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Adjuvant osimertinib in patients with stage IB–IIIA EGFR mutation-positive NSCLC after complete tumour resection: ADAURA China subgroup analysis

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Objective

- To assess efficacy and safety data from an exploratory subgroup analysis of 159 Chinese patients enrolled in mainland China from ADAURA (NCT02511106)

Conclusions

- Demographics and characteristics in the China population were generally well balanced between treatment arms
  - Compared with the global population, a higher percentage of patients in the China population were aged <65 years, had stage IB disease and L858R mutation
  - Consistent with the global population, 67% of patients in the China population received adjuvant chemotherapy, in line with Chinese treatment guidelines for stage II / III NSCLC[9]
- Consistent with the global population, adjuvant osimertinib demonstrated a clinically meaningful improvement in DFS in Chinese patients with stage IB / II / IIIA EGFR mutation-positive (EGFRm) NSCLC
- The safety profile of osimertinib in Chinese patients was consistent with the global population and with the established safety profile of osimertinib
- **Efficacy and safety results in the ADAURA China population were consistent with the global population, supporting 3 years of adjuvant osimertinib as an effective treatment for Chinese patients with resected stage IB–IIIA EGFRm NSCLC**

Plain language summary

Why did we perform this research?

Osimertinib is a medication used to treat a type of non-small cell lung cancer (NSCLC), with a change (mutation) in the EGFR gene, known as EGFR-mutated NSCLC. In the ADAURA clinical study, which was conducted all over the world, participants had resectable EGFR-mutated NSCLC, which means they had tumours that can be removed by surgery. Participants had NSCLC that is described to be in the early stages of disease, classified as either stage IB, IIA/B or IIIA NSCLC. Participants in the study took either osimertinib or a placebo for up to 3 years after having their tumours surgically removed. Results from the study showed that participants who took osimertinib stayed cancer-free for longer than those who took the placebo. The proportion of Chinese patients with EGFR-mutated disease is reported to be higher than patients from the rest of the world. We conducted an analysis of patients from mainland China who participated in the ADAURA study to see whether they benefitted from osimertinib in a similar way to the global study population.

How did we perform this research?

We analysed how long Chinese participants taking part at study sites in China would remain alive and cancer-free with osimertinib, after having their tumours removed by surgery, and what side effects from taking osimertinib these participants experienced.

What are the findings of this research and what are the implications?

Results from Chinese participants in ADAURA were similar to the global population. There was an 82% reduction in the risk of the cancer returning or death in Chinese participants who took osimertinib compared with placebo. Chinese participants experienced similar side effects to those observed in the global population, which were consistent with what we already know about osimertinib. The findings show that osimertinib is a useful treatment for Chinese patients with stage IB / II / IIIA EGFR-mutated NSCLC.

Where can I access more information?

ADAURA (NCT02511106): https://clinicaltrials.gov/ct2/show/NCT02511106

Poster

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please click on the link below.

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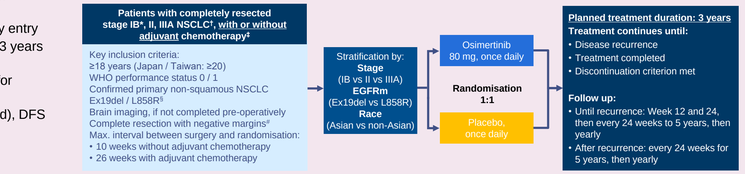
Introduction

- In Chinese patients with non-small cell lung cancer (NSCLC), the prevalence of epidermal growth factor receptor mutation-positive (EGFRm) disease is high (36–50%) compared with other parts of the world, such as Europe (14%) and the USA (24%)[1–4]
- Based on results from the global Phase III ADAURA study, osimertinib was approved for the adjuvant treatment of patients with stage IB–IIIA EGFRm (Ex19del/L858R) NSCLC after tumour resection[5–8]
  - Stage II / IIIA: disease free survival (DFS) hazard ratio (HR) vs placebo: 0.17 (99.06% CI 0.11, 0.26); p<0.0001
  - Stage IB–IIIA: DFS HR vs placebo: 0.20 (99.12% CI 0.14, 0.30); p<0.0001
- Here we present an exploratory efficacy and safety subgroup analysis of 159 Chinese patients enrolled in mainland China from ADAURA

