BERLIN 2025 ESMO congress

2001P

Molecular factors and ctDNA dynamics associated with clinical outcomes in patients with HER2-mutant NSCLC treated with sevabertinib (BAY 2927088): Exploratory analysis of the SOHO-01 study

N. Girard[1], L. Li[2], T.M. Kim[3], X. Dong[4], H.H.F. Loong[5], S. Lu[6], H.R. Kim[7], B-C. Goh[8], A. Prelaj[9], Y. Fang[10], L. Wu[11], Y. Shinno[12], G. Daniele[13], T-Y. Yang[14], G. Ruiter[15], J. Zhao[16], P. Grassi[17], T. Descamps[18], J.C. Brase[19], X. Le[20]

[1] Department of Medical Oncology, Institut Curie, Paris, France, [2] Department of Medical Oncology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China, [3] Internal Medicine Department, Seoul National University Hospital, Seoul, Republic of Korea, [4] Thoracic Oncology Department, Oncology Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [5] Department of Clinical Oncology, The Chinese University of Hong Kong - Prince of Wales Hospital, Hong Kong SAR, China, [6] Department of Oncology, Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China, [7] Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center Yonsei University, Seoul, Republic of Korea, [8] Department of Haematology-Oncology, National University Cancer Institute Singapore, National University Health System, Singapore, [9] Dipartimento di Oncologia Medica, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, [10] Medical Oncology Department, Sir Run Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China, [11] Thoracic Medicine Department II, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China, [12] Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan, [13] Phase 1 Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [14] Department of Chest Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, [15] Departments of Clinical Pharmacology and Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands, [16] Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Thoracic Oncology, Peking University Cancer Hospital and Institute, Beijing, China, [17] SBU Oncology, Bayer S.p.A., Milan, Italy, [18] ODO Statistics UK, Bayer UK Ltd. - Bayer plc, Reading, United Kingdom, [19] Translational Sciences Oncology, Bayer Consumer Care AG, Basel, Switzerland[20] Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, United States of America

Background

Sevabertinib produced durable responses in patients with advanced *HER2*-mutant NSCLC who had not previously received HER2-targeted therapies (Group D, n=81) and those treated with a HER2-targeted antibody-drug conjugate (Group E, n=55). We analyzed molecular factors associated with response and outcomes to sevabertinib in SOHO-1 (NCT05099172).

Methods

Plasma collected from patients at baseline (BL) and on-treatment (OT) was used to identify co-alterations and detectable (D, *HER2* mutation positive) and nondetectable (ND, *HER2* mutation negative) ctDNA at BL and after 2 and 6 weeks of treatment using the Thermo Fisher Scientific Oncomine™ Precision Assay. Longitudinal ctDNA results were used to classify patients into subgroups: “never detected” (BL and OT - ND), “clearance” (BL – D, ND for at least one OT time point) and “persistent detection” (BL and OT - D). Historical *HER2* variant information from local testing and ctDNA were correlated with treatment response and outcomes.

Results

Sevabertinib was active across *HER2* variants and protein domains in SOHO-01 Groups D and E. In Group D, enhanced efficacy was seen in patients with *HER2* mutations in the tyrosine kinase domain (89% of Group D; ORR 69.4%), especially those with the *HER2 Y772_A775dup* (YVMA) mutation (59% of Group D; ORR 77.1%). *TP53* mutations were the most frequent co-alterations at BL in 17/61 patients (27.9%) with detectable *HER2* ctDNA and were associated with less favorable responses and outcomes. The ctDNA subgroups “never detected” and “clearance” had prolonged PFS (HR 0.347 [95% CI 0.116, 1.040] and 0.430 [95% CI 0.204, 0.906], respectively) compared to “persistent detection” subgroup. ctDNA subgroups were statistically distinct in a multivariate analysis.

Conclusions

This exploratory analysis suggests that molecular features such as the presence of the HER2 YVMA variant, absence of TP53 co-alteration, early ctDNA clearance, are associated with favorable outcomes in patients with HER2-mutant NSCLC treated with sevabertinib. Associations between ctDNA dynamics and PFS, despite the limited follow-up information, align with previous findings in NSCLC cohorts treated with TKIs.

Clinical trial identification

NCT05099172.

Editorial acknowledgement

Caudex, IPG Health Medical Communications, provided medical writing and editorial assistance in the development of this abstract, funded by Bayer AG.

Legal entity responsible for the study

Bayer AG.

Funding

Bayer AG.

