elcc European Lung Cancer Congress 2025

Phase I / II SOHO-01 study of BAY 2927088 in patients with previously treated *HER2*-mutant NSCLC: safety and efficacy results from 2 expansion cohorts

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Disclosures

Nicolas Girard, MD, PhD

I have the following financial relationships to disclose:

- Consulting or advisory role: AbbVie, Amgen, AstraZeneca, BeiGene, Bristol Myers Squibb, Daiichi Sankyo / AstraZeneca, Gilead Sciences, Ipsen, Janssen, LEO Pharma, Lilly, MSD Avenir, Novartis, Pfizer, Roche, Sanofi, Takeda
- Research funding (institutional): AstraZeneca, BMS, MSD Avenir, Roche
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- Employment (immediate family): AstraZeneca

Background: BAY 2927088

- Activating mutations in *HER2* are reported in approximately 2-4% of NSCLC and are associated with poor prognosis[1,2,3]
- BAY 2927088 is an oral tyrosine kinase inhibitor targeting *HER2*-activating mutations[3,4]
- BAY 2927088 has manageable safety and encouraging anti-tumor activity in patients with advanced NSCLC with *HER2*-activating mutations[3,4]
- BAY 2927088 was granted Breakthrough Therapy Designation by the US FDA and Chinese NMPA for patients with unresectable or metastatic NSCLC with *HER2*-activating mutations who have already received therapy[5,6]

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 (17 Suppl): LBA8598; 4. Loong HHF et al. *Ann Oncol* 2023; 34 (2 Suppl): S761; 5. Bayer. Bayer receives U.S. FDA Breakthrough Therapy designation for BAY 2927088 for non-small cell lung cancer harboring HER2 activating mutations. February 26, 2024. Accessed February 5, 2025. https://www.bayer.com/en/us/news-stories/fda-breakthrough-therapy-designation; 6. Bayer. Bayer receives Breakthrough Therapy designation in China for BAY 2927088 in high unmet need patients with HER2-mutant non-small cell lung cancer. June 11, 2024. Accessed February 5, 2025. https://www.bayer.com/media/en-us/bayer-receives-breakthrough-therapy-designation-in-china-for-bay-2927088-in-high-unmet-need-patients-with-her2-mutant-non-small-cell-lung-cancer

FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; NMPA, National Medical Products Administration; NSCLC, non-small cell lung cancer

