SOHO-02: Phase III trial of BAY 2927088 in patients with locally advanced or metastatic NSCLC with *HER*-activating mutations

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Introduction

- Activating human epidermal growth factor receptor 2 (*HER2*) mutations account for ~2-4% of non-small cell lung cancer (NSCLC), the majority of which are exon 20 insertions[1,2]
- Presence of *HER2*-activating mutations in NSCLC is associated with Asian ethnicity, non-smoking status, and adenocarcinoma histology[2,3]
- As no targeted therapies are approved for first-line treatment of patients with *HER2*-mutant metastatic NSCLC, platinum-based doublet chemotherapy with or without immunotherapy is recommended as the first-line standard of care[4]; however, treatment outcomes within this context remain unsatisfactory[5,6]
- BAY 2927088 is an oral, reversible tyrosine kinase inhibitor (TKI) that potently targets *HER2* and mutant epidermal growth factor receptor (*EGFR*)[7]
- Preliminary evidence from the Phase I / II SOHO-01 trial has demonstrated anti-tumor activity and a manageable safety profile for BAY 2927088 in previously treated patients with NSCLC harboring *HER2*-activating mutations[8]

BAY 2927088 mechanism of action

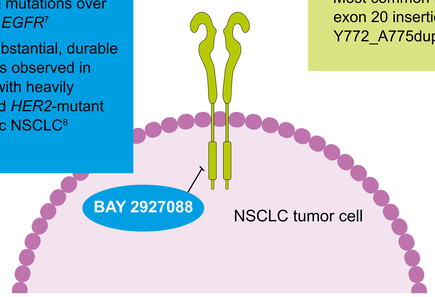
BAY 2927088

- Oral, reversible TKI[7]
- Selectivity for *HER2*-activating mutations over wild-type *EGFR*[7]
- Rapid, substantial, durable responses observed in patients with heavily pretreated *HER2*-mutant metastatic NSCLC[8]

Mutant *HER2*

***HER2*-activating mutations**

- ~2-4% of NSCLC cases[1,2]
- Most common mutation is exon 20 insertion Y772_A775dup (YVMA)[3]



Key patient enrollment features

Key inclusion criteria

- Aged ≥18 years
- Documented histologically or cytologically confirmed locally advanced or metastatic NSCLC (stage III or IV)
- Documented activating *HER2* mutation in the tyrosine kinase domain (TKD)
- No previous systemic therapy for locally advanced or metastatic disease
- Eligible to receive treatment with the selected platinum-based doublet chemotherapy (cisplatin / pemetrexed or carboplatin / pemetrexed) and pembrolizumab

Key exclusion criteria

- Known history of malignancy except if the patient has undergone potentially curative therapy with no evidence of that disease recurrence for 5 years since initiation of that therapy[a]
- Tumors with targetable alterations with approved available therapy (excluding *HER2* TKD mutations)
- Unresolved toxicity of grade ≥2 from previous anti-cancer treatment
- History of severe hypersensitivity reaction to treatment with a monoclonal antibody
- Uncontrolled intercurrent illness

SOHO-02 will recruit ~278 patients across 36 countries

Europe

Austria, Belgium, Bulgaria, Czechia, Denmark, Finland, France, Germany, Greece, Hungary, Israel, Italy, Netherlands, Poland, Portugal, Romania, Slovakia, Spain, Sweden, Switzerland, Turkey, Ukraine, UK

Asia

China, Hong Kong, Japan, Malaysia, Republic of Korea, Singapore, Taiwan

Americas

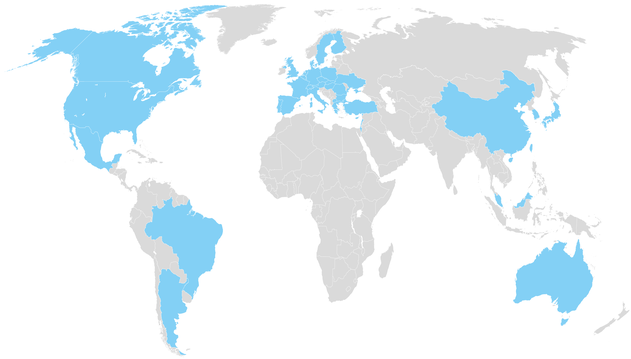
Argentina, Brazil, Canada, Mexico, USA

Oceania

Australia

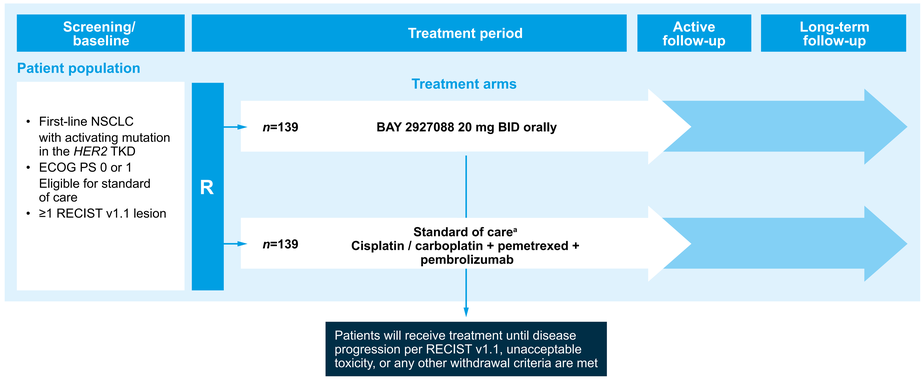
[a]The following cancer types are acceptable within 5 years if curatively treated or under surveillance: *in situ* cancers of cervix, breast, or skin; superficial bladder cancer (Ta, Tis, and T1); limited-stage prostate cancer; basal or squamous cancers of the skin

Geographical distribution



SOHO-02 overall study design

A Phase III open-label, randomized, active-controlled, multicenter trial in patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations



Primary endpoints

- PFS per RECIST v1.1 by BICR

Secondary endpoints

- Overall survival
- ORR per RECIST v1.1 by BICR
- Safety and tolerability
- PFS per RECIST v1.1 by investigator
- ORR by investigator
- Disease control rate per RECIST v1.1 by BICR and investigator
- Duration of response by BICR and investigator
- Patient-reported outcomes

[a]Standard of care based on National Comprehensive Cancer Network / European Society for Medical Oncology treatment guidelines and dosing based on approved labels: cisplatin (75 mg/m² Q3W) or carboplatin (area under the concentration-vs-time curve 5 Q3W) + pemetrexed (500 mg/m² Q3W) + pembrolizumab (200 mg Q3W or 400 mg Q6W) via i.v. infusion

BICR, blinded independent central review; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Summary

Intervention / treatment
BAY 2927088 is an oral, reversible TKI that potently targets *HER2* mutations

Study
Phase III open-label, randomized, active-controlled, multicenter trial (NCT06452277)

- Progression-free survival (PFS)
- Overall survival
- Overall response rate (ORR)

Status[9]
Ongoing

Participants
Patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations

Acknowledgments

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1. Remon J et al. *Cancer Treat Rev* 2020; 90: 102105; 2. Tan AC et al. *JCO Precis Oncol* 2022; 6: e2200278; 3. Riudavets M et al. *ESMO Open* 2021; 6: 100260; 4. Hendriks LE et al. *Ann Oncol* 2023; 34: 339-357; 5. Wang Y et al. *BMC Cancer* 2018; 18: 326; 6. Zhang J et al. *J Cancer Res Clin Oncol* 2024; 150: 42; 7. Siegel F et al. *Cancer Res* 2023; 83 (7 Suppl): abs 4035; 8. Girard N et al. Poster LBA8598 presented at ASCO, Chicago, IL, USA, May 31-June 4, 2024; 9. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT06452277

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