Disclosure

N. Girard: Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, MSD, Roche, Pfizer, Janssen, Regeneron, AbbVie, Amgen, Lilly, Takeda, Owkin, Leo Pharma, Daiichi Sankyo, Ipsen, Pierre Fabre, BeiGene; Financial Interests, Personal, Invited Speaker: AstraZeneca, BMS, Pfizer, Amgen, MSD, Sanofi, Gilead, Janssen; Financial Interests, Personal, Officer: Edimark; Financial Interests, Institutional, Research Grant, Local: Roche, Sivan, Janssen; Financial Interests, Institutional, Funding: BMS, Leo Pharma; Financial Interests, Institutional, Research Grant: MSD; Other, Other, Family member is an employee: AstraZeneca. T.M. Kim: Financial Interests, Institutional, Sponsor/Funding: Bayer AG; Financial Interests, Institutional, Speaker, Consultant, Advisor: AstraZeneca, Janssen, Regeneron, Samsung Bioepis, Takeda, Yuhan; Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, IMBDx, Inc., Takeda, Yuhan; Financial Interests, Institutional, Research Grant: AstraZeneca-KHIDI; Non-Financial Interests, Advisory Board: AstraZeneca, Janssen, Regeneron, Takeda. H.H.F. Loong: Financial Interests, Institutional, Invited Speaker: Boehringer Ingelheim, MSD; Financial Interests, Personal, Invited Speaker: Eli Lilly, Illumina, Bayer, Guardant Health; Financial Interests, Personal, Advisory Board: Novartis, Takeda. S. Lu: Financial Interests, Personal, Leadership Role: Innovent BIOLOGICS, INC; Financial Interests, Personal, Advisory Role: AstraZeneca, Pfizer, Boehringer Ingelheim, Hutchison MediPharma, Simcere Pharmaceutical Group, Zai Lab, GenomiCare, Yuhan Corporation, Roche, Menarini, InventisBio Co. Ltd; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, Roche, Hansoh Pharmaceutical Group Co. Ltd., Hengrui Therapeutics; Financial Interests, Institutional, Research Funding: AstraZeneca, Hutchison MediPharma, BMS, Hengrui Therapeutics, BeiGene, Roche, Hansoh, Lilly Suzhou Pharmaceutical Co.Ltd. B. Goh: Financial Interests, Institutional, Funding: Bayer AG; Financial Interests, Personal, Leadership Role: Drug Advisory Committee, Ministry of Health, Singapore. A. Prelaj: Financial Interests, Personal, Other, Training of personnel: AstraZeneca, Italfarma; Financial Interests, Personal, Invited Speaker, The Hive Project: Discussant: Roche; Financial Interests, Personal, Advisory Board, Advisory board in Lung Cancer project: BMS; Financial Interests, Personal, Other, Travel Grant: Janssen; Financial Interests, Personal, Advisory Board: Janssen, AstraZeneca; Financial Interests, Personal, Invited Speaker: Medsir, Novartis, Lilly; Financial Interests, Institutional, Local PI: Bayer, BMS, Lilly, MSD, Roche; Financial Interests, Institutional, Coordinating PI: AstraZeneca, Spectrum. L. Wu: Financial Interests, Personal, Speaker's Bureau: AstraZeneca, Bristol Myers Squibb, Hengrui Medicine, Innovate Biopharmaceuticals, Lilly, MSD, Pfizer, Roche China. Y. Shinno: Financial Interests, Institutional, Research Funding: ONO PHARMACEUTICAL, Janssen Pharmaceutical, Japan Clinical Research Operations, Taiho Pharmaceutical, Bayer; Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, Bristol Myers Squibb, CHUGAI PHARMACEUTICAL, ONO PHARMACEUTICAL, Eli Lilly Japan. G. Daniele: Financial Interests, Personal, Speaker, Consultant, Advisor: Gilead, GSK; Financial Interests, Institutional, Research Grant: Gilead. G. Ruiter: Financial Interests, Institutional, Research Funding: AstraZeneca, AbbVie, Daiichi Sankyo, Cullinan Oncology, Boehringer Ingelheim, Merus, Bayer, Navire, BridgeBio, Bristol Myers Squibb, Scorpion, Taiho Oncology, Revolution Medicine, Pierre Fabre; Financial Interests, Institutional, Speaker, Consultant, Advisor: Boehringer Ingelheim. J. Zhao: Financial Interests, Personal, Member of Board of Directors: AstraZeneca, BeiGene, Pfizer. P. Grassi: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer S.p.A. Pharmaceuticals. T. Descamps: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer Public Limited Company. J.C. Brase: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer Consumer Care AG. X. Le: Financial Interests, Personal, Advisory Board: AstraZeneca, Merck KGaA, Spectrum Pharmaceutics, Novartis, Boehringer Ingelheim, Eli Lilly, Hengrui, Janssen, Blueprint, Daiichi Sankyo, Regeneron, ArriVent, Abion, Pinetree therapeutics, AbbVie, Aviston, Allist, Bayer; Financial Interests, Institutional, Coordinating PI: Eli Lilly, EMD Serono, Regeneron, Janssen; Financial Interests, Institutional, Research Grant: Arrivent; Financial Interests, Institutional, Funding: Teligene. All other authors have declared no conflicts of interest.