Methods

- ADAURA enrolled adult patients with completely resected stage IB / II / IIIA EGFRm (Ex19del/L858R) NSCLC (**Figure 1**)[6]
- Adjuvant chemotherapy was allowed, per physician and patient choice before study entry
- Patients were randomised 1:1 to osimertinib 80 mg once daily or placebo for up to 3 years (treatment completion) or until disease recurrence or discontinuation
- Primary endpoint: DFS in stage II / IIIA patients (investigator assessed), designed for superiority under the assumed DFS HR of 0.70
- Secondary endpoints included: DFS in the overall population (investigator assessed), DFS at 2, 3, 4, and 5 years, overall survival, safety, health-related quality of life
- Statistical analyses for this China population subgroup were exploratory; p-values are nominal. Data cut-off was 17 January 2020
- The sample size of the China population was calculated to demonstrate consistency with the results of the global population (i.e. to provide at least 75% probability of a 50% retention of global effect size, in terms of the primary endpoint)

Figure 1. Study design



Patients were stratified based on entry of disease characteristics into the interactive voice response system at randomisation.
*Tumour ≥3 cm. †AJCC 7th edition. ‡Per physician and patient choice before study entry. Prior, post, or planned radiotherapy was not allowed; §Centrally confirmed in tissue.
#Patients received a CT scan after resection and within 28 days prior to treatment
AJCC, American Joint Committee on Cancer; DFS, disease-free survival; EGFRm, epidermal growth factor receptor mutation-positive; Ex19del, exon 19 deletion; HR, hazard ratio; NSCLC, non-small cell lung cancer; WHO, World Health Organization

Results and interpretation

Patients

- Of 682 patients randomised globally, 159 Chinese patients from 30 centres in mainland China were included in this subgroup analysis: osimertinib n=77, placebo n=82
- The full analysis set comprised all randomised patients. All 159 patients received at least one dose of study treatment
- Baseline characteristics were generally balanced across arms (**Table 1**). Compared with the global population, a higher proportion of patients in the China population were aged <65 years (74% vs 56%), had stage IB disease (43% vs 32%) and L858R mutation (58% vs 45%)

Table 1. Baseline characteristics (overall population)

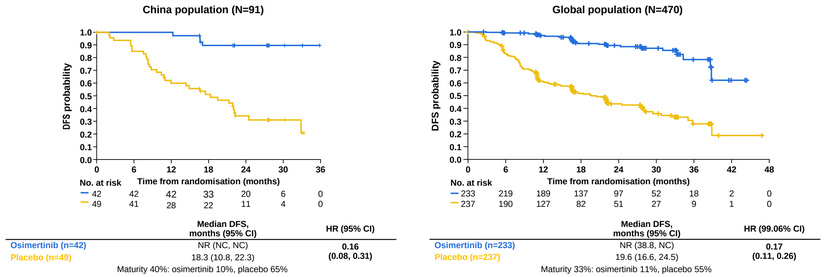
Characteristics, %	China population (N=159)		Global population (N=682)	
	Osimertinib (n=77)	Placebo (n=82)	Osimertinib (n=339)	Placebo (n=343)
Sex: male / female	40 / 60	40 / 60	32 / 68	28 / 72
Age: median (range), years	61 (32–78)	60 (31–76)	64 (30–86)	62 (31–82)
Age: ≥65 years	30	23	45	43
Smoking history*: yes / no	29 / 71	24 / 76	32 / 68	25 / 75
WHO PS: 0 / 1	56 / 44	62 / 38	64 / 36	64 / 36
AJCC staging at diagnosis (7th edition): IB / II / IIIA	45 / 21 / 34	40 / 28 / 32	32 / 34 / 35	32 / 34 / 34
EGFR mutation at randomisation†: Ex19del / L858R	47 / 53	38 / 62	55 / 45	55 / 45
Adjuvant chemotherapy: yes / no	62 / 38	71 / 29	60 / 40	60 / 40

*Global population smoking history: previous: osimertinib n=104, placebo n=83; current: osimertinib n=4, placebo n=3; never: osimertinib n=231, placebo n=257; China population smoking history: previous: osimertinib n=21, placebo n=20; current: osimertinib n=1, placebo n=0; never: osimertinib n=55, placebo n=62. †Central test.
AJCC, American Joint Committee on Cancer; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; PS, performance status; WHO, World Health Organization