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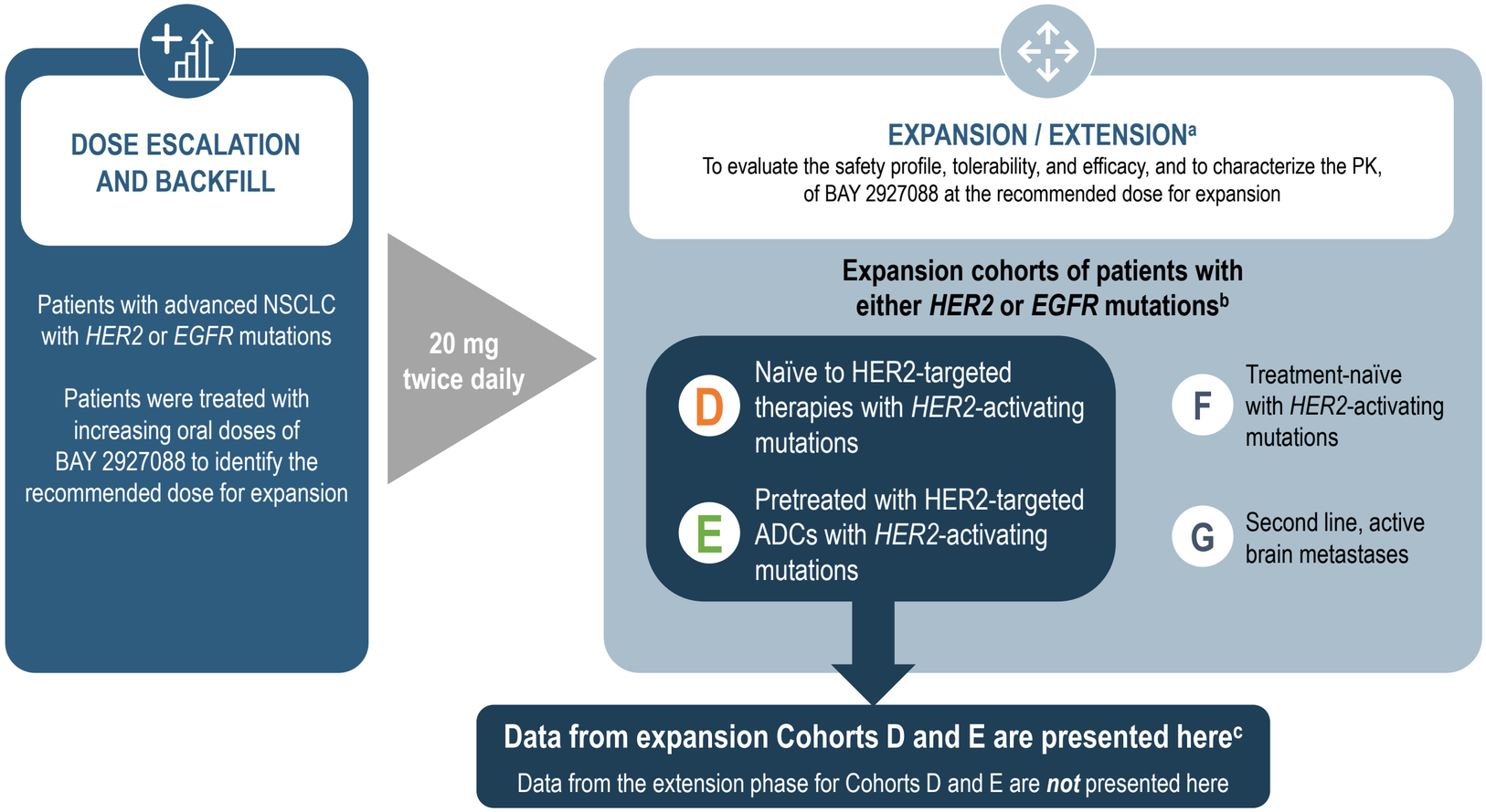
SOHO-01 study design (NCT05099172)



PRIMARY ENDPOINTS

- Safety and tolerability
- PK

SECONDARY ENDPOINTS

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

[a]Extension phase ongoing in selected cohorts; [b]*EGFR* cohorts not shown here; [c]Includes patients treated with 20mg BID of study drug from dose escalation/backfill meeting the same eligibility criteria for Cohorts D and E. Data cut-off was October 14, 2024.
ADC, antibody-drug conjugate; BID, twice daily; DCR, disease control rate; DoR, duration of response; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival; PK, pharmacokinetics

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Demographics and disease characteristics

	Cohort D[a] (*n*=44)	Cohort E[b] (*n*=34)
Sex, *n* (%)		
Male	16 (36.4)	13 (38.2)
Female	28 (63.6)	21 (61.8)
Race, *n* (%)		
White	10 (22.7)	10 (29.4)
Black or African American	0	3 (8.8)
Asian	30 (68.2)	18 (52.9)
Not reported	4 (9.1)	3 (8.8)
Median age, years (range)	62.0 (29-82)	62.5 (48-91)
Baseline ECOG PS, *n* (%)		
0	19 (43.2)	10 (29.4)
1	25 (56.8)	24 (70.6)
Smoking habits at informed consent, *n* (%)		
Never	31 (70.5)	22 (64.7)
Former	11 (25.0)	11 (32.4)
Current	2 (4.5)	1 (2.9)
NSCLC histology, *n* (%)		
Squamous cell carcinoma, NOS	2 (4.5)	0
Adenocarcinoma, mixed or NOS[c]	42 (95.5)	34 (100)

