SINGAPORE 2025 ESMO ASIA

Phase I / II SOHO-01 study of sevabertinib (BAY 2927088) in *HER2*-mutant non-small cell lung cancer: safety and efficacy in Asian patients

Daniel Shao-Weng Tan

National Cancer Centre Singapore and Duke–National University of Singapore Medical School, Singapore

Friday, December 5

Daniel Shao-Weng Tan,[1,2] Boon Cher Goh,[3,4] Lin Li,[5,6] Yong Fang,[7] Shun Lu,[8] Xiaorong Dong,[9] Lin Wu,[10] Yuki Shinno,[11] Tsung-Ying Yang,[12] Hye Ryun Kim,[13,14] Jun Zhao,[15] Liyun Miao,[16] Koichi Goto,[17] Seigo Katakura,[18] Kazumi Nishino,[19] Cheng Huang,[20] Rui Li,[21] Paolo Grassi,[22] Herbert H. Loong,[23,24] Tae Min Kim[25]

[1]Division of Medical Oncology, National Cancer Centre Singapore, Singapore; [2]Duke–National University of Singapore Medical School, Singapore; [3]Department of Hematology–Oncology, National University Cancer Institute, Singapore; [4]Cancer Science Institute of Singapore, National University of Singapore, Singapore; [5]Department of Medical Oncology, Beijing Hospital, Beijing, China; [6]National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China; [7]Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; [8]Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [9]Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [10]Department of Thoracic Medical Oncology, Hunan Cancer Hospital, Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [11]National Cancer Center Hospital, Tokyo, Japan; [12]Department of Chest Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [13]Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Seoul, South Korea; [14]Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, South Korea; [15]Key Laboratory of Carcinogenesis and Translational Research, Ministry of Education, Department I of Thoracic Oncology, Peking University Cancer Hospital and Institute, Beijing, China; [16]Nanjing Drum Tower Hospital, Affiliated Hospital of Nanjing University Medical School, Nanjing, China; [17]National Cancer Center Hospital East, Kashiwa, Japan; [18]Kanagawa Cancer Center, Yokohama, Japan; [19]Osaka International Cancer Institute, Osaka, Japan; [20]Fujian Provincial Cancer Hospital, Fuzhou, China; [21]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; [22]Bayer, Milan, Italy; [23]Department of Clinical Oncology, Chinese University of Hong Kong, Hong Kong; [24]Phase 1 Clinical Trial Center, Chinese University of Hong Kong, Hong Kong; [25]Seoul National University Hospital, Seoul, South Korea

Declaration of interests

Daniel Shao-Weng Tan

I have the following financial relationships to disclose:

- Consulting fees: Amgen, Astellas, AstraZeneca, Bayer, BeiGene, Boehringer Ingelheim, DKSH, Genmab, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, Regeneron, Roche, Takeda, and Zymeworks
- Research grants: ACM Biolabs, Amgen, AstraZeneca, Bayer, GlaxoSmithKline, Novartis, and Pfizer

Presented by: Daniel Shao-Weng Tan

Sevabertinib is an oral, reversible HER2 TKI

- Sevabertinib is an oral, reversible TKI with anti-*HER2* activity in preclinical models[1]
- The ongoing Phase I / II SOHO-01 study is evaluating sevabertinib in patients with advanced *EGFR*- or *HER2*-mutant NSCLC[2]
- Sevabertinib has demonstrated anti-tumor activity and manageable safety in patients with *HER2*-mutant NSCLC who had already received treatment, including HER2-targeted ADCs, as well as in the first-line setting[2]
- The Chinese Center for Drug Evaluation has accepted the New Drug Application for sevabertinib for patients with advanced NSCLC characterized by activating *HER2* mutations who have already undergone systemic treatment[3]
- Here, we report the safety and efficacy of sevabertinib in Asian patients from the dose-expansion and dose-extension phases of the SOHO-01 study

ADC, antibody-drug conjugate; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

1. Siegel F et al. *Cancer Discov* 2025; doi: 10.1158/2159-8290.CD-25-0605; 2. Le X et al. *N Engl J Med* 2025; doi: 10.1056/NEJMoa2511065; 3. Bayer. 2025. Bayer's sevabertinib (BAY 2927088) accepted for review in China. Accessed October 2025

Presented by: Daniel Shao-Weng Tan

SOHO-01 study design (NCT05099172)

