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LUNG CONNECT

ONCOGENE-ADDICTED NSCLC HIGHLIGHTS FROM ELCC 2025

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This programme is developed by LUNG CONNECT, an international group of experts in the field of thoracic oncology and brought to you alongside PRECISION ONCOLOGY CONNECT, an international group of experts in the field of detection and treatment of targetable genetic/genomic alterations in various cancers

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CLINICAL TAKEAWAYS

- **SOHO-01:** Treatment with BAY 2927088 led to durable responses in *HER2*m NSCLC patients naïve to HER2-targeted therapy and in those who had received a HER2-targeted ADC
- **MARIPOSA:** A highly meaningful and practice changing OS benefit was observed, further establishing amivantamab plus lazertinib as a new SoC in patients with first-line *EGFR*m advanced NSCLC
- **COCOON:** Early onset AEs experienced with amivantamab + lazertinib treatment can be significantly reduced with proactive prophylactic approaches
- **SAVANNAH:** Savolitinib plus osimertinib may offer a chemotherapy-free treatment option in patients with *EGFR*m, MET overexpressed and/or amplified advanced NSCLC after progression on osimertinib
- **ORCHARD:** Osimertinib + Dato-DXd showed promising efficacy and manageable safety in patients with *EGFR*m advanced NSCLC who progressed on first-line osimertinib

ADC, antibody-drug conjugate; AE, adverse event; Dato-DXd, datopotamab deruxtecan; EGFRm, EGFR mutated; HER2m, HER2 mutated; NSCLC; non-small cell lung cancer; OS, overall survival; SoC, standard of care

EDUCATIONAL OBJECTIVES

- Understand the clinical trial data and emerging profile of targeted therapies for the treatment of molecularly driven lung cancer

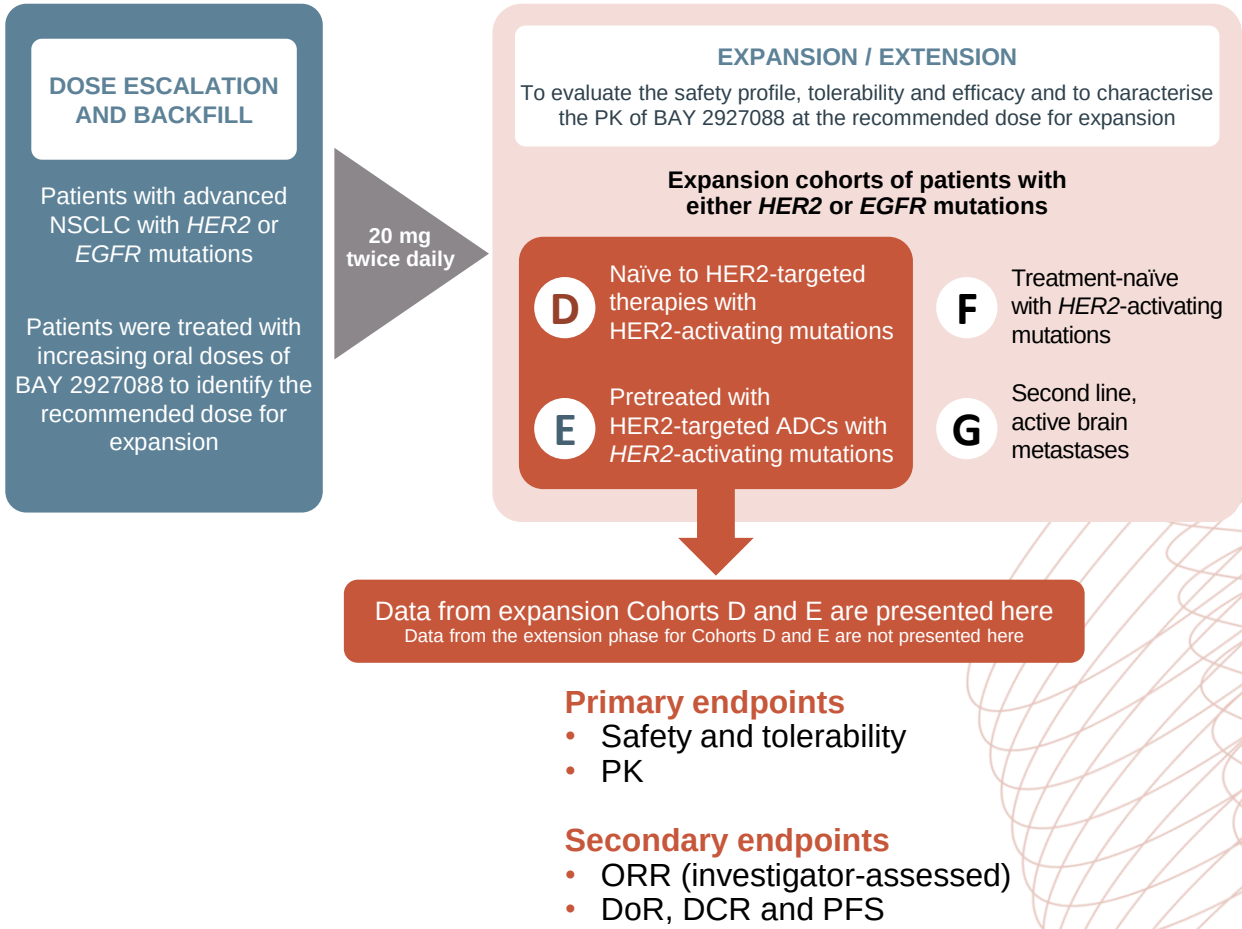
PHASE 1/2 SOHO-01 STUDY OF BAY 2927088 IN PATIENTS WITH PREVIOUSLY TREATED *HER2*-MUTANT NSCLC: SAFETY AND EFFICACY RESULTS FROM 2 EXPANSION COHORTS

Girard N, et al. Abstract 3O, ELCC 2025

NSCLC, non-small cell lung cancer

SOHO-01: BACKGROUND[1-5] AND STUDY DESIGN[6]

- *HER2*-activating mutations have been reported in approximately 2-4% of patients with NSCLC and are associated with poor prognosis[1-3]
- BAY 2927088 is an oral, reversible tyrosine kinase inhibitor that potently inhibits *HER2* and mutant *EGFR* in preclinical models[3,4]
- Encouraging anti-tumour activity and manageable safety were observed in patients with NSCLC harbouring a *HER2* activating mutation treated with BAY 2927088[3,4]
- The FDA has granted Breakthrough Therapy designation for BAY 2927088 for previously-treated patients with advanced NSCLC and activating *HER2* mutations.[3,5] Here we report results from 2 expansion cohorts of SOHO-01 (NCT05099172)[6]



