LBA57 Overall survival results of ceritinib in ALKi-naïve patients with ALK-rearranged NSCLC (ASCEND-3)

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Background: The previous analysis of phase 2, ASCEND-3 study (NCT01685138; data cutoff: November 15, 2015) demonstrated prolonged median progression-free survival (mPFS) with ceritinib 750 mg/d (fasted) in ALKi-naïve patients with ALK+ NSCLC, who had received ≤3 prior lines of chemotherapy. The current analysis (data cutoff: January 22, 2018) from ASCEND-3 study reports the final safety and efficacy results including overall survival (OS).

Methods: ASCEND-3 is a multicenter, single-arm, open-label, phase 2 study in ALKi-naïve patients (aged, ≥18 years) with locally advanced or metastatic ALK+ NSCLC, who had received ≤3 lines of chemotherapy. Patients received oral ceritinib 750 mg/d (fasted). Primary endpoint was overall response rate (ORR) per RECIST v1.1 (by investigator). Secondary endpoints were ORR (by blinded independent review committee [BIRC]); overall intracranial response rate (OIRR), duration of response (DOR), disease control rate (DCR), PFS (by investigator and BIRC); OS; and safety.

Results: Of 124 ceritinib-treated patients, 123 (99.2%) had received prior antineoplastic regimens (31 patients [25.0%], ≥3 regimens), and 49 (39.5%) had baseline brain metastases. Median follow-up time was 52.14 months (range, 48.4-60.1). Median duration of drug exposure was 23.2 months (range, 0.1-55.2). Median OS was 51.3 months (95% CI: 42.7, 55.3). Other efficacy results are shown in the table below. The most common adverse events (AEs [all grades], ≥60% of patients), suspected to be drug related, were diarrhea (83.1%), nausea (76.6%), and vomiting (69.4%). Grade 3/4 AEs suspected to be drug related were reported in 81 patients (65.3%). Overall, 18 patients (14.5%) had an AE leading to treatment discontinuation.

Table: LBA57

	Investigator Assessment (N* = 124)	BIRC Assessment (N* = 124)
Overall response rate, n (%) (95% CI)	84 (67.7) (58.8, 75.9)	79 (63.7) (54.6, 72.2)
Disease control rate, n (%) (95% CI)	112 (90.3) (83.7, 94.9)	107 (86.3) (79.0, 91.8)
Median duration of response (in responders), months (95% CI)	M‡ = 84 24.0 (14.8, 37.5)	M‡ = 79 27.3 (16.6, 44.3)
Median progression-free survival, months (95% CI)	16.6 (11.0, 23.2)	19.4 (10.9, 29.3)

*Total number of patients included in the full analysis set. ‡Total number of patients with confirmed complete response or partial response.

Conclusions: Ceritinib demonstrated prolonged and clinically meaningful OS, PFS, and DOR in chemotherapy pretreated (≤3 lines), ALKi-naïve patients with ALK+ NSCLC. The safety profile is consistent with the previous studies.

Clinical trial identification: NCT01685138.

Legal entity responsible for the study: Novartis Pharmaceuticals Corporation.

Funding: Novartis Pharmaceuticals Corporation.

Disclosure: E. Felip: Speakers or advisory board: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Guardanthealth, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Takeda, Abbvie, Merck. M. Nishio: Speakers or advisory board: Ono Pharmaceutical, Bristol Myers Squibb, Pfizer, Chugai Pharmaceutical, Eli Lilly, Taiho Pharmaceutical, AstraZeneca, Boehringer Ingelheim, MSD, Novartis; Grants, research support: MSD, Novartis, Ono Pharmaceutical, Chugai Pharmaceutical, Bristol-Myers Squibb, Taiho Pharmaceutical, Eli Lilly, AstraZeneca, Pfizer, Astellas. S. Orlov: Speakers or advisory board: BMS, Boehringer Ingelheim, MSD, Novartis, Roche. K. Park: Speakers or advisory board: Astellas, AZ, Boehringer Ingelheim, BMS, Clovis, Eli Lilly, Hanmi, KHK, MSD, Novartis, Ono, Roche; Grants, research support: AstraZeneca. C-J. Yu: Speakers or advisory board: AstraZeneca, Boehringer-Ingelheim, Novartis, GSK, MSD, Ono, Roche. C-M. Tsai: Speakers or advisory board: Novartis, Eli Lilly, Pfizer, MSD, BMS, Roche, AstraZeneca; Honoraria: Novartis, Eli Lilly, Pfizer, MSD, BMS, Roche, AstraZeneca. T.SK Mok: Speakers or advisory board: AstraZeneca, Roche/Genentech, Pfizer, Eli Lilly, BI, Clovis Oncology, Merck Serono, MSD, Novartis, SFJ Pharmaceutical, Acea Biosciences, Inc., Vertex Pharmaceuticals, BMS, GeneDecode Co., Ltd., OncoGenex Technologies Inc., Celgene, Ignyta, Inc., Cirina, Fishawack Facilitate Ltd., Janssen, Takeda, ChiMed; Stock ownership or options: Sanomics Ltd.; Honoraria: AstraZeneca, Roche/Genentech, Pfizer, Eli Lilly, BI, Merck Serono, MSD, Novartis, SFJ Pharmaceutical, Acea Biosciences, Inc., Vertex Pharmaceuticals, BMS, OncoGenex Pharmaceuticals, Inc., Celgene, Ignyta, Inc., Fishawack Facilitate Ltd, Takeda Oncology, Janssen; Grants, research support: AstraZeneca, BMS, Clovis Oncology, MSD, Novartis, Pfizer, Roche, SFJ, XCovery; Employment: The Chinese University of Hong Kong. G.V. Scagliotti: Speakers or advisory board: MSD, Eli Lilly; Honoraria: Eli Lilly, Roche, AstraZeneca, Abbvie. V.Q. Passos: Full-time employee of Novartis Pharmaceuticals. Z. Chen: Stock ownership or options: Novartis; Employee: Novartis Pharmaceuticals Corporation. A.T. Shaw: Advisory board: Novartis, Pfizer, Genentech/Roche, Blueprint Medicines, Loxo, Ariad/Takeda; Honoraria: Novartis, Pfizer, Genentech/Roche, Takeda, Foundation Medicine. All other authors have declared no conflicts of interest.