DOSE ESCALATION AND BACKFILL

Patients with advanced NSCLC with *HER2* or *EGFR* mutations

Patients were treated with increasing oral doses of sevabertinib to identify the RDE (5 QD dose levels and 3 BID dose levels, from 10 mg QD to 40 mg BID)

20 mg BID

EXPANSION AND EXTENSION[a]
Cohorts of patients with *HER2* mutations[b]

To evaluate the safety, tolerability, and efficacy, and to characterize the pharmacokinetics, of sevabertinib at the RDE

- **D** Previously treated, naïve to HER2-targeted therapies
- **E** Previously treated with HER2-targeted ADCs
- **F** Naïve to systemic therapy for advanced disease

Cut-off date: March 28, 2025

Efficacy and safety from expansion and extension Cohorts D, E, and F

PRIMARY ENDPOINT (extension phase)

- ORR per RECIST v1.1 by BICR

SECONDARY ENDPOINTS

- DoR and PFS (per RECIST v1.1) by BICR and investigator assessment
- Safety and tolerability

[a]Patients from dose escalation and backfill treated with 20 mg BID and who met the same eligibility criteria were combined for statistical analysis;
[b]Cohorts of patients with *EGFR* mutations are not shown
BICR, blinded independent central review; BID, twice daily; DoR, duration of response; ORR, objective response rate; QD, once daily;
PFS, progression-free survival; RDE, recommended dose for expansion; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Presented by: Daniel Shao-Weng Tan

Baseline characteristics (Asian patients in Cohorts D, E, and F)

	Cohort D[a] (*n*=57)	Cohort E[b] (*n*=32)	Cohort F[c] (*n*=51)
Female, *n* (%)	33 (58)	20 (63)	31 (61)
Median age, years (range)	59 (29-82)	61 (35-79)	66 (34-80)
Baseline ECOG PS, *n* (%)			
0	21 (37)	9 (28)	10 (20)
1	36 (63)	23 (72)	41 (80)
Smoking habits at informed consent, *n* (%)			
Never	42 (74)	23 (72)	44 (86)
Former or current	15 (26)	9 (28)	7 (14)
Adenocarcinoma histology[d], *n* (%)	54 (95)	32 (100)	49 (96)
Brain metastases at baseline[e], *n* (%)	12 (21)	10 (31)	4 (8)
Activating *HER2* mutations, *n* (%)			
Y772_A775dupYVMA	35 (61)	27 (84)	40 (78)
Other *HER2* ex20ins	14 (25)	5 (16)	8 (16)
HER2 point mutation	7 (12)	0	1 (2)
Not applicable[f]	1 (2)	0	2 (4)

	Cohort D[a] (*n*=57)	Cohort E[b] (*n*=32)	Cohort F[c] (*n*=51)
***HER2* TKD mutation, *n* (%)**			
Yes	50 (88)	32 (100)	50 (98)
No	6 (11)	0	1 (2)
Not applicable[g]	1 (2)	0	0
Number of previous systemic anti-cancer therapies, *n* (%)			
0	0	0	46 (90)
1	31 (54)	7 (22)	4 (8)[h]
≥2	26 (46)	25 (78)	1 (2)[h]
Previous anti-cancer therapies, *n* (%)			
Chemotherapy	54 (95)	26 (81)	5 (10)
Platinum and no immunotherapy	16 (28)	8 (25)	3 (6)
Platinum and immunotherapy	36 (63)	18 (56)	2 (4)
Trastuzumab deruxtecan	2 (4)[i]	20 (63)	0

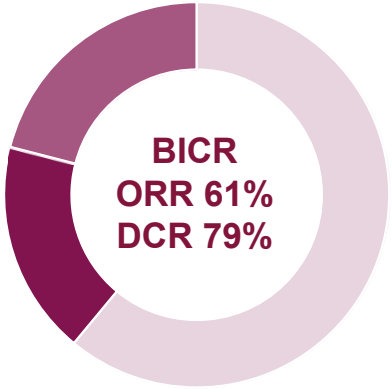
[a]Patients were naïve to HER2-targeted therapies; [b]Patients were pretreated with HER2-targeted ADCs; [c]Patients were naïve to systemic therapy for advanced disease; [d]Acinar adenocarcinoma, acinar cell carcinoma, mixed subtype adenocarcinoma, adenocarcinoma (NOS), bronchiolar adenocarcinoma, papillary adenocarcinoma (NOS), or solid adenocarcinoma with mucin formation; [e]Patients with brain lesions, including previously treated and asymptomatic brain metastases at baseline; [f]Specific variant is not an ex20ins or point mutation or unspecified *HER2* driver that could not be classified as Y772_A775dupYVMA or other *HER2* ex20ins per local assessment; [g]TKD and non-TKD *HER2* variants detected; [h]4 patients in Cohort F received and completed adjuvant or neoadjuvant therapy for stage I-III disease ≥12 months before first study dose (eligible); 1 patient completed therapy <12 months before first dose (protocol deviation); [i]Patients who had previously received ≤2 months of *HER2* ex20ins-targeted therapy and stopped for reasons other than progression were eligible if treatment was not tolerated