Primary endpoints
- Safety and tolerability
- PK

Secondary endpoints
- ORR (investigator-assessed)
- DoR, DCR and PFS

ADC, antibody-drug conjugate; DCR, disease control rate; DoR, duration of response; FDA, Food and Drug Administration; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PK, pharmacokinetics

1. Riudavets M, et al. ESMO Open 2021; 6:100260; 2. Remon J, et al. Cancer Treat Rev. 2020;90:102105; 3. Girard N, et al. J Clin Oncol. 2024;42(suppl 17). Abstr LBA8598; 4. Loong HHF, et al. Ann Oncol. 2023;34(Supplement 2):S761-S762; 5. Bayer receives U.S. FDA Breakthrough Therapy designation for BAY 2927088 for non-small cell lung cancer harboring HER2 activating mutations. Available here (accessed April 2025); 6. Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S9. ELCC 2025 (oral presentation, Abstract 3O)

SOHO-01: EFFICACY RESULTS

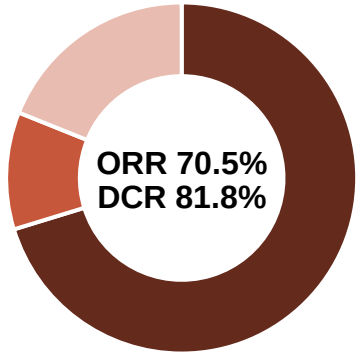
DEMOGRAPHY

- Median age: 62.0 years (D) and 62.5 years (E); Females: 63.6% (D) and 61.8% (E); Never smokers: 70.5% (D) and 64.7% (E)
- 54.5% (D) and 76.5% (E) had received ≥2 therapy lines, and 82.4% (E) had received trastuzumab deruxtecan

ORR BY INVESTIGATOR

N (%)	Cohort D (N=44)	Cohort E (N=34)
CR, n (%)	1 (2.3)	0
PR, n (%)	30 (68.2)	12 (35.3)
SD, n (%)	7 (15.9)	11 (32.4)
PD, n (%)	5 (11.4)	9 (26.5)
NE, n (%)	1 (2.3)	2 (5.9)
ORR, n (%) [95% CI]	**31 (70.5)** [54.8, 83.2]	**12 (35.3)** [19.7, 53.5]
DCR, n (%) [95% CI]	**36 (81.8)** [67.3, 91.8]	**18 (52.9)** [35.1, 70.2]
mDoR, months (95% CI)	8.7 (4.5, NE)	9.5 (4.1, NE)

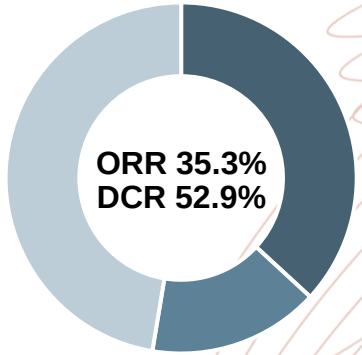
Cohort D:
Naïve to HER2-targeted therapy



Median follow-up:
17.2 months
(range 0.95-24.38)

Median duration of treatment:
7.2 months
(range 0.20-24.4)

Cohort E:
Progressed on HER2-targeted ADCs



Median follow-up:
10.3 months
(range 2.69-14.91)

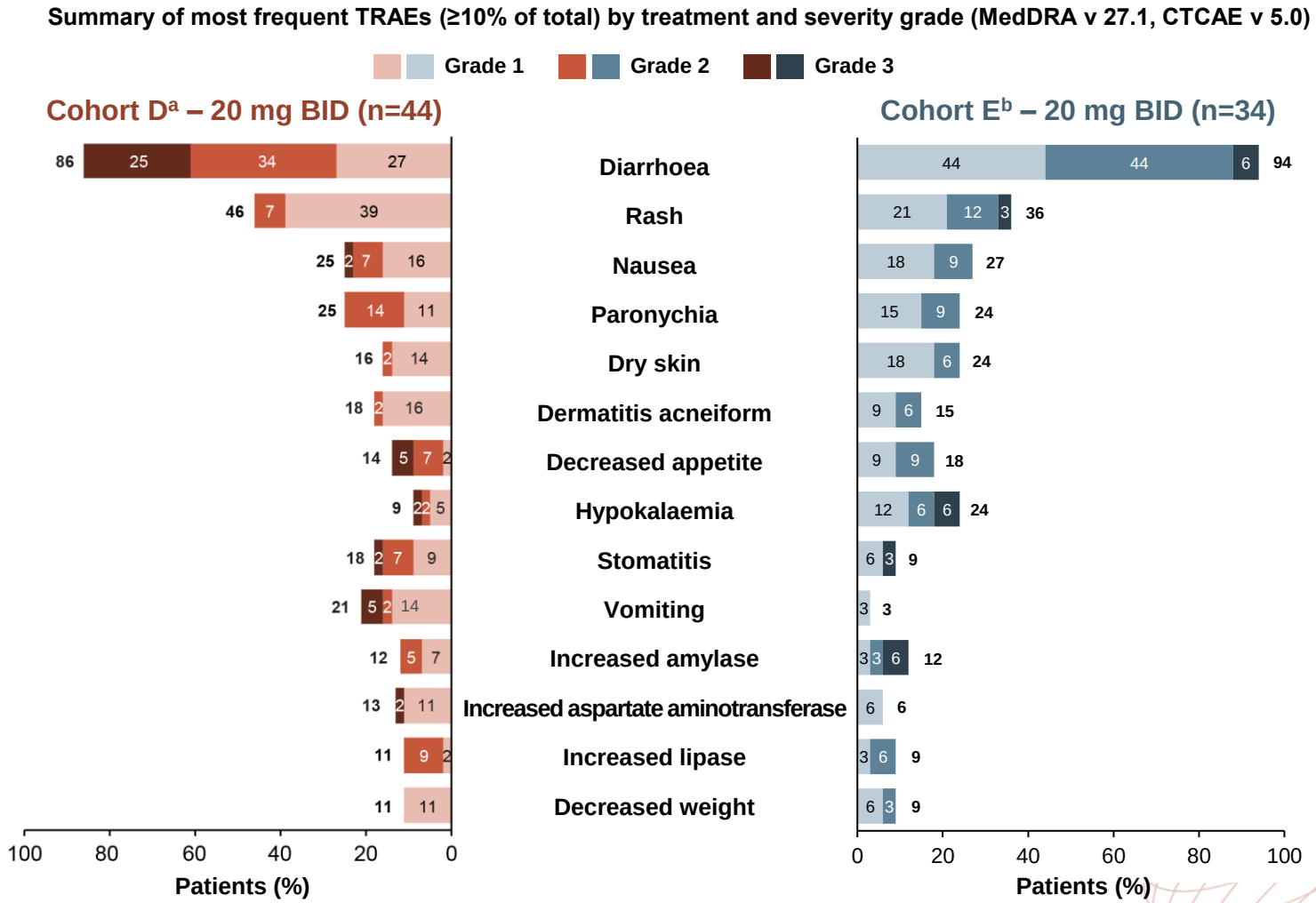
Median duration of treatment:
4.8 months
(range 0.43-14.78)

