LBA4

Plenary Session

Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study.

Suresh S. Ramalingam, Terufumi Kato, Xiaorong Dong, Myung-Ju Ahn, Le-Van Quang, Nopadol Soparattanapaisarn, Takako Inoue, Chih-Liang Wang, Meijuan Huang, James Chih-Hsin Yang, Manuel Cobo, Mustafa Özgüroğlu, Ignacio Casarini, Dang-Van Khiem, Virote Sriuranpong, Eduardo Cronemberger, Xiangning Huang, Toon van der Gronde, Dana C. Ghiorghiu, Shun Lu; Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA; Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Department of Hematology-Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Department of Oncology, Hanoi Medical University, Hanoi, Viet Nam; Mahidol University, Sriraj Hospital, Bangkok, Thailand; Department of Thoracic Oncology, Osaka International Cancer Institute, Osaka, Japan; Division of Pulmonary Oncology and Interventional Bronchoscopy, Department of Thoracic Medicine, Linkou Chang Gung Memorial Hospital, Medical College of Chang Gung University, Taoyuan, Taiwan; Division of Thoracic Tumor Multimodality Treatment and Department of Medical Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, China; Department of Oncology, National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan; Unidad de Gestión Clínica Intercentros de Oncología Médica, Hospitales Universitarios Regional y Virgen de la Victoria, IBIMA, Málaga, Spain; Department of Internal Medicine, Division of Medical Oncology, Clinical Trial Unit, Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Istanbul, Turkey; Servicio Oncología, Hospital Bernardo Houssay, Mar del Plata, Buenos Aires, Argentina; Vietnam National Lung Hospital, Hanoi, Viet Nam; Division of Medical Oncology, Faculty of Medicine, Chulalongkorn University and the King Chulalongkorn Memorial Hospital, Bangkok, Thailand; Centro de Pesquisa Clínica CRIO, Centro Regional Integrado de Oncologia, Fortaleza, Ceará, Brazil; Biometrics, Late-stage Development, Oncology R&D, AstraZeneca, Cambridge, United Kingdom; Late-stage Development, Oncology R&D, AstraZeneca, New York, NY; Late-stage Development, Oncology R&D, AstraZeneca, Baar, Switzerland; Department of Medical Oncology, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Background: EGFR mutations occur in up to one-third of pts with unresectable stg III NSCLC. Consolidation durvalumab is standard of care (SoC) for pts who do not progress after concurrent CRT (cCRT), yet the benefit of consolidation immunotherapy specifically for EGFRm NSCLC remains uncertain, with limited data available. Osi, a 3rd-generation CNS-active EGFR-TKI, is recommended for EGFRm advanced/metastatic NSCLC and as adjuvant therapy for resectable EGFRm NSCLC. We report primary results from the global, double-blind, placebo (PBO)-controlled Phase 3 LAURA study (NCT03521154), assessing efficacy/safety of osi in unresectable stg III EGFRm NSCLC without progression after definitive CRT. **Methods:** Eligible pts: aged ≥18 years (≥20 in Japan), WHO PS 0/1, unresectable stg III EGFRm (Ex19del/L858R) NSCLC, had received definitive platinum-based cCRT/sequential CRT (sCRT) with no progression. Pts were stratified (cCRT vs sCRT; stg IIIA vs IIIB/IIIC; Chinese vs non-Chinese) and randomized 2:1 to receive osi 80 mg or PBO QD until progression (blinded independent central review [BICR]-confirmed)/discontinuation. Imaging, including brain MRI, was mandated at baseline, every 8 wks to wk 48, then every 12 wks, until progression by BICR. Open-label osi was offered after progression by BICR. Primary endpoint: progression-free survival (PFS; RECIST v1.1) assessed by BICR. Secondary endpoints included overall survival (OS) and safety. Data cut-off: January 5, 2024. **Results:** Overall, 216 pts were randomly assigned: osi n=143, PBO n=73. Baseline characteristics were generally balanced across osi/PBO arms: female 63/58%, stg IIIA 36/33%, IIIB 47/52%, IIIC 17/15%, Ex19del 52/59%. Osi significantly improved PFS by BICR vs PBO: HR 0.16; 95% CI 0.10, 0.24; p<0.001. Median PFS was 39.1 mo (95% CI 31.5, not calculable) for osi vs 5.6 mo (95% CI 3.7, 7.4) for PBO; 12-mo PFS rate was 74% (osi) vs 22% (PBO); 24-mo PFS rate was 65% (osi) vs 13% (PBO). Investigator-assessed PFS (HR 0.19; 95% CI 0.12, 0.29; nominal p<0.001) was consistent with PFS by BICR. PFS benefit was consistent across predefined subgroups. Interim OS analysis (20% maturity) showed a trend in favor of osi: HR 0.81; 95% CI 0.42, 1.56; p=0.530; 81% of pts (PBO arm) received osi after progression. All-causality AEs were reported in 98% vs 88% pts; ≥Grade 3 AEs in 35% vs 12%; serious AEs in 38% vs 15% for osi vs PBO, respectively. Radiation pneumonitis AEs (grouped term): 48% (osi) vs 38% (PBO), majority Grade 1/2. Any AEs leading to discontinuation were reported in 13% vs 5% for osi vs PBO, respectively. **Conclusions:** Osi after definitive CRT demonstrated a statistically significant and clinically meaningful improvement in PFS, for unresectable stg III EGFRm NSCLC, with no unexpected safety signals. These results establish osi as the new SoC for EGFRm NSCLC in this setting. Clinical trial information: NCT03521154. Research Sponsor: AstraZeneca.