	Cohort D[a] (*n*=44)	Cohort E[b] (*n*=34)
Activating *HER2* mutations, *n* (%)		
HER2 exon 20 insertions	41 (93.2)	31 (91.2)
HER2 point mutation	3 (6.8)	2 (5.9)
Other	0	1 (2.9)
Median time since initial diagnosis, months (range)	16.0 (4-77)	23.1 (2-72)
Median time since most recent progression / relapse to first administration of study treatment, months (range)[d]	1.5 (0-14)	0.8 (0-14)
Brain metastases at baseline, *n* (%)[e]		
Yes	8 (18.2)	10 (29.4)
No	36 (81.8)	24 (70.6)
Number of previous systemic anti-cancer therapies, *n* (%)		
1	20 (45.5)	8 (23.5)
2	10 (22.7)	8 (23.5)
≥3	14 (31.8)	18 (52.9)
Previous anti-cancer therapies, *n* (%)[f]		
Platinum and no immunotherapy	16 (36.4)	9 (26.5)
Platinum and immunotherapy	27 (61.4)	19 (55.9)
Trastuzumab deruxtecan[g]	1 (2.3)	28 (82.4)
Other HER2-targeted ADCs	0	7 (20.6)

[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; [c]Adenocarcinoma defined as acinar adenocarcinoma, adenocarcinoma with mixed subtypes, adenocarcinoma, NOS, bronchiolar adenocarcinoma, papillary adenocarcinoma, NOS, solid adenocarcinoma with mucin formation per medical review; [d]Based on 69 patients with non-missing data; [e]Previously treated and asymptomatic brain metastases at baseline; [f]Other previous ADCs include trastuzumab emtansine, DX126-262, and SHR-A1811; [g]Patients who had received HER2 ex20ins-targeted therapy, including trastuzumab deruxtecan, for ≤2 months and stopped treatment due to reasons other than progressive disease were eligible
ADC, antibody-drug conjugate; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; NOS, not otherwise specified; NSCLC, non-small cell lung cancer

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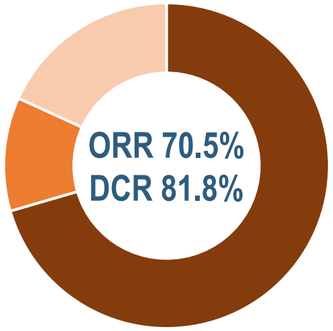
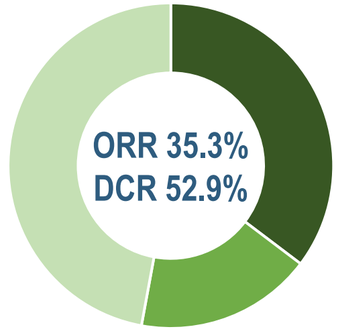
ORR by investigator (RECIST v1.1)

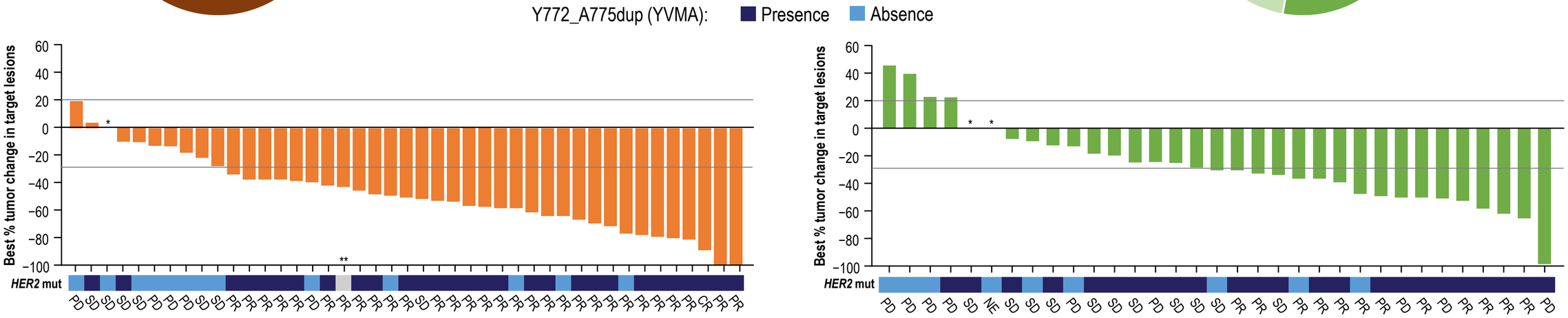
Cohort D:
Naïve to HER2-targeted therapy