ADC, antibody-drug conjugate; CI, confidence interval; CR, complete response; DCR, disease control rate; mDoR, median duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S9. ELCC 2025 (oral presentation, Abstract 3O)

SOHO-01: SAFETY RESULTS

- TRAEs were reported in 97.4% of pts
- Diarrhoea was the most common TRAE, mostly G1 or 2, leading to dose reduction
- No patients discontinued treatment due to diarrhoea
- No cases of interstitial lung disease
- 7 patients (9.0%) had serious TRAEs



[a] Patients with NSCLC with *HER2*-activating mutations who are naïve to HER2-targeted therapies; [b] Patients with NSCLC with *HER2*-activating mutations who have received and progressed on HER2-targeted ADCs

ADC, antibody-drug conjugate; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; G, grade; MedDRA, Medical Dictionary for Regulatory Activities; NSCLC, non-small cell lung cancer; TRAE, treatment-related adverse events

Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S9. ELCC 2025 (oral presentation, Abstract 3O)

SOHO-01: SUMMARY

- Treatment with BAY 2927088 led to durable responses in patients naïve to HER2-targeted therapy and in those who had received a HER2-targeted ADC
- The safety profile of BAY 2927088 was manageable across cohorts and consistent with previous reports
- The safety and efficacy of BAY 2927088 as first-line therapy for locally or mNSCLC with HER2 mutations are being investigated in the ongoing phase 3 SOHO-02 trial

Clinical perspective

- The durable responses in heavily pre-treated patients with *HER2*m NSCLC are clinically meaningful
- SOHO-01 provides insight into potential future treatment sequences for these patients. T-DXd is expected to become a potential 1st line option for those patients based on DESTINY-Lung04. SOHO-01 suggests that BAY 2927088 could be a potential 2nd line option irrespective of prior therapy (including ADC)
- SOHO-02 trial will provide more information on the efficacy of BAY 2927088 in the 1st line setting versus chemotherapy + immune checkpoint inhibitor

ADC, antibody-drug conjugate; HER2m, HER2 mutated; mNSCLC, metastatic non-small cell lung cancer; T-DXd, trastuzumab deruxtecan

Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S9. ELCC 2025 (oral presentation, Abstract 3O)

AMIVANTAMAB PLUS LAZERTINIB VS OSIMERTINIB IN FIRST-LINE *EGFR*-MUTANT ADVANCED NSCLC: FINAL OVERALL SURVIVAL FROM THE PHASE 3 MARIPOSA STUDY

Chih-Hsin Yang J, et al. Abstract 4O, ELCC 2025

NSCLC, non-small cell lung cancer

MARIPOSA: BACKGROUND[1] AND STUDY DESIGN[2]

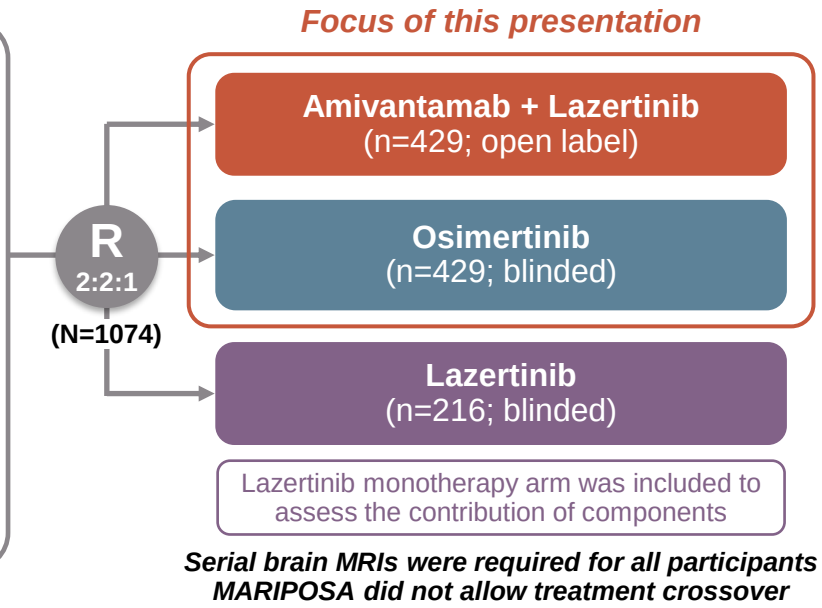
- In MARIPOSA (NCT04487080); 1st line amivantamab plus lazertinib significantly improved progression-free survival vs osimertinib in patients with *EGFR*m advanced NSCLC, with consistent benefit across risk groups[1]
- Favourable OS trends were seen for amivantamab plus lazertinib vs osimertinib at interim OS analysis and after 31.1 months follow-up[2]
- The final analysis of OS for amivantamab plus lazertinib vs osimertinib from MARIPOSA is reported[3]

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Treatment naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Stratification factors

- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases (yes or no)



Primary endpoint:

- PFS by BICR per RECIST v1.1

Key secondary endpoint:

