysis. Similarly, the primary population for the OS analyses was the stage II-IIIA population, and the analysis in the overall population was secondary; both OS analyses were multiplicity-controlled.

At the DCO of the current analysis, in patients with stage II-IIIA disease, the majority of patients (98.7%) had had the opportunity for at least 1 year of follow-up, with 18.3% of patients having had the opportunity for at least 3 years of follow-up. In patients with stage II-IIIA disease, 26 patients (11.2%) in the osimertinib arm and 130 patients (54.9%) in the placebo arm had experienced a DFS event at the DCO of the current analysis. For these patients, a statistically significant and clinically meaningful improvement in DFS for patients randomised to receive osimertinib compared to patients randomised to receive placebo was observed (HR: 0.17; 99.06% CI: 0.11, 0.26; p-value < 0.0001), based on a total of 156 DFS events having been recorded in 470 evaluable patients (33.2% maturity of data). The KM estimate of median duration of DFS was not reached for patients in the osimertinib arm (95% CI: 38.8, NC) compared to 19.6 months (95% CI: 16.6, 24.5) for patients in the placebo arm, with a greater proportion of osimertinib arm patients alive and disease-free at all assessed timepoints compared with those in the placebo arm. Separation in the KM curves between the treatment groups was observed early (after the first scan at 12 weeks post-randomisation), with separation clearly maintained.

In the overall study population (FAS; all patients with stage IB-IIIA disease), almost all patients (99.1%) had had the opportunity for at least 1 year of follow-up, with 19.5% of patients having had the opportunity for at least 3 years of follow-up. In the overall study population, 37 patients (10.9%) in the osimertinib arm and 159 patients (46.4%) in the placebo arm had experienced a DFS event at the DCO of the current analysis. In this overall study population, a statistically significant and clinically meaningful improvement in DFS for patients randomised to receive osimertinib compared to patients randomised to receive placebo was observed (HR: 0.20; 99.12% CI: 0.14, 0.30; p-value < 0.0001), based on 196 DFS events having been recorded in 682 evaluable patients (28.7% maturity of data). The KM estimate of median duration of DFS was not reached in the osimertinib arm (95% CI: NC, NC) compared to 27.5 months (95% CI: 22.0, 35.0) in the placebo arm, with a greater proportion of osimertinib arm patients alive and disease-free at all assessed timepoints compared with those in the placebo arm. Separation in the KM curves between the treatment groups was observed early (after the first scan at 12 weeks post-randomisation), with separation clearly maintained. A benefit with osimertinib was consistently observed in all pre-specified subgroups with sufficient events for analysis (subgroups with < 20 events were excluded from the analysis).

In the osimertinib arm, the majority of disease recurrence events were local/regional only (in 23/37 patients). In the placebo arm, the majority of disease recurrence events (in 78/157 patients) were distant only. A variety of sites of tumour recurrence were reported in both treatment arms; the most common site of recurrence (in both treatment arms) was lung (osimertinib: 19 patients; placebo: 61 patients) and lymph nodes (osimertinib: 10 patients; placebo: 48 patients).

At the DCO of the current analysis, OS data are considered not mature, as only 29 events had been reported in the overall population (4.3% maturity of data). The majority of patients were still in survival follow up (616 patients [90.3%) overall: 309 patients [91.2%] in the osimertinib arm, and 307 patients [89.5%] in the placebo arm). At the DCO, 25 deaths had occurred in stage II-IIIA patients (5.3% maturity of data), comprising 8 patients (3.4%) in the osimertinib arm and 17 patients (7.2%) in the placebo arm. The HR was 0.40 (99.98% CI: 0.09, 1.83; p = 0.0244), which did not reach statistical significance (p-value < 0.0002 required).

Overall, HRQoL was maintained in both arms. More than 75% of stage IIA-IIIA patients in either arm did not experience a clinically meaningful deterioration in the Physical Component Score or death (osimertinib: 75.1%; placebo: 83.5%), or a clinically meaningful deterioration in the Mental Component Score or death (osimertinib: 77.7%; placebo: 78.1%) in the SF-36. There was no difference between the arms in the time to confirmed deterioration for the mental component or death. A trend of shorter time to confirmed deterioration for the physical component or death was observed in the osimertinib arm.

