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Sevabertinib (BAY 2927088) in advanced *HER2*-mutant non-small cell lung cancer (NSCLC): Results from the SOHO-01 study

X. Le¹, T.M. Kim², X. Dong³, H.H.F. Loong⁴, N. Girard⁵, S. Lu⁶, H.R. Kim⁷, B.-C. Goh⁸, A. Prelaj⁹, Y. Fang¹⁰, L. Wu¹¹, Y. Shinno¹², G. Daniele¹³, T.-Y. Yang¹⁴, G. Ruiter¹⁵, J. Zhao¹⁶, J.C. Brase¹⁷, R. Li¹⁸, P. Grassi¹⁹, L. Li²⁰

¹ Thoracic Head & Neck, MD Anderson Cancer Center, Houston, United States of America, ² Internal Medicine Department, Seoul National University Hospital, Seoul, Republic of Korea, ³ Cancer Center, Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, ⁴ Department of Clinical Oncology and Phase 1 Clinical Trial Centre, The Chinese University of Hong Kong, Hong Kong SAR, China, ⁵ Department of Medical Oncology, Institut Curie, Paris, France, ⁶ Department of Oncology, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, ⁷ Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Seoul, Republic of Korea, ⁸ Department of Haematology-Oncology, National University Cancer Institute, Singapore, ⁹ Oncologia Medica Toracica Dept., Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, ¹⁰ Medical Oncology Dept., Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China, ¹¹ Department of Thoracic Medical Oncology, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China, ¹² Thoracic Oncology, National Cancer Center Hospital, Chuo-ku, 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 I of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China, ¹⁷ Translational Sciences Oncology, Bayer Consumer Care AG, Basel, Switzerland, ¹⁸ Clinical Statistics, Bayer HealthCare Pharmaceuticals Inc., Whippany, United States of America, ¹⁹ SBU Oncology, Bayer S.p.A., Milan, Italy, ²⁰ Department of Medical Oncology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China

Background

Sevabertinib is a potent, reversible, oral *HER2* tyrosine kinase inhibitor with FDA Breakthrough Therapy Designation and Priority Review for pretreated patients (pts) with advanced *HER2*-mutant NSCLC. We report updated efficacy and safety in pretreated and treatment-naïve pts with *HER2*-mutant NSCLC in the open-label, multicenter Phase I/II SOHO-01 study.

Methods

Pts with *HER2*-mutant NSCLC were treated with sevabertinib 20 mg twice daily in 3 cohorts: Cohort D, previous systemic therapy but naïve to *HER2* ex20ins-targeted therapy; Cohort E, previous *HER2*-targeted antibody-drug conjugates; Cohort F, naïve to systemic anti-cancer therapy for advanced disease. The primary endpoint was objective response rate (ORR) by RECIST v1.1 and blinded independent central review. Secondary endpoints were duration of response (DoR) and progression-free survival (PFS).

Results

At the data cut-off (June 27, 2025), 209 pts with *HER2*-mutant NSCLC were treated: 81 (D), 55 (E), and 73 (F). ORR (95% CI) was 64% (53, 75; D), 38% (25, 52; E), and 71% (59, 81; F). Median (95% CI) DoR was 9.2 (6.3, 13.5; D), 8.5 (5.6, 16.4; E), and 11.0 (8.1, not evaluable; F) months; 12-month DoR rates (95% CI) were 42% (27, 57; D) and 29% (5, 53; E). Median PFS (95% CI) was 8.3 (6.9, 12.3; D) and 5.5 (4.3, 8.3; E) months, and not reached (F). In Cohort D, pts with baseline brain metastases had a similar ORR to those without (61% vs 65%). Among pts with *HER2* tyrosine kinase domain (TKD) mutations, those with Y772_A775dupYVMA had a higher ORR (78% vs 57%) and median PFS (12.2 vs 7.0 months) than those with other *HER2* TKD mutations. Overall, grade ≥ 3 treatment-related adverse events (TRAEs) were reported in 31% of pts. Diarrhea was the most commonly reported TRAE, mostly grade 1/2 (grade 3: 14%). TRAEs led to treatment discontinuation in 3% of pts; none due to diarrhea. There were no reports of interstitial lung disease or pneumonitis.

Conclusions

Sevabertinib showed rapid and durable responses with a manageable safety profile in pretreated and treatment-naïve pts with advanced *HER2*-mutant NSCLC. These data support sevabertinib as a potential practice-changing, new targeted therapy for pts with *HER2*-mutant NSCLC.

Clinical trial identification

NCT05099172, March 28, 2025.

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Bayer AG.

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Disclosure

X. Le: Financial Interests, Personal, Advisory Board: AstraZeneca, Merck KGaA, Spectrum Pharmaceuticals, 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. 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. 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. 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 Therapeutics, 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. J.C. Brase: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer Consumer Care AG. R. Li: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer AG. P. Grassi: Financial Interests, Personal and Institutional, Full or part-time Employment: Bayer S.p.A. Pharmaceuticals. All other authors have declared no conflicts of interest.

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