- Protocol-specified final overall survival

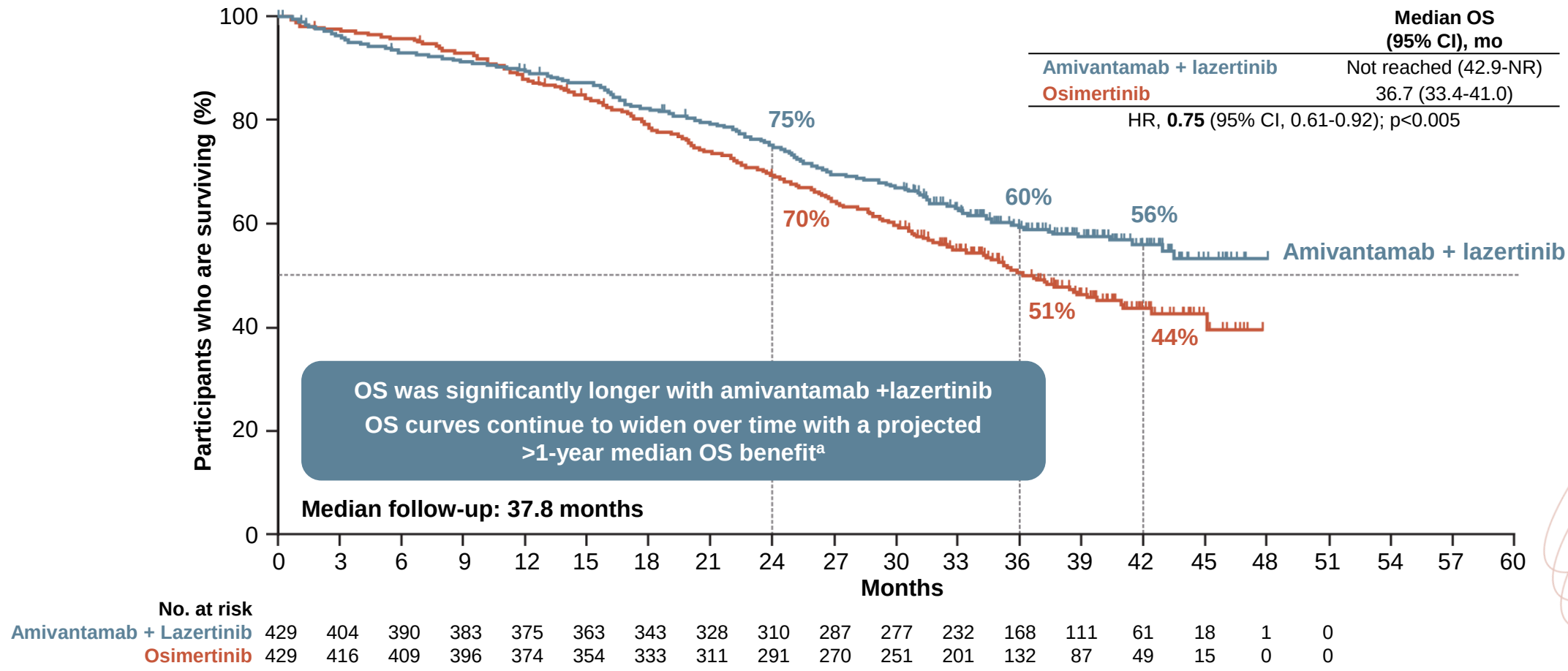
Other endpoints reported in this presentation:

- Intracranial PFS (icPFS)
- Intracranial ORR (icORR)
- Intracranial DoR (icDoR)
- Time to symptomatic progression (TTSP)
- Safety

BICR, blinded independent central review; DoR, duration of response; ECOG PS, Easter Cooperative Oncology Group performance status; EGFRm, EGFR mutated; Ex19del, exon 19 deletion; ic, intracranial; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours

1. Cho BC, et al. N Engl J Med. 2024;391:1486-1498; 2. Gadgeel S, et al. J Thorac Oncol. 2024;19 (10):S10-S11; 3. Chih-Hsin Yang J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 4O)

MARIPOSA: EFFICACY RESULTS (OVERALL SURVIVAL)



- A generally consistent OS benefit for amivantamab + lazertinib over osimertinib was observed across all predefined subgroups

[a] Based on an exponential distribution assumption of OS in both arms, the improvement in median OS is projected to exceed 1 year

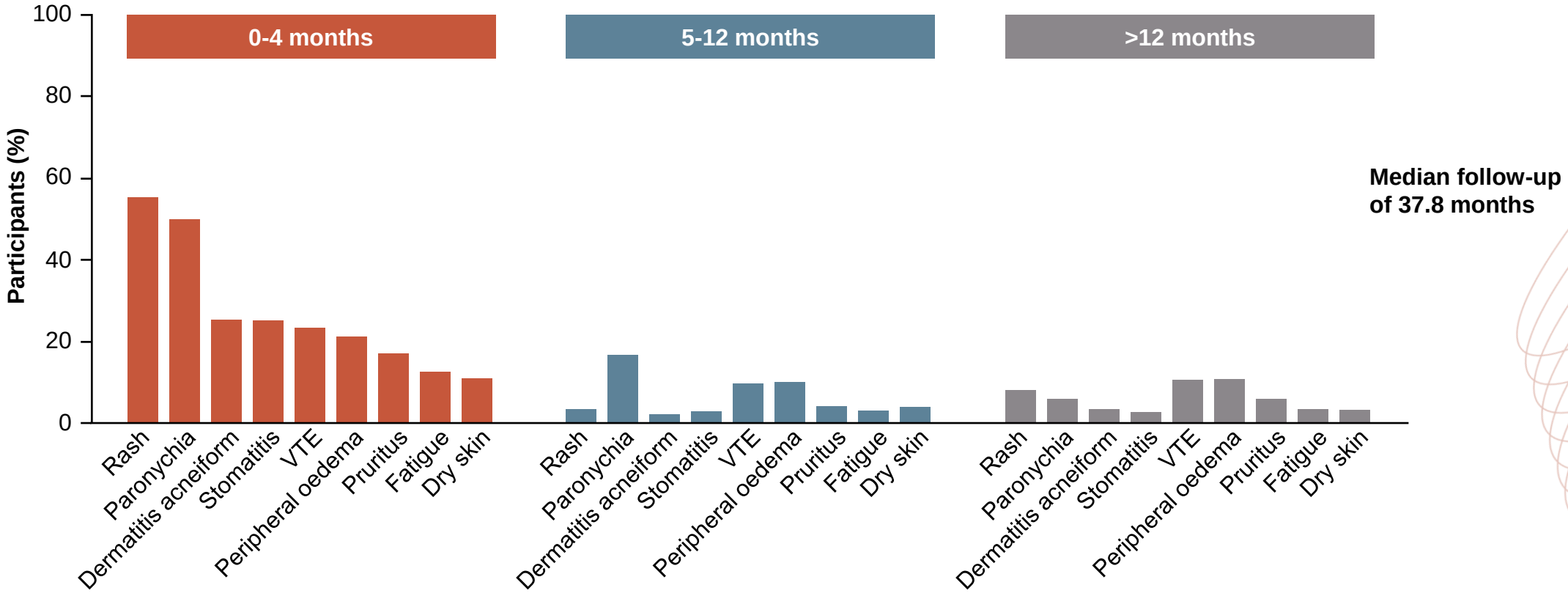
CI, confidence interval; HR, hazard ratio; mo, months; NR, not reached; OS, overall survival