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

Cohort E:
Progressed on HER2-targeted ADCs





*Patient exhibited 0% tumor reduction; **Exact *HER2* variant not reported by local test

[a]Requirement for CR/PR/SD/PD not met; [b]Patients with confirmed CR or PR; [c]Patients with confirmed CR or confirmed PR or SD for at least 12 weeks

ADC, antibody-drug conjugate; CI, confidence interval; CR, complete response; DCR, disease control rate; HER2, human epidermal growth factor receptor 2; mut, mutation; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria for Solid Tumors; SD, stable disease

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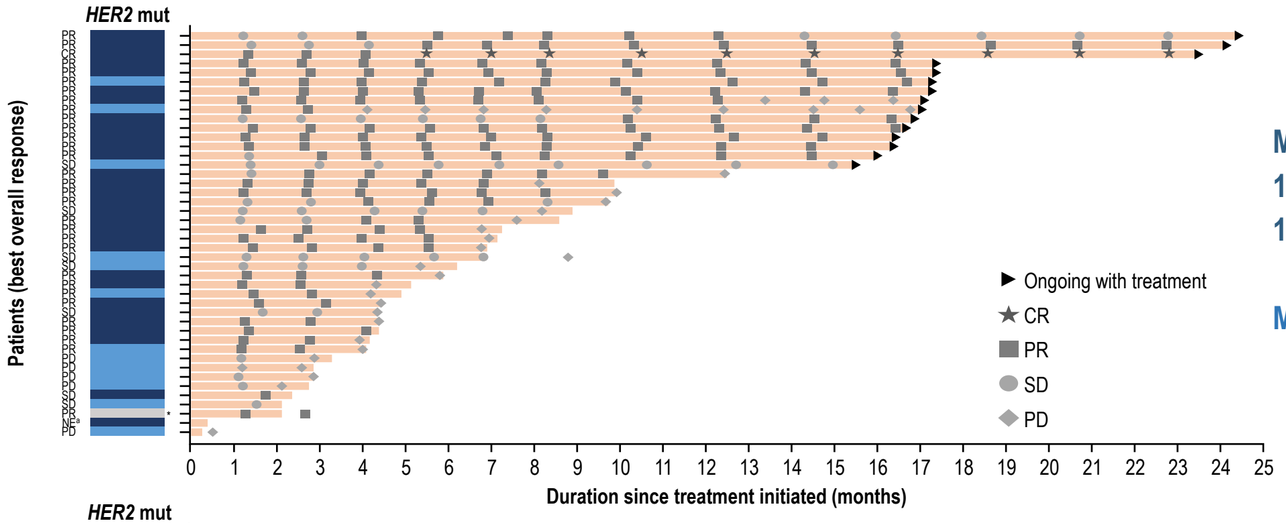
Treatment duration and time of responses

