BERLIN 2025 ESMO congress

1817MO

Molecular residual disease (MRD) analysis from the LAURA study of osimertinib (osi) in unresectable (UR) stage III EGFR-mutated (EGFRm) NSCLC

E. Arriola Aperribay[1], J.P. Robichaux[2], V.Q. Le[3], T. Inoue[4], N. Soparattanapaisarn[5], C-L. Wang[6], J. Chindaprasirt[7], T. Kato[8], F.V. Moiseenko[9], D. Vicente Baz[10], K. Dang Van[11], T.H. Le[12], T. Ohira[13], P. Bhetaryia[14], A.L. Bolanos[15], R.J. Hartmaier[2], S.S. Ramalingam[16]

[1] Medical Oncology Department, Hospital del Mar, Barcelona, Spain, [2] Translational Medicine, Oncology R&D, AstraZeneca, Boston, United States of America, [3] Department of Oncology, Hanoi Medical University, Hanoi, Vietnam, [4] Department of Thoracic Oncology, Osaka International Cancer Institute, Osaka, Japan, [5] Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [6] Department of Thoracic Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan, [7] Department of Internal Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, [8] Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan, [9] Chemotherapy Department, N.P. Napalkov Saint-Petersburg Clinical Scientific and Practical Center for Specialized Types of Medical Care (Oncological), St. Petersburg, Russian Federation, [10] Medical Oncology Department, Hospital Universitario Virgen de Macarena, Seville, Spain, [11] Department of Oncology, Vietnam National Lung Hospital, Hanoi, Vietnam, [12] Department of Medical Oncology, Hanoi Oncology Hospital, Hanoi, Vietnam, [13] Department of Surgery, Tokyo Medical University, Shinjuku-ku, Japan, [14] Oncology Data Science, Oncology R&D, AstraZeneca, Boston, United States of America, [15] Late-stage Development, Oncology R&D, AstraZeneca, Mississauga, Canada[16] Department of Hematology and Medical Oncology, Emory University School of Medicine, Winship Cancer Institute, Atlanta, United States of America

Background

Osi demonstrated significant improvement in progression-free survival (PFS; HR 0.16; 95% CI 0.10, 0.24; p<0.001) vs placebo (pbo) after definitive chemoradiotherapy (CRT) in the LAURA study (NCT03521154) in UR stage III EGFRm NSCLC. Tumour-informed MRD assays have greater sensitivity than traditional ctDNA genotyping assays, making them useful for ctDNA monitoring. We assessed the ability of high-sensitivity MRD testing to predict progressive disease (PD) in pts from LAURA.

Methods

Eligible pts (≥18 yrs [Japan ≥20], WHO PS 0/1) with UR stage III EGFRm (Ex19del/L858R) NSCLC who had received CRT with no PD, were randomised 2:1 to osi 80 mg or pbo QD until BICR-assessed PD per RECIST 1.1, or discontinuation. Personalised MRD panels (NeXT Personal®, Personalis) based on tumour whole genome sequencing achieved a high median sensitivity of 2.6 ppm. Plasma samples (at baseline [BL; randomisation post-CRT], Wks 2, 4, Q4W to Wk 24, Q8W to Wk 48 and Q12W to PD) were analysed by MRD panels to detect ctDNA (ie MRD+). In pts with BL MRD+, MRD clearance was defined as a 10-fold ctDNA decrease or MRD– for 2 consecutive timepoints by Wk 12. Molecular PD (MolPD) was defined previously (Gray JTO 2024). LAURA primary endpoint: BICR-assessed PFS.

Results

Of 216 pts randomised, 65 had samples/consent to create MRD panels; panels were evaluable in 52 pts (80%; osi n=34, pbo n=18). At BL, 57% (29/51) of pt samples were MRD+; 43% (22/51) MRD– (sample unavailable for 1 pt). BL MRD status did not correlate with best overall response to CRT (14/24 pts with SD had MRD+, 12/24 PR, 2/2 CR, 1/1 NE). BL MRD+ was cleared in 84% (16/19, osi) and 0% (0/10, pbo) of pts. Similar benefit of osi vs pbo was observed in pts with BL MRD+ (median PFS [95% CI] 38.8 [16.6, NR] vs 5.8 [1.9, 9.5] mo) and MRD– (39.3 [9.0, NR] vs 11.1 [3.5, 13.8] mo). MRD had 63% clinical sensitivity and 86% specificity to detect PFS events. In pts with both PFS and MRD events (both arms), MolPD preceded PFS events in 79% (15/19); median lead time 5.1 mo (95% CI 3.8, 8.5).

Conclusions

All pts in the MRD set had evidence of disease post-CRT (molecular or clinical). Osi treatment cleared MRD in most pts with BL MRD+, supporting the overall benefit of osi in LAURA. MRD may predict progression in UR stage III EGFRm NSCLC.

Clinical trial identification

NCT03521154.

Editorial acknowledgement

Medical writing support for the development of this abstract, under the direction of the authors, was provided by Neil R. Smith PhD, of Ashfield MedComms, an Inizio Company, and was funded by AstraZeneca in accordance with Good Publications Practice (GPP) guidelines

(http://www.ismpp.org/gpp-2022).

Legal entity responsible for the study

AstraZeneca.

Funding

AstraZeneca.

Disclosure

E. Arriola Aperribay: Financial Interests, Personal, Advisory Board: Roche, Pfizer, Lily, AstraZeneca, Boehringer Ingelheim; Financial Interests, Personal, Advisory Role: AstraZeneca, Roche, MSD, BMS, Takeda, Amgen, Pfizer, Janssen; Financial Interests, Personal and Institutional, Full or part-time Employment: Department of Medical Oncology, Hospital del Mar-CIBERONC; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, Roche, Merck Sharp & Dohme, Pfizer, Lily, AstraZeneca, Boehringer Ingelheim, Takeda, Janssen; Non-Financial Interests, Personal, Member: ESMO, IASLC; Financial Interests, Personal and Institutional, Other, Financial co-founder: Training Health S.L.; Financial Interests, Personal, Principal Investigator: Roche, Merck Sharp & Dohme, Pfizer, Lily, AstraZeneca, Boehringer Ingelheim, Janssen, Amgen; Financial Interests, Institutional, Research Grant: Roche, Pfizer, AstraZeneca, Bristol Myers Squibb; Financial Interests, Personal, Writing Engagement: Pfizer. J.P. Robichaux: Financial Interests, Personal and Institutional, Full or part-time Employment: AstraZeneca; Financial Interests, Personal and Institutional, Licencing Fees or royalty for IP, Inventor on patents held by UT MD Anderson Cancer Center licenced to SP for treatment of EGFR/HER2 exon 20 mutant cancers: UT MD Anderson Cancer Center and Spectrum Pharmaceuticals; Non-Financial Interests, Personal and Institutional, Advisory Board, Inventor on patent held by UT MDACC regarding EGFR mutation subtypes and methods of: UT MD Anderson Cancer Center; Financial Interests, Personal, Stocks/Shares: AstraZeneca. V.Q. Le: Financial Interests, Personal, Advisory Role: AstraZeneca, Roche; Financial Interests, Personal, Other, Honoraria: AstraZeneca, Roche, MSD, Pfizer, Novartis. T. Inoue: Financial Interests, Personal, Speaker's Bureau: Ono Pharmaceutical, MSD K.K., Chugai Pharceutical Co. Ltd AstraZeneca K.K. Eli Lilly Japan K.K. N. Soparattanapaisarn: Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Board, Honoraria: AstraZeneca, Pfizer, Takeda, Roche. T. Kato: Financial Interests, Personal, Advisory Role: AstraZeneca, BeiGene, Chugai, Daiichi Sankyo, Janssen, Merck KGaA, MSD, Novartis, Pfizer; Financial Interests, Personal, Other, Honoraria: Amgen, AstraZeneca, BeiGene, Boehringer Ingelheim, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Eli Lilly, GSK, Janssen, Merck KGaA, MSD, Novartis, Ono, Pfizer, Taiho, and Takeda; Financial Interests, Personal, Other, Family member employment: Lilly; Financial Interests, Personal, Research Grant: AbbVie, Amgen, Arrivent, AstraZeneca, Bayer, BeiGene, BluePrint, Boehringer Ingelheim, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Eli Lilly, Gilead, GSK, Haihe, Janssen, Merck KGaA, MSD, Novartis, Novocure, Pfizer, Regeneron and Takeda. F.V. Moiseenko: Financial Interests, Personal, Invited Speaker: AstraZeneca, Pfizer, Roche – Genentech, Biocad; Financial Interests, Personal, Advisory Board: AstraZeneca, AstraZeneca; Financial Interests, Personal and Institutional, Steering Committee Member: Biocad; Financial Interests, Personal and Institutional, Local PI: AstraZeneca. D. Vicente Baz: Financial Interests, Personal, Advisory Board: Pfizer, AstraZeneca, Roche, Takeda, BMS, MSD, Merck, Amgen, Janssen; Financial Interests, Personal, Invited Speaker: Pfizer, AstraZeneca, Roche, Takeda, BMS, MSD, Merck, Amgen, Janssen; Financial Interests, Personal, Local PI: Zailab, BioNTech; Financial Interests, Personal, Speaker, Consultant, Advisor: Pfizer, AstraZeneca, Roche, Takeda, BMS, MSD, Merck, Amgen, Janssen; Financial Interests, Personal, Steering Committee Member: Pfizer. K. Dang Van: Financial Interests, Personal, Advisory Role: AstraZeneca, Boehringer Ingelheim, Roche, MSD; Financial Interests, Personal, Other, Travel, accommodations, expenses: AstraZeneca, Boehringer Ingelheim; Financial Interests, Personal, Speaker's Bureau: Boehringer Ingelheim, Roche, MSD. P. Bhetaryia: Financial Interests, Personal and Institutional, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Other, https://patents.google.com/patent/WO2012023020A1/en?q=(Bhetariya)&oq=Bhetariya: Patent: WO2012023020A1; Financial Interests, Personal, Other, https://patents.google.com/patent/EP3902607A4/en?q=(Bhetariya)&oq=Bhetariya: Intellectual property: EP3902607A4; Financial Interests, Personal, Stocks/Shares: AstraZeneca. A.L. Bolanos: Financial Interests, Personal and Institutional, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks or ownership: AstraZeneca. R.J. Hartmaier: Financial Interests, Personal and Institutional, Full or part-time Employment: AstraZeneca; Non-Financial Interests, Personal, Other, Inventor on patent: US11066709B2; Financial Interests, Personal, Stocks/Shares: AstraZeneca. S.S. Ramalingam: Non-Financial Interests, Institutional, Research Funding: Amgen, AstraZeneca, GSK, Pfizer, BMS; Financial Interests, Personal, Other, Travel, accommodations, expenses: AbbVie, AstraZeneca. All other authors have declared no conflicts of interest.