Chih-Hsin Yang J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 4O)

MARIPOSA: SAFETY RESULTS

FIRST ONSET OF KEY AEs FOR 1ST LINE AMIVANTAMAB + LAZERTINIB

- Most first onset AEs occur early (0-4 months), with longer-term follow up showing no new safety signals and indicating that long-term treatment is feasible



AE, adverse event; VTE, venous thromboembolism

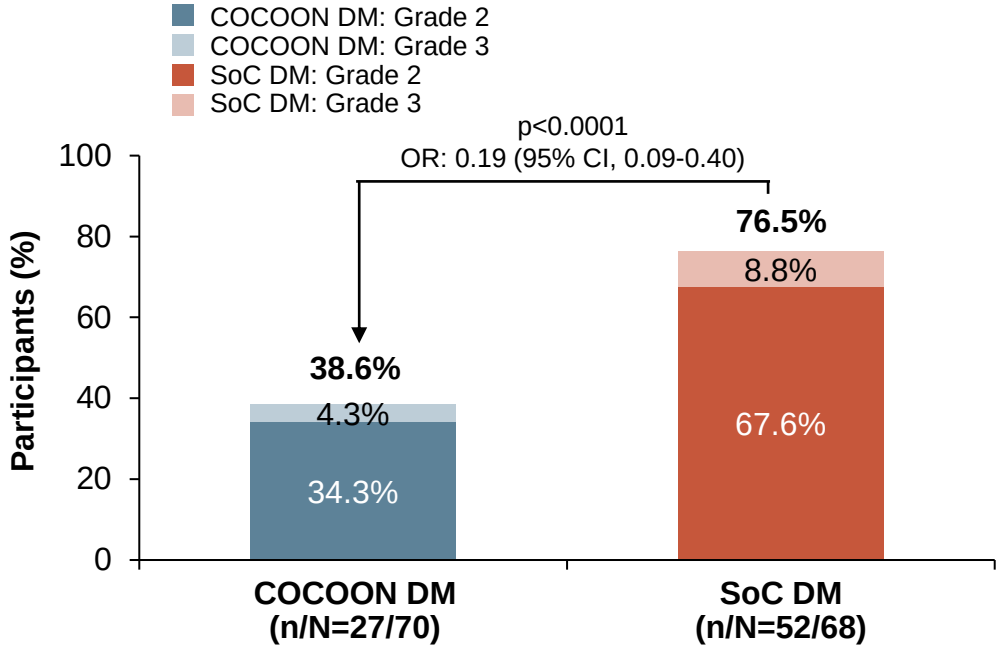
Chih-Hsin Yang J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 4O)

PREVENTING AEs WITH AMIVANTAMAB + LAZERTINIB

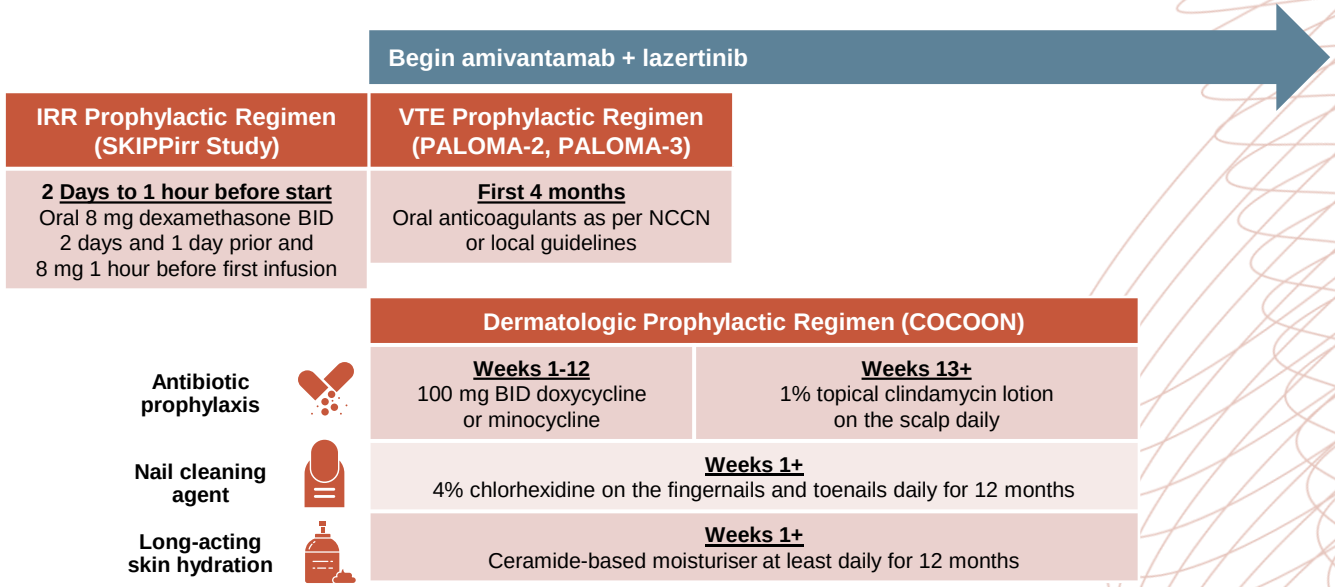
COCOON TRIAL

- The prophylactic COCOON DM regimen reduced the incidence of grade ≥ 2 dermatologic AEs by 50% versus standard of care[1]

Primary endpoint: incidence of G≥2 dermatologic AEs in first 12 weeks of treatment[1,2]



Preventing AEs with amivantamab + lazertinib[1]



AE, adverse event; BID, twice daily; CI, confidence interval; DM, dermatologic management; G, grade; IRR, infusion-related reaction; OR, odds ratio; SoC, standard of care; VTE, venous thromboembolism

1. Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 10MO); 2. Chih-Hsin Yang J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 4O);

MARIPOSA: SUMMARY

- Amivantamab plus lazertinib significantly reduced the risk of death vs osimertinib in patients with previously untreated *EGFR*m advanced NSCLC[1]
- While the median has not yet been reached for amivantamab plus lazertinib, it is expected to provide an OS benefit of at least 12 months[1]
- Safety profile was consistent with the primary analysis, with most AEs being EGFR- and MET-related and grades 1-2[2]
- Early onset AEs can be significantly reduced with prophylactic approaches as seen in the COCOON trial[3]

