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Final overall survival and long-term safety outcomes of savolitinib in patients with locally advanced or metastatic NSCLC harboring MET exon 14 (METex14) mutation: An update from a phase IIb study

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Background: Savolitinib (Savo) is a potent and highly selective oral MET inhibitor. We previously reported robust and durable activity of savo from a phase IIb confirmatory study (data cut: Oct 20, 2023; Shun L, et al. ELCC 2024), with ORR of 62.1% and 39.2%, median PFS (mPFS) of 13.7 mo and 11.0 mo, median OS (mOS) of not mature, in treatment-naïve and previously treated patients (pts), respectively. Here we report the final OS and long-term safety outcomes of this 3b study (data cut: Nov 30, 2024).

Methods: Treatment-naïve (1 L) or previously treated (≥ 2 L) pts with advanced or metastatic METex14 NSCLC were enrolled. Eligible pts received savo QD at 600 mg (body weight ≥ 50 kg) or 400 mg (< 50 kg). OS analysis was conducted via Kaplan-Meier method.

Results: Among the 166 pts who received savo, the median follow-ups for 87 treatment-naïve pts and 79 previously treated pts were 34.5 and 25.1 mo, respectively. 48.8% of pts (48.3% of treatment-naïve and 49.4% of previously treated) received subsequent anti-tumor therapies, with chemotherapy (27.7%) and targeted therapy (23.5%) being most frequent. In 87 treatment-naïve pts, mOS (95%CI) was 28.3 mo (17.5, NE), and 36-mo OS rate was 44.7% (33.7%, 55.0%). In 79 previously treated pts, mOS was 25.3 mo (20.5, 30.5), and 24-mo OS rate was 51.7% (39.1%, 62.9%). Post-hoc OS subgroup suggested that pts with baseline brain metastasis (BM) might also gain survival benefit; mOS was 15.3 mo and 25.3 mo in treatment-naïve pts with BM (10/87 pts) and previously treated pts with BM (21/79 pts), respectively. Treatment-related Grade ≥ 3 treatment-emergent adverse events occurred in 103 out of 166 pts (62.0%), and the common events were hepatic function abnormal (17.5%), alanine aminotransferase increased (15.1%), and aspartate aminotransferase increased (12.0%).

Conclusions: The final OS results of this 3b study further demonstrate survival benefits of savo in advanced or metastatic METex14 NSCLC, particularly in treatment-naïve pts. No new safety signal was observed.

Clinical trial identification: NCT04923945.

Editorial acknowledgement: Writing and editing assistance was provided by Dr. Haoyun Shi of HUTCHMED Limited.

Legal entity responsible for the study: HUTCHMED Limited.

Funding: HUTCHMED Limited and AstraZeneca.

Disclosure: Q. Song, S. Fan: Financial Interests, Personal, Full or part-time Employment: HUTCHMED Limited. M. Shi: Financial Interests, Personal, Full or part-time Employment: HUTCHMED Limited; Financial Interests, Personal, Member of Board of Directors: HUTCHMED Limited; Financial Interests, Personal, Officer: HUTCHMED Limited. W. Su: Financial Interests, Personal, Full or part-time Employment: HUTCHMED Limited; Financial Interests, Personal,

Member of Board of Directors: HUTCHMED Limited; Financial Interests, Personal, Officer: HUTCHMED Limited. All other authors have declared no conflicts of interest.

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Tepotinib in patients (pts) with MET exon 14 (METex14) skipping non-small cell lung cancer (NSCLC) from the VISION study: ≥ 3 -year follow-up outcomes

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Background: Tepotinib, a highly selective MET inhibitor has demonstrated robust and durable efficacy and safety in pts with METex14 skipping NSCLC in Cohorts A+C (data cut-off: Nov 20, 2022; follow-up: Cohort A > 35 months, Cohort C > 18 months) and in pts with high-level MET amplification (METamp) NSCLC in Cohort B of the Phase II VISION study (NCT02864992). We report long-term efficacy and safety outcomes from VISION in pts with ≥ 3 -years follow-up (data cut-off: May 20, 2024).

Methods: Pts with advanced NSCLC and METex14 skipping or METamp received tepotinib 500 mg (450 mg active moiety) once daily. Primary endpoint was objective response by independent review using RECIST v1.1. Secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety.

Results: Of 313 pts enrolled in Cohorts A+C (male: 49.2%; median age [range]: 72 years [41–94]; ECOG PS 1: 73.8%; smoking history: 47.6%), the median duration of treatment was 7.5 months (range: 0.03–83.12) and treatment was ongoing in 18 pts (first-line [1L]: 12/164; second-or-

later line [2L+]: 6/149). Overall, objective response rate (ORR) was 51.8% (95% CI: 46.1, 57.4) and median (m) DOR was 18.0 months (12.6, 31.8). In 1L pts, ORR was 57.9% (50.0, 65.6) and mDOR was 31.7 months (13.8, 46.4), while in 2L+ pts, ORR was 45.0% (36.8, 53.3) and mDOR was 12.6 months (9.5, 18.5) (Table). No new safety concerns were observed. Grade ≥ 3 treatment-related adverse events (TRAEs) occurred in 36.1% of pts, while 15.7% of pts discontinued treatment due to TRAEs. Long-term outcomes from Cohort B will also be presented.