Cohort D (*n*=44): Naïve to HER2-targeted therapy

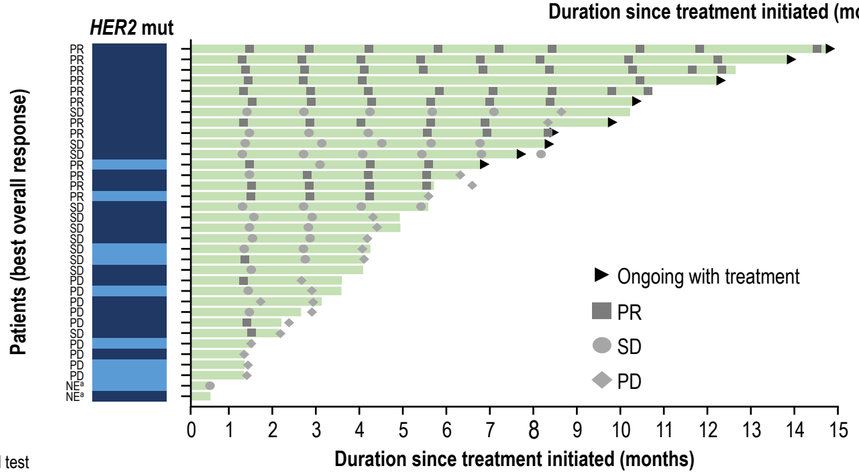


Y772_A775dup (YVMA):
- Presence
- Absence

Median follow-up: 17.2 months (range 0.95-24.38)
15 of 44 patients (34.1%) had ongoing treatment
16 patients (36.4%) had treatment duration >12 months

Median duration of treatment: 7.16 months (range 0.20-24.4)

Cohort E (*n*=34): Progressed on HER2-targeted ADCs



Median follow-up: 10.3 months (range 2.69-14.91)
9 of 34 patients (26.5%) had ongoing treatment
4 patients (11.8%) had treatment duration >12 months

Median duration of treatment: 4.83 months (range 0.43-14.78)

*Exact *HER2* variant not reported by local test
[a]Requirement for CR / PR / SD / PD not met
ADC, antibody-drug conjugate; CR, complete response; HER2, human epidermal growth factor receptor 2; mut, mutation; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease

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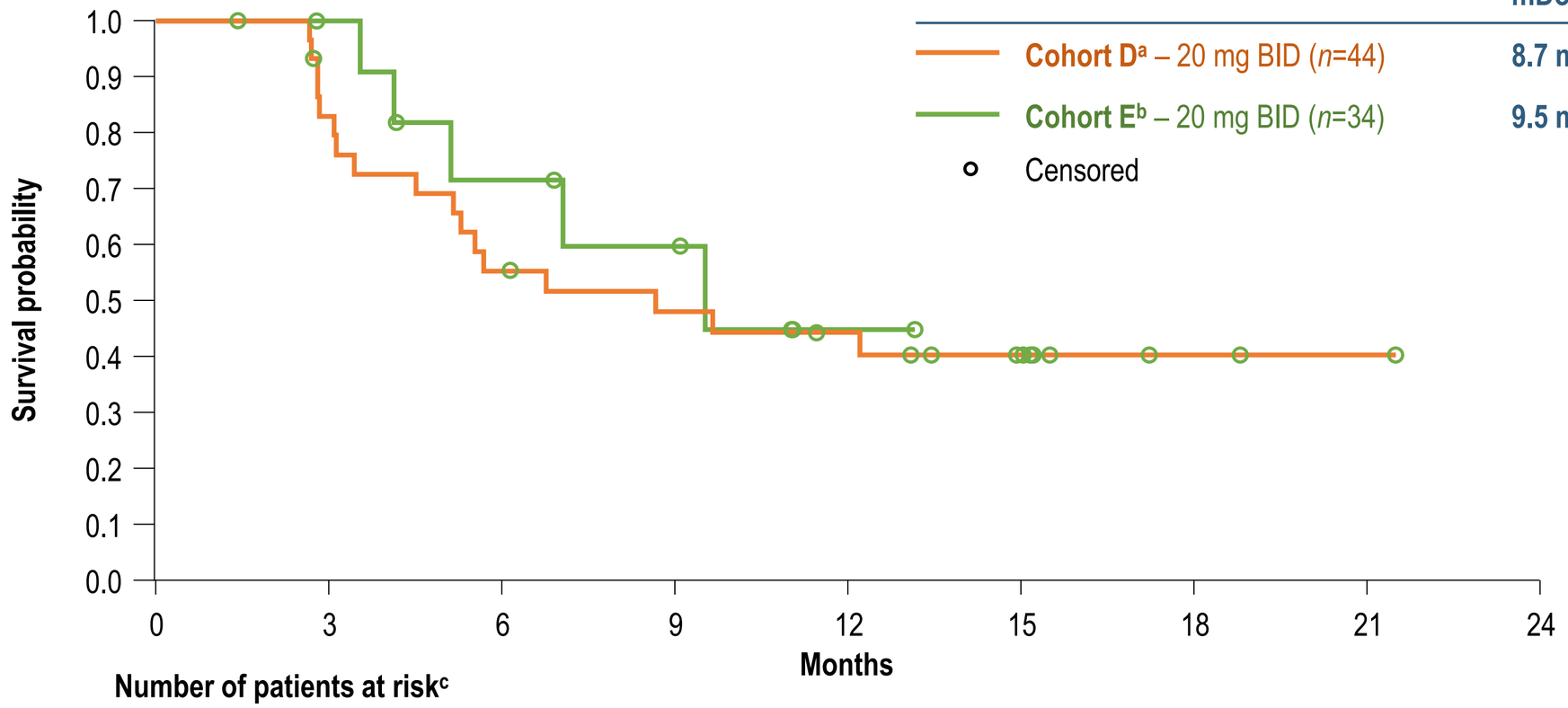
Duration of response