Clinical perspective

- The OS benefit seen in MARIPOSA is highly meaningful and practice changing and further establishes amivantamab plus lazertinib as a new SoC in patients with first-line *EGFR*m advanced NSCLC
- The efficacy is accompanied by early and long-lasting toxicity but this, particularly dermatologic toxicities, can be managed with proactive prophylactic treatment regimen
- The benefit:risk ratio of the amivantamab plus lazertinib combination must be considered alongside the patient's treatment objectives as part of the shared decision-making process

AE, adverse event; EGFRm, EGFR mutant; NSCLC, non-small cell lung cancer; OS, overall survival; SoC, standard of care

1. Chih-Hsin Yang J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 4O); 2. Cho BC, et al. N Engl J Med. 2024;391:1486-1498; 3. Girard N, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 10MO)

SAVANNAH: SAVOLITINIB + OSIMERTINIB IN PATIENTS WITH *EGFR*m ADVANCED NSCLC AND MET OVEREXPRESSION AND/OR AMPLIFICATION FOLLOWING PROGRESSIVE DISEASE ON OSIMERTINIB

Ahn M-J, et al. Abstract 2O, ELCC 2025

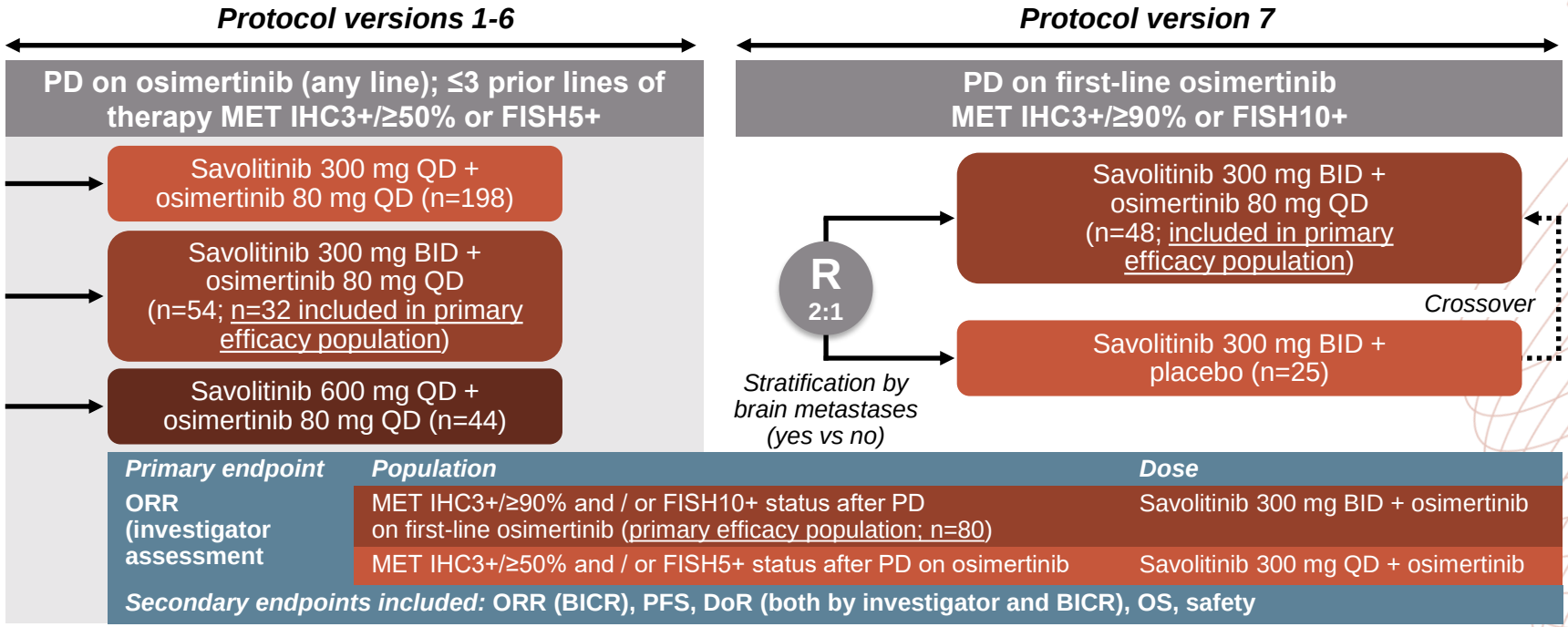
NSCLC, non-small cell lung cancer

SAVANNAH: BACKGROUND AND STUDY DESIGN

- Savolitinib is an oral, potent and highly selective MET-TKI that when combined with osimertinib, an oral, third-generation EGFR-TKI, may overcome acquired MET-driven resistance in *EGFR*m advanced NSCLC post-osimertinib
- The primary results from the phase 2 SAVANNAH study (NCT03778229), assessing the efficacy and safety of savolitinib + osimertinib in this setting are reported

Key inclusion criteria

- ≥18 years (Japan: ≥20 years)
- Locally advanced or metastatic *EGFR*m NSCLC
- PD on osimertinib
- Centrally confirmed MET overexpression (IHC) or amplification (FISH)
- ECOG PS 0/1
- Stable CNS metastases permitted



BICR, blinded independent central review; BID, twice daily; CNS, central nervous system; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFRm, EGFR mutated; FISH, fluorescence in situ hybridisation; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; QD, once daily; R, randomised; TKI, tyrosine kinase inhibitor

Ahn M-J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 2O)

SAVANNAH: RESULTS

EFFICACY

	Patients with PD on 1L osi and MET IHC 3+/≥90% or FISH10+ status who received savo 300 mg BID + osi (primary efficacy population; n=80)	
	Inv assessment	BICR assessment
Confirmed ORR (95% CI), %	56 (45, 67)	55 (43, 66)
Median DoR (95% CI), months	7.1 (5.6, 9.6)	9.9 (6.0, 13.7)
Median PFS (95% CI), months	7.4 (5.5, 7.6)	7.5 (6.4, 11.3)
PFS events, n (%)	65 (81)	49 (61)

SAFETY

- Grade ≥3 AEs occurred in 57% (Grade ≥3 TRAEs 32%); SAEs 31%; AEs leading to discontinuation of savolitinib/osimertinib 16%/12%
- Most common all-grade AEs (>20%): peripheral oedema 58%, nausea 45%, diarrhoea 33%, vomiting 21%. No new safety concerns emerged

1L, first line; AE, adverse event; BICR, blinded independent central review; BID, twice daily; CI, confidence interval; DoR, duration of response; FISH, fluorescence in situ hybridisation; IHC, immunohistochemistry; Inv, investigator; ORR, objective response rate; osi, osimertinib; PD, progressive disease; PFS, progression-free survival; SAE, serious AE; savo, savolitinib; TRAE, treatment-related AEs

Ahn M-J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 2O)

SAVANNAH: SUMMARY

- After progressive disease on 1st line osimertinib, treatment with savolitinib plus osimertinib was well tolerated and demonstrated clinically meaningful and durable response in patients with *EGFR*m advanced NSCLC with MET IHC 3+/≥90% and/or FISH10+ status
- This combination offers a potential treatment option in this setting and is under further investigation in the ongoing phase 3 SAFFRON study (NCT05261399)

Clinical perspective

- The results of the SAVANNAH trial lend support to the approach of combining osimertinib with another matched targeted therapy based on the acquired resistance mechanism
- Rebiopsy for molecular testing of patients exhibiting resistance to 1st line treatment can identify targets such as MET overexpression which may be effectively treated with savolitinib, an oral MET inhibitor in combination with osimertinib

EGFRm, EGFR mutated; FISH, fluorescence in situ hybridisation; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer

Ahn M-J, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstract 2O)

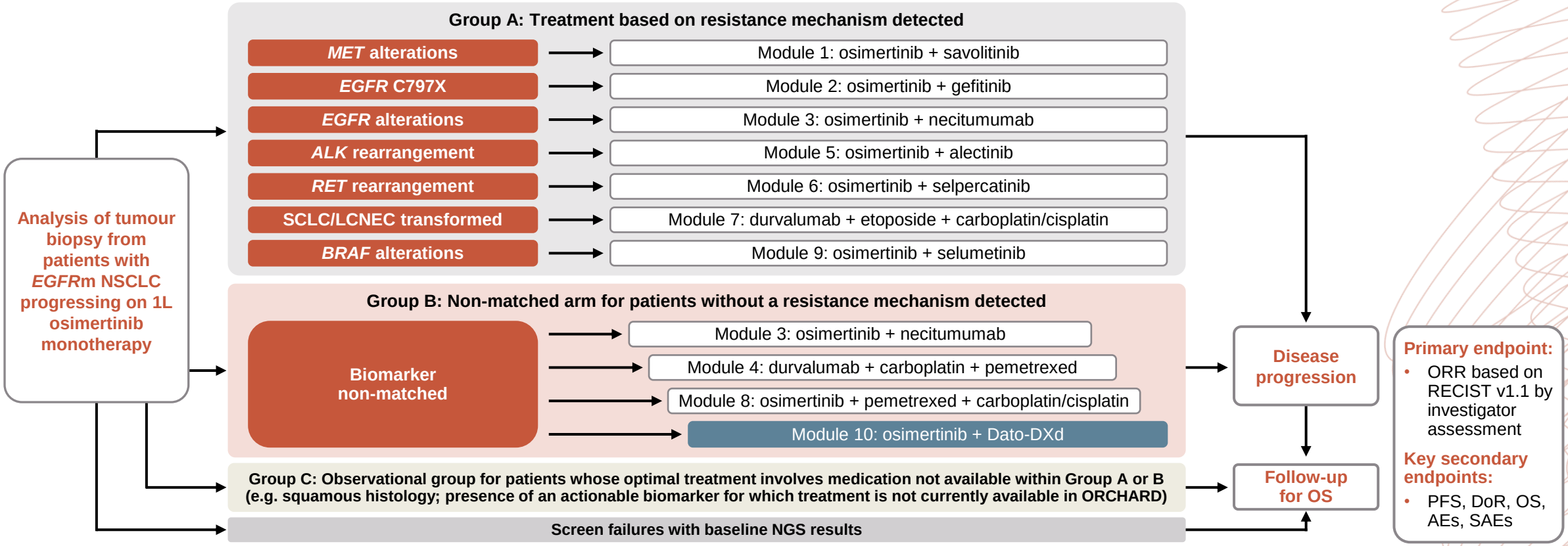
OSIMERTINIB + DATOPOTAMAB DERUXTECAN IN PATIENTS WITH *EGFR*-MUTATED ADVANCED NSCLC WHOSE DISEASE PROGRESSED ON FIRST LINE OSIMERTINIB: ORCHARD

Le X, et al. Abstract 1O, ELCC 2025

NSCLC, non-small cell lung cancer

ORCHARD: BACKGROUND AND STUDY DESIGN

- ORCHARD (NCT03944772) is a global, phase 2, biomarker directed platform study aiming to characterise first-line osimertinib resistance and identify post-progression treatments in patients with *EGFR*m advanced NSCLC.[1] Data from module 10 of the study is presented here[2]



1L, first line; AE, adverse event; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; EGFRm, EGFR mutated; LCNEC, large cell neuroendocrine carcinoma; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; SAE, serious adverse event; SCLC, small cell lung carcinoma

1. Yu HA, et al. Clin Lung Cancer. 2021;22:601-606; 2. Le X, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstr 1O)

ORCHARD: RESULTS

- Overall, 69 patients received osimertinib + Dato-DXd; 68 patients were evaluable
- Median treatment duration was 9.0 and 9.8 months for the 4 mg (n =35) and 6 mg (n =34) cohorts, respectively; median duration of follow-up was 13.4 and 13.8 months, respectively

EFFICACY SUMMARY

	Osimertinib + Dato-DXd 4 mg/kg (n=35)	Osimertinib + Dato-DXd 6 mg/kg (n=33)
PFS mPFS (95% CI), months 6-month rate (95% CI), % 9-month rate (95% CI), % 12-month rate (95% CI), %	 **9.5 (7.2, 9.8)** 74 (56, 85) 50 (33, 65) 21 (9, 35)	 **11.7 (8.3, NC)** 80 (61, 91) 70 (49, 83) 39 (21, 57)
ORR, % (80% CI)	**43 (31, 55)**	**36 (25, 49)**
DoR mDoR (95% CI), months 6-month rate (95% CI), % 9-month rate (95% CI), %	 **6.3 (3.8, 8.2)** 60 (32, 80) 15 (2, 38)	 **20.5 (6.2, NC)** 92 (54, 99) 64 (30, 85)
Median time to onset of response (Q1, Q3), months	2.7 (1.5, 4.1)	1.4 (1.2, 2.1)
Median duration of follow-up, months	13.4	13.8
OS events, n (%)	16 (46)	9 (27)