Table: 81P

		Overall N = 313	1L n = 164	2L+ n = 149
Efficacy				
ORR, %		51.8	57.9	45.0
(95% CI)		(46.1, 57.4)	(50.0, 65.6)	(36.8, 53.3)
DOR	Median	18.0	31.7	12.6
	(95% CI), months	(12.6, 31.8)	(13.8, 46.4)	(9.5, 18.5)
	Events, n (%)	77 (47.5)	40 (42.1)	37 (55.2)
PFS	Median	11.2	12.6	11.0
	(95% CI), months	(9.5, 13.8)	(9.7, 17.7)	(8.2, 13.7)
	Events, n (%)	172 (55.0)	88 (53.7)	84 (56.4)
OS	Median	19.7	21.1	19.3
	(95% CI), months	(16.2, 22.3)	(14.2, 24.5)	(15.6, 21.0)
	Events, n (%)	234 (74.8)	119 (72.6)	115 (77.2)

1L, first-line; 2L+, second-or-later line; CI, confidence interval; DOR, duration of response; m, median; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Conclusions: In VISION pts with ≥ 3 -years follow-up, tepotinib continued to demonstrate robust and durable activity across treatment lines. Importantly, outcomes in pts with METex14 skipping were consistent with previous results, reinforcing tepotinib as a meaningful treatment option in this setting.

Clinical trial identification: NCT02864992.

Editorial acknowledgement: Medical writing assistance (funded by Merck) was provided by Bhartendu K Srivastava, PhD of Syneos Health, London, UK.

Legal entity responsible for the study: Merck Healthcare KGaA, Darmstadt, Germany.

Funding: Merck (CrossRef Funder ID: 10.13039/100009945).

Disclosure: J. Mazieres: Financial Interests, Personal, Advisory Board: Roche, BMS, MSD, AstraZeneca, Pfizer, Novartis, Merck, Amgen, Takeda, Daiichi Sankyo; Financial Interests, Institutional, Other, Research funding: Roche/Genentech, AstraZeneca, Bristol Myers Squibb. R. Veillon: Financial Interests, Personal, Other, Research funding: Merck; Financial Interests, Personal, Other, Consulting fees: Janssen; Financial Interests, Personal, Other, Speaker fees: BMS, Takeda; Financial Interests, Personal, Speaker's Bureau: Amgen, Sanofi, Roche, AstraZeneca; Financial Interests, Personal, Other, Travel fees: Pfizer, Janssen. A.B. Cortot: Financial Interests, Personal, Other, Research funding: Novartis, Merck; Financial Interests, Personal, Other, Honoraria: AstraZeneca, BMS, Novartis, MSD, Pfizer, Roche, Takeda; Financial Interests, Personal, Advisory Role: AstraZeneca, BMS, Novartis, Pfizer, Roche, Takeda; Financial Interests, Personal, Other, Travel expenses: AstraZeneca, MSD, Novartis, Pfizer, Roche, Takeda. R. Ferrara: Financial Interests, Personal, Advisory Board: MSD, BeiGene. E. Felip: Financial Interests, Personal, Advisory Role: Pfizer, Roche, Boehringer Ingelheim, AstraZeneca, BMS, Guardant Health, Novartis, Takeda, AbbVie, Blue Print Medicines, Lilly, Merck, MSD, Janssen, Samsung; Financial Interests, Personal, Other, Speaker's bureau/expert testimony: Pfizer, Roche, AstraZeneca, BMS, Novartis, Takeda, Lilly, MSD, Medscape, prIME Oncology, Touchtime; Financial Interests, Personal, Research Grant, Grant for Oncology Innovation (GOI): Fundación Merck Salud, a private non-profit institution founded by Merck, S.L.U., Madrid, Spain, an affiliate of Merck KGaA; Financial Interests, Personal, Officer, Independent member: Grifols. M.C. Garassino: Financial Interests, Personal, Other, Honoraria: MSD Oncology, AstraZeneca/MedImmune, GSK, Takeda, Roche, BMS; Financial Interests, Personal, Advisory Role: BMS, MSD, AstraZeneca, Novartis, Takeda, Roche, Tiziana Life Sciences, Sanofi-Aventis, Celgene, Daiichi Sankyo, Inivata, Incyte, Pfizer, Seattle Genetics, Eli Lilly, GSK, Bayer Healthcare Pharmaceuticals, Blueprint Medicines, Janssen, Regeneron; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, Takeda, MSD Oncology, Celgene, Incyte, Roche, BMS, Otsuka, Eli Lilly; Financial Interests, Institutional, Other, Research funding: BMS, MSD, Roche/Genentech, AstraZeneca/MedImmune, AstraZeneca, Pfizer, GSK, Novartis, Merck, Incyte, Takeda, Spectrum Pharmaceuticals, Blueprint