Number of patients at risk[c]

Cohort D	31	24	16	13	11	7	2	1	0
Cohort E	12	11	7	5	1	0	0	0	0

[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; [c]At-risk patient counts were calculated as the start of time point
ADC, antibody-drug conjugate; BID, twice daily; CI, confidence interval; HER2, human epidermal growth factor receptor 2; mDoR, median duration of response; NE, not estimable; NSCLC, non-small cell lung cancer

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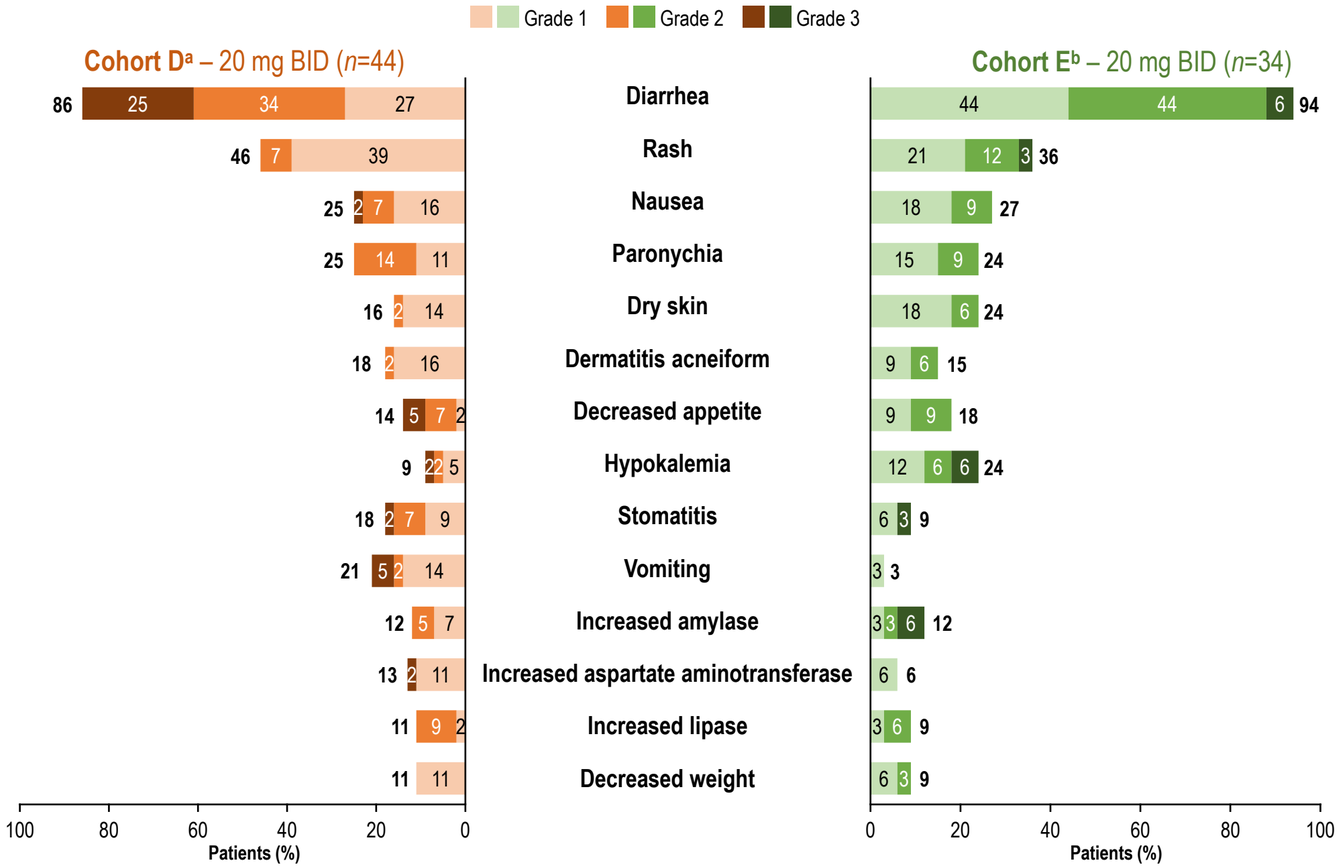
Safety and tolerability

Summary of most frequent TRAEs (≥10% of total) by treatment and severity grade (MedDRA v 27.1, CTCAE v 5.0)



Among all patients (*N*=78):

Diarrhea was the most common TRAE and mostly grade 1 or 2

- No patients discontinued treatment due to diarrhea

There was 1 grade 4 TRAE (dyspnea) and no grade 5 TRAEs

There were no reports of interstitial lung disease or pneumonitis

7 patients (9.0%) had serious TRAEs

- Diarrhea (*n*=2), duodenitis (*n*=1), vomiting (*n*=1), abnormal hepatic function (*n*=2), dyspnea (*n*=1), and rash (*n*=1)

24 patients (30.8%) had dose reductions due to TRAEs, most commonly due to diarrhea (*n*=9)[c]

4 patients (5.1%) had TRAEs leading to treatment discontinuation[d]

[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; [c]≥2 patients: diarrhea (*n*=9), nausea (*n*=2), stomatitis (*n*=2), abnormal hepatic function (*n*=2), increased alanine aminotransferase (*n*=2), decreased weight (*n*=2); [d]Corneal epithelial microcysts and reduced visual acuity (*n*=1), abnormal hepatic function (*n*=1), pain in extremity (*n*=1), and dyspnea (*n*=1)

ADC, antibody-drug conjugate; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; HER2, human epidermal growth factor receptor 2; MedDRA, Medical Dictionary for Regulatory Activities; NSCLC, non-small cell lung cancer; TRAE, treatment-related adverse event

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Summary and conclusions

Treatment with BAY 2927088 led to durable responses in pretreated patients with advanced *HER2*-mutant NSCLC who were naïve to HER2-targeted therapy (Cohort D) or who had previously received a HER2-targeted ADC (Cohort E)

- In Cohort D: ORR was 70.5%, DCR was 81.8%, and mDoR was 8.7 months (median follow-up 17.2 months)
- In Cohort E: ORR was 35.3%, DCR was 52.9%, and mDoR was 9.5 months (median follow-up 10.3 months)

The safety profile of BAY 2927088 was manageable and consistent with previous reports

The safety and efficacy of BAY 2927088 as first-line therapy for locally advanced or metastatic NSCLC with *HER2* mutations are being investigated in the ongoing Phase III SOHO-02 trial (NCT06452277)

ADC, antibody-drug conjugate; DCR, disease control rate; HER2