ECOG PS, Eastern Cooperative Oncology Group performance status; ex20ins, exon 20 insertion; NOS, not otherwise specified; TKD, tyrosine kinase domain

Presented by: Daniel Shao-Weng Tan

Response by BICR: Asian patients in Cohort D

Cohort D
(previously treated but naïve to HER2-targeted therapies)
n=57
Median follow-up: 12.2 months



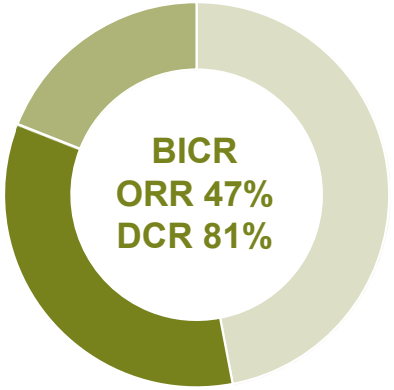
Best objective response, *n* (%)	
CR	1 (2)
PR	34 (60)
SD	16 (28)
PD	4 (7)
Not evaluable[a]	2 (4)
Not available	0
ORR[b], *n* (%) [95% CI]	35 (61) [47.6, 74.0]
DCR[c], *n* (%) [95% CI]	45 (79) [66.1, 88.6]
Median DoR[d], months [95% CI]	12.6 [6.3, 15.9]
Median PFS, months [95% CI]	8.3 [6.7, 16.5]

Analysis cut-off date was March 28, 2025. Response was assessed per RECIST v1.1
[a]Requirement for CR, PR, SD, or PD was not met; [b]Confirmed CR or PR; [c]Confirmed CR, PR, or SD for ≥12 weeks;
[d]Data from subset of patients with confirmed PR or CR
CI, confidence interval; CR, complete response; DCR, disease control rate; PD, progressive disease; PR, partial response; SD, stable disease

Presented by: Daniel Shao-Weng Tan

Response by BICR: Asian patients in Cohort E

Cohort E
(previously treated with HER2-targeted ADCs)
n=32
Median follow-up: 10.8 months



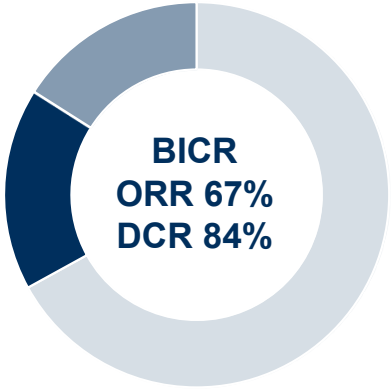
Best objective response, *n* (%)	
CR	2 (6)
PR	13 (41)
SD	14 (44)
PD	2 (6)
Not evaluable[a]	1 (3)
Not available	0
ORR[b], *n* (%) [95% CI]	15 (47) [29.1, 65.3]
DCR[c], *n* (%) [95% CI]	26 (81) [63.6, 92.8]
Median DoR[d], months [95% CI]	8.5 [4.1, NE[e]]
Median PFS, months [95% CI]	6.7 [4.3, 16.3]

Analysis cut-off date was March 28, 2025. Response was assessed per RECIST v1.1
[a]Requirement for CR, PR, SD, or PD was not met; [b]Confirmed CR or PR; [c]Confirmed CR, PR, or SD for ≥12 weeks;
[d]Data from subset of patients with confirmed PR or CR; [e]Cannot be estimated due to censored data
NE, not estimable

Presented by: Daniel Shao-Weng Tan

Response by BICR: Asian patients in Cohort F

Cohort F
(naïve to systemic therapy for advanced disease)
n=51
Median follow-up: 7.6 months