Medicines, Eli Lilly, Ipsen, Janssen, Exelixis, MedImmune, Sanofi, Pfizer, Amgen; Financial Interests, Personal, Other, Travel and accommodation expenses: Pfizer; Financial Interests, Personal, Invited Speaker, Travel and accommodation expenses: Roche, AstraZeneca. X. Le: Financial Interests, Personal, Advisory Role: AstraZeneca, Eli Lilly, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Novartis, Daiichi Sankyo, Hengrui Therapeutics; Financial Interests, Personal, Other, Research funding: Eli Lilly, Boehringer Ingelheim. M. Thomas: Financial Interests, Personal, Other, Honoraria – Scientific Meetings (self): AbbVie, BMS, MSD, AstraZeneca, Novartis, Roche, Takeda, Lilly, Chugai, Celgene, Boehringer Ingelheim, Pfizer, Janssen, GSK, Merck, Sanofi, Amgen; Financial Interests, Personal, Other, Travelling support (self): AbbVie, BMS, MSD, AstraZeneca, Novartis, Roche, Takeda, Lilly, Chugai Pharma, Celgene, Boehringer Ingelheim, Pfizer; Financial Interests, Personal, Advisory Board: AbbVie, BMS, MSD, AstraZeneca, Novartis, Roche, Takeda, Lilly, Chugai Pharma, Celgene, Boehringer Ingelheim, Pfizer, Janssen, Daiichi Sankyo, GSK, Merck, Sanofi, Amgen; Financial Interests, Institutional, Other, Research funding: BMS, AstraZeneca, Roche, Takeda. H. Sakai: Financial Interests, Personal, Speaker's Bureau: BMS, Ono Pharmaceutical, MSD K.K., AstraZeneca, Chugai Pharma, Taiho Pharmaceutical, Boehringer Ingelheim. E.F. Smit: Financial Interests, Institutional, Advisory Role: Lilly, AstraZeneca, Boehringer Ingelheim, Roche/Genentech, BMS, MSD Oncology, Takeda, Bayer, Regeneron, Novartis, Daiichi Sankyo, Seattle Genetics; Financial Interests, Institutional, Other, Research funding: Boehringer Ingelheim, Bayer, Roche/Genentech, AstraZeneca, BMS. J. Raskin: Financial Interests, Personal, Advisory Role: Merck, Lilly, AstraZeneca, Pfizer, BMS. S. Viteri: Financial Interests, Personal, Advisory Role: AbbVie, BMS, Roche, Takeda, AstraZeneca, MSD; Financial Interests, Personal, Speaker's Bureau: BMS, MSD, Roche, AstraZeneca; Financial Interests, Personal, Other, Travel expenses: Roche, OSE Pharma, BMS, MSD, Merck, Puma Biotechnology, Janssen Cilag. J.C. Yang: Financial Interests, Personal, Advisory Role: Amgen, Bayer, Boehringer Ingelheim, BMS, Daiichi Sankyo, MSD, Novartis, Roche/Genentech, Takeda Oncology, Yuhon Pharmaceuticals, Ono Pharmaceuticals, Pfizer. M. Ahn: Financial Interests, Personal, Advisory Role: AstraZeneca, Lilly, Amgen, Merck, MSD, Takeda, ONO, Pfizer, Yuhon, Alpha-pharmaceuticals, Daiichi Sankyo, Roche. Y. Wu: Financial Interests, Personal and Institutional, Other, Institute grants and personal fees: AstraZeneca, Roche, Boehringer Ingelheim; Financial Interests, Personal, Invited Speaker, Personal fees: BMS, MSD, Eli Lilly, Pfizer. V. Ghori: Financial Interests, Personal, Full or part-time Employment: Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA. R. Bruns: Financial Interests, Personal, Full or part-time Employment: Merck; Financial Interests, Personal, Stocks/Shares: Merck. A. John: Financial Interests, Personal, Full or part-time Employment: Merck; Financial Interests, Personal, Stocks/Shares: Merck. P.K. Paik: Financial Interests, Institutional, Other, Grants or contracts (institutional research): EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Bicara; Financial Interests, Personal, Other, Consulting fees: Novartis, AstraZeneca, Janssen, Bicara; Financial Interests, Personal, Other, Honoraria: IDEology, Touch IME, Excerpta Medica, ACE Oncology, Physicians Education Resource, Axis Medical Education, PeerVoice, Aptitude Health, MJH. All other authors have declared no conflicts of interest.

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A retrospective real-world evidence study of MTAP status and clinical outcomes in patients with advanced non-small cell lung cancer

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Background: In non-small cell lung cancer (NSCLC) resistance to immunotherapy and targeted therapy remain an unmet need. Methylthioadenosine phosphorylase (MTAP) deletion emerged as a promising therapeutic vulnerability present in 15% of solid tumors including NSCLC. This study characterizes demographic, clinical, and molecular features, treatment modalities, and real-world overall survival (rwOS) in advanced NSCLC patients, stratified by MTAP deletion status.