Efficacy

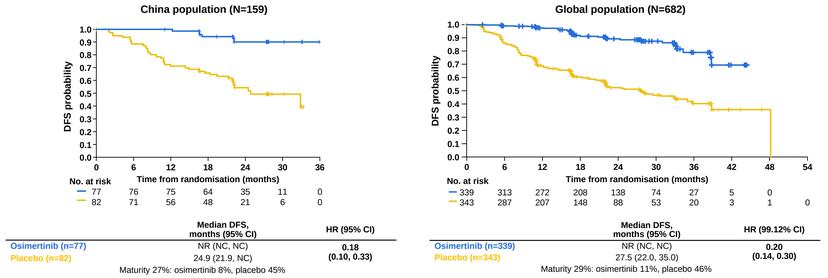
- In the China population, osimertinib demonstrated an improvement in DFS vs placebo in patients with stage II / IIIA disease and in the overall population (stage IB / II / IIIA) (**Figures 2 and 3**). A DFS benefit was observed across all pre-specified patient subgroups with sufficient events for analysis (**Figure 4**)

Figure 2. Primary endpoint: DFS in patients with stage II / IIIA NSCLC



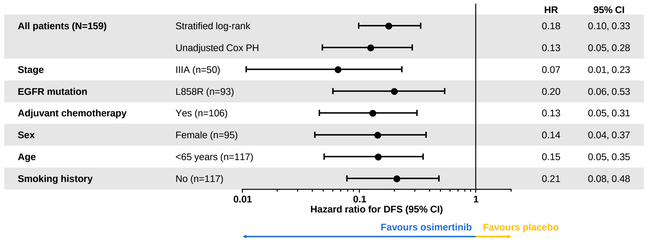
CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; NC, not calculable; NR, not reached; NSCLC, non-small cell lung cancer

Figure 3. Secondary endpoint: DFS in patients with stage IB–IIIA NSCLC



CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; NC, not calculable; NR, not reached; NSCLC, non-small cell lung cancer

Figure 4. China population – DFS across subgroups (stage IB–IIIA)



Performed using a Cox proportional hazards model including treatment, subgroup and a treatment-by-subgroup interaction term. Includes all pre-specified subgroups with sufficient events for analysis (≥20 DFS events). A hazard ratio of less than 1 favours osimertinib.
CI, confidence interval; DFS, disease-free survival; EGFR, epidermal growth factor receptor; HR, hazard ratio; PH, proportional hazards

Safety

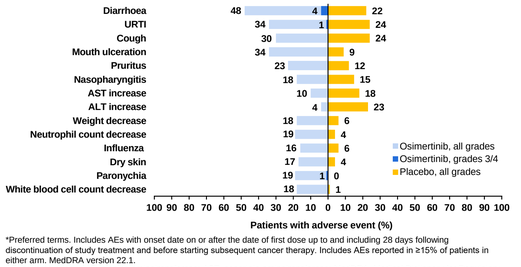
- In the China population, the median duration of exposure for osimertinib and placebo was 26.1 months (range: 0–36) and 22.8 months (0–36), respectively. In the global population the median duration of exposure for osimertinib and placebo was 22.5 months (0–38) and 18.7 months (0–36), respectively
- The safety profile of osimertinib was consistent with the global population (**Table 2; Figure 5**)
- In the China population, Grade 2 interstitial lung disease (grouped term) was reported in one (1%) patient in the osimertinib arm
- QTc prolongation was reported in 5 (6%) patients in the osimertinib arm and one (1%) patient in the placebo arm

Table 2. Safety summary

AE, any cause, n (%)	China population (N=159)		Global population (N=680)	
	Osimertinib (n=77)	Placebo (n=82)	Osimertinib (n=337)	Placebo (n=343)
Any AE	77 (100)	81 (99)	329 (98)	306 (89)
Any AE CTCAE grade ≥3	19 (25)	14 (17)	68 (20)	46 (13)
Any AE leading to death	0	0	0	1 (<1)
Any serious AE	15 (19)	12 (15)	54 (16)	42 (12)
Any AE leading to discontinuation	4 (5)	2 (2)	37 (11)	10 (3)
Any AE leading to dose reduction	6 (8)	0	29 (9)	3 (1)
AE, possibly causally related*, n (%)				
Any AE	73 (95)	64 (78)	305 (91)	192 (56)
AE CTCAE grade ≥3	5 (6)	1 (1)	32 (9)	8 (2)
Any AE leading to death	0	0	0	0
Any serious AE	2 (3)	1 (1)	8 (2)	2 (1)

Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category counted once in each of those categories. MedDRA version 22.1. CTCAE version 4.03. *As assessed by the investigator. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities

Figure 5. China population – all causality adverse events* (≥15% of patients)



*Preferred terms. Includes AEs with onset date on or after the date of first dose up to and including 28 days following discontinuation of study treatment and before starting subsequent cancer therapy. Includes AEs reported in ≥15% of patients in either arm. MedDRA version 22.1.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MedDRA, Medical Dictionary for Regulatory Activities; URTI, upper respiratory tract infection

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Disclosures

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