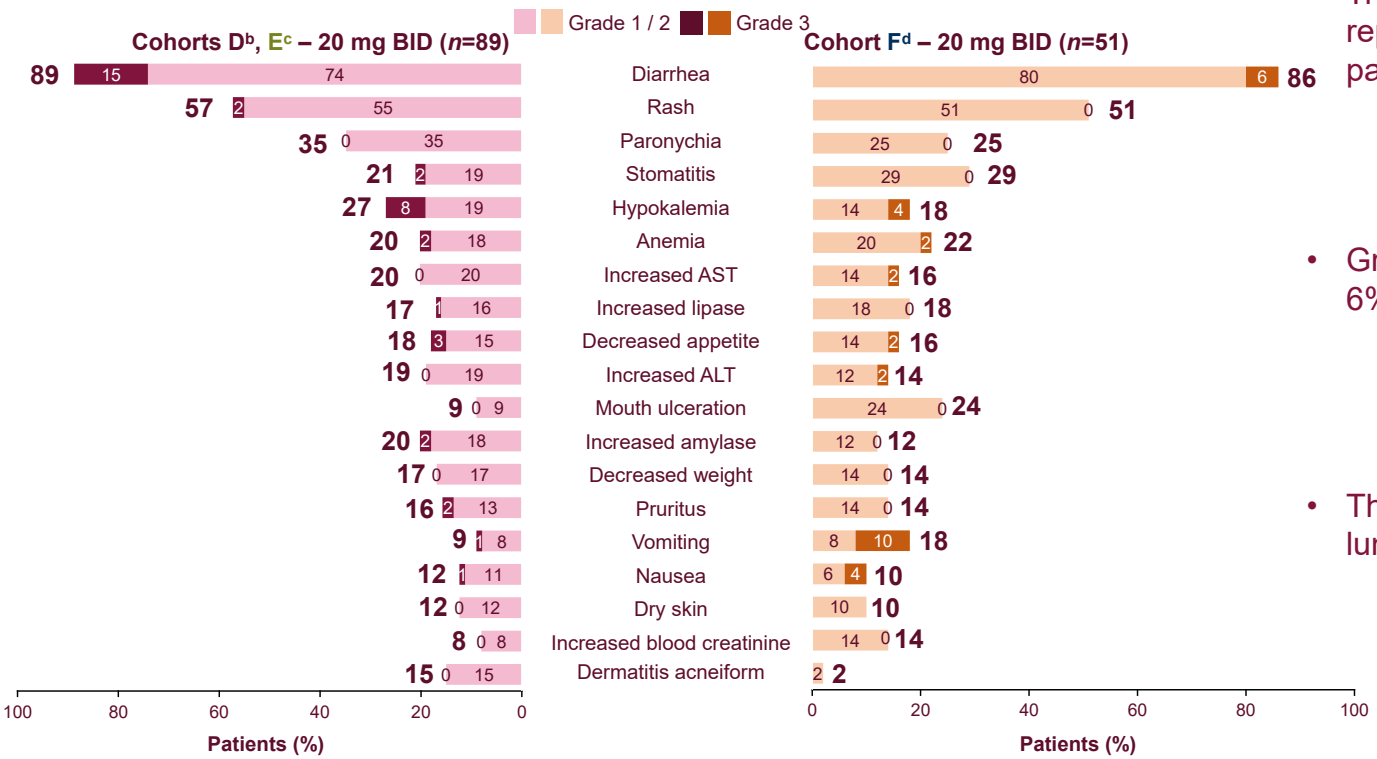
Best objective response, *n* (%)	
CR	2 (4)
PR	32 (63)
SD	13 (26)
PD	3 (6)
Not evaluable[a]	0
Not available	1 (2)
ORR[b], *n* (%) [95% CI]	34 (67) [52.1, 79.2]
DCR[c], *n* (%) [95% CI]	43 (84) [71.4, 93.0]
Median DoR[d], months [95% CI]	NE[e] [8.1, NE[e]]
Median PFS, months [95% CI]	NE[e] [9.9, NE[e]]

Analysis cut-off date was March 28, 2025. Response was assessed per RECIST v1.1
[a]Requirement for CR, PR, SD, or PD was not met; [b]Confirmed CR or PR; [c]Confirmed CR, PR, or SD for ≥12 weeks; [d]Data from subset of patients with confirmed PR or CR; [e]Cannot be estimated due to censored data

Presented by: Daniel Shao-Weng Tan

Sevabertinib safety and tolerability in Asian patients

Most frequent treatment-related adverse events (≥10% of total)[a]