Summary of pharmacokinetic results

Osimertinib concentrations at pre-dose, 0.5-1.5 hr and 2-4 hr at Week 4, Week 24, Week 48, and Week 96 showed a flat profile, suggesting steady-state concentrations are maintained throughout the dosing period.

Summary of safety results

Per protocol, the maximum study treatment duration was 3 years (36 months). The median total duration of exposure to treatment was 22.5 months for patients in the osimertinib arm and 18.7 months for patients in the placebo arm. This is consistent with a longer median DFS in the osimertinib arm and is limited by the analysis being performed earlier than planned; the median follow up duration for the primary endpoint was 22.1 months in the osimertinib arm (FAS). Patients in the osimertinib arm had a longer exposure to study drug (609.5 treatment-years vs. 532.1 treatment-years for the placebo arm). The actual median exposure in the osimertinib arm was similar to the total median exposure, indicating that the frequency of dosing interruptions for any reason and their median duration had almost no impact on osimertinib exposure.

Whilst almost all patients treated with osimertinib reported an AE (97.6%), the majority were non-serious, mild or moderate in severity, and did not lead to treatment discontinuation. The majority of patients in the placebo arm (89.2%) also experienced at least 1 AE.

The most frequently reported (≥ 15% of patients) individual AEs in the osimertinib arm were diarrhoea, paronychia, dry skin, pruritus, cough, and stomatitis. These AEs have previously been identified as osimertinib ADRs, and no differences in nature of these AEs (in terms of reporting frequency and severity) was noted from the established osimertinib safety profile. The most frequently reported AEs in the placebo arm were diarrhoea and cough.

Overall, the proportion of patients who had a CTCAE ≥ Grade 3 AE was low in both treatment arms (osimertinib: 20.2%; placebo: 13.4%). The most common AEs of CTCAE ≥ Grade 3 were diarrhoea, stomatitis and pneumonia in the osimertinib arm, and pneumonia and hypertension in the placebo arm. Similarly, SAEs were reported in a comparable proportion of patients in both treatment arms (16.0% in the osimertinib arm, and 12.2% in the placebo arm), with pneumonia the most frequently reported SAE in both treatment arms.

None of the patients in the osimertinib arm were reported to have died from an AE. In the placebo arm, 1 patient (0.3%) was reported to have experienced an AE with a fatal outcome while on study treatment (pulmonary embolism, considered unrelated to study treatment by the reporting Investigator). The death of this patient was also attributed to disease progression by the Investigator.

Interstitial lung disease (grouped term) was reported in 10 patients (3.0%) in the osimertinib arm (Preferred Terms (PTs) of ILD in 8 patients and Pneumonitis in 2 patients), and 0 patients in the placebo arm. Adverse events of ILD (grouped term) were generally considered to be less clinically impactful to patients in the ADAURA study than previously observed in osimertinib clinical studies in the advanced/metastatic setting. All AEs of ILD in the current study were mild to moderate in severity, with patient recovery reported in all cases.

No notable differences between treatment arms were observed in relation to cardiac contractility (as characterised by LVEF measurements), and no new safety signal was identified from a review of AEs indicative of cardiac failure.

Whilst worsening Common Terminology Criteria for Adverse Events (CTCAE) grade shifts in haematology and clinical chemistry parameters were noted in both treatment arms (primarily 1- and 2-grade shifts), none of the changes in laboratory parameters were deemed to have a significant clinical impact on the individual patient by way of reporting of a concurrent AEs, or requiring any clinical intervention.

Conclusion(s)

This ongoing, phase 3, double-blind, randomised, placebo-controlled study in patients with stage IB-IIIA EGFRm NSCLC who have undergone complete tumour resection (with or without postoperative adjuvant chemotherapy) demonstrated:

- Patients randomised to osimertinib had a highly statistically significant and clinically meaningful improved DFS in comparison to patients randomised to placebo.
- Osimertinib has an acceptable safety and tolerability profile for treating patients with EGFRm NSCLC in the adjuvant setting, consistent with previous clinical studies and post-marketing experience in the advanced/metastatic setting.
- Overall, the benefit-risk balance was positive for long-term use in patients in the curative setting.