CI, confidence interval; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; (m)PFS, (median) progression-free survival; NC, not calculable; ORR, objective response rate; OS, overall survival; Q, quartile

Le X, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstr 1O)

ORCHARD: SAFETY RESULTS

- No new safety signals were identified in either cohort

n (%)	Osimertinib + Dato-DXd 4 mg/kg (n=35)	Osimertinib + Dato-DXd 6 mg/kg (n=34)
Treatment-related AE Grade ≥3 Grade ≥3 possibly related to osimertinib only Grade ≥3 possibly related to Dato-DXd only	34 (97) 12 (34) 2 (6) 5 (14)	33 (97) 19 (56) 0 12 (35)
Any Grade ≥3 AE	17 (49)	25 (74)
SAE	11 (31)	14 (41)
AE with outcome of death, n (%)	1 (3)	0
Dose reduction AE leading to osimertinib dose reduction AE leading to Dato-DXd dose reduction	 6 (17) 8 (23)	 0 20 (59)
Dose interruption AE leading to osimertinib dose interruption AE leading to Dato-DXd dose interruption	 15 (43) 16 (46)	 12 (35) 22 (65)
Discontinuation AE leading to osimertinib discontinuation AE leading to Dato-DXd discontinuation	 6 (17) 6 (17)	 8 (24) 9 (26)

AE, adverse event; Dato-DXd, Datopotamab deruxtecan; SAE, serious AE

Le X, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstr 1O)

ORCHARD: SUMMARY

- Osimertinib + Dato-DXd showed promising efficacy and manageable safety in patients with *EGFR*m advanced NSCLC who progressed on first-line osimertinib
- No new safety signals were identified in either cohort
- Considering the overall benefit/risk profile, 6 mg/kg should be the preferred Dato-DXd starting dose for combination with 80 mg osimertinib
- Longer-term follow-up data for OS are awaited

Clinical perspective

- ORCHARD helps further inform optimal post-osimertinib treatment strategies for *EGFR-mutated* NSCLC and demonstrates promising efficacy with osimertinib plus ADCs in the 2nd line setting

ADC, antibody-drug conjugate; Dato-DXd, datopotamab deruxtecan; EGFRm, EGFR mutated; NSCLC, non-small cell lung cancer; OS, overall survival

Le X, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (oral presentation, Abstr 1O)

PHASE 1B OPEN-LABEL STUDY OF TRASTUZUMAB DERUXTECAN + RILVEGOSTOMIG ± CARBOPLATIN AS FIRST LINE TREATMENT FOR METASTATIC HER2-OVEREXPRESSING NSCLC: DESTINY-LUNG03 (DL-03) PART 4

Planchard D, et al. Poster 132TiP, ELCC 2025

NSCLC, non-small cell lung cancer

DESTINY-LUNG03: BACKGROUND AND STUDY DESIGN

- **HER2 overexpression** has been reported in **2-30% of patients with NSCLC**, and is associated with a poor prognosis[1,2]
- Currently there are **no first-line HER2 directed therapies approved for HER2 overexpressing NSCLC[3]**
- Trastuzumab deruxtecan is approved in the US, Russia, Israel and Brazil for patients with unresectable or metastatic HER2-positive solid tumours who have received prior treatment or have no alterative treatment options available[3]
- **DESTINY-Lung03** is an ongoing phase 1b, open-label, multipart study **assessing T-DXd-based regimens in HER2-overexpressing NSCLC[3]**
  - **Part 4 of the study will assess T-DXd in combination with rilvegostomig ± carboplatin**, as first-line therapy for unresectable, advanced or metastatic HER2-overexpressing NSCLC[3]

DESTINY-Lung03 study design

Part 1: dose escalation (enrolment complete)

Arm 1A: T-DXd + durvalumab + cisplatin (N=18)
Arm 1B: T-DXd + durvalumab + carboplatin (N=18)

Part 1: T-DXd monotherapy (enrolment complete)

Arm 1D: T-DXd 5.4 mg/kg IV Q3W (N=36)

Part 3: dose confirmation (N~6 per arm) and expansion (N~34 per arm) (currently open)

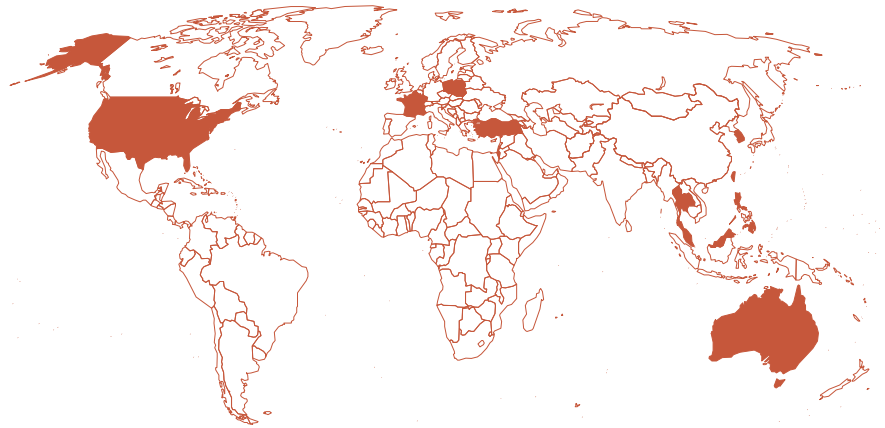
Arm 3A: T-DXd + volrustomig
Arm 3B: T-DXd + volrustomig + carboplatin

Part 4: safety run-in (N~6 per arm) and expansion (N~34 per arm) (currently recruiting)

Arm 4A: T-DXd + rilvegostomig
Arm 4B: T-DXd + rilvegostomig + carboplatin

Part 1 Arm 1C: T-DXd + durvalumab + pemetrexed treatment was planned but not initiated. For more information about DESTINY-Lung03, please visit https://clinicaltrials.gov/study/NCT04686305

Part 4 enrolment start: August 22, 2024, | Currently recruiting



Countries with participating study sites

Australia, France, Israel, Malaysia, Philippines, Poland, Republic of Korea, Taiwan, Thailand, Turkey, United States

IV, intravenous; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan; US, United States

1. Riudavets M, et al. ESMO Open. 2021;6:100260; 2. Ren S, et al. ESMO Open. 2022;7:100395; 3. Planchard D, et al. J Thorac Oncol. 2025;20 (3):S1-S97. ELCC 2025 (poster, Abstract 132TiP)

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