- Treatment-related adverse events were reported in 98%, 100%, and 100% of Asian patients in Cohorts D, E, and F, respectively
  - Grade 3 treatment-related adverse events were reported in 18 (32%), 13 (41%), and 10 (20%) patients[e]
- Grade 3 diarrhea was reported in 19% (D), 6% (E), and 6% (F) of patients
  - No grade 4 diarrhea
  - No treatment discontinuations due to diarrhea
- There were no cases of interstitial lung disease or pneumonitis

Analysis cut-off date was March 28, 2025. Grade categories do not necessarily equal total due to rounding
[a]Medical Dictionary for Regulatory Activities version 27.1, Common Terminology Criteria for Adverse Events version 5.0; [b]Patients were naïve to HER2-targeted therapies; [c]Patients were pretreated with HER2-targeted ADCs; [d]Patients were naïve to systemic therapy for advanced disease; [e]Grade 4 event of elevated ALT was reported, and 1 grade 5 event of cardiorespiratory arrest (this patient had baseline cardiopulmonary comorbidities and experienced renal failure, and the role of sevabertinib and renal failure in this outcome remains unclear and was reported by the investigator as "possibly related" to the study drug)
ALT, alanine aminotransferase; AST, aspartate aminotransferase

Presented by: Daniel Shao-Weng Tan

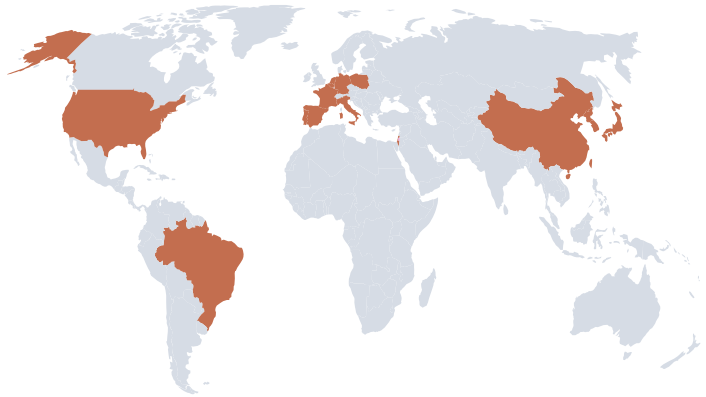
Conclusions

- Sevabertinib demonstrated robust and durable responses in Asian patients with *HER2*-mutant advanced NSCLC in both pretreated and first-line settings
- The most common side effect of sevabertinib was diarrhea, which was manageable; there were no reported cases of interstitial lung disease or pneumonitis
- These data support sevabertinib as a potential new targeted therapy for patients with *HER2*-mutant NSCLC
- The safety and efficacy of sevabertinib as first-line therapy for locally advanced or metastatic NSCLC with *HER2* mutations are being investigated in the ongoing Phase III, randomized SOHO-02 study (NCT06452277)

Presented by: Daniel Shao-Weng Tan

Acknowledgments

- We thank the patients and their families for participation in the SOHO-01 study
- We thank the investigators and their team members at each of the 90 study sites
- This study was sponsored by Bayer AG
- Caudex, an IPG Health company, provided medical writing and editorial assistance for this presentation, funded by Bayer AG



Participating countries in SOHO-01

Europe		Asia		Americas
Belgium	Netherlands	China	Singapore	Brazil
France	Poland	Hong Kong	Taiwan	USA
Israel	Portugal	Japan		
Italy	Spain	Republic of Korea		

Presented by: Daniel Shao-Weng Tan

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sevabertinib in Advanced *HER2*-Mutant Non–Small-Cell Lung Cancer

X. Le,[1] T.M. Kim,[2] H.H. Loong,[3,4] A. Prelaj,[5] B.C. Goh,[6,7] L. Li,[8,9] Y. Fang,[10] S. Lu,[11] X. Dong,[12] L. Wu,[13] Y. Shinno,[14] G. Daniele,[15] T.-Y. Yang,[16] H.R. Kim,[17,18] G. Ruiter,[19] J. Zhao,[20] S. Novello,[21] L. Miao,[22] P.A. Jänne,[23] K. Goto,[24] D. Rüttinger,[25] T. Descamps,[26] J.C. Brase,[27] W. Bao,[28] R. Li,[28] N. Brega,[27] P. Grassi,[29] N. Girard,[30] and D.S.-W. Tan,[31,32] for the SOHO-01 Investigators*

Presented by: Daniel Shao-Weng Tan

SINGAPORE 2025 ESMO ASIA

Thank you!

European Society for Medical Oncology (ESMO)
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
esmo@esmo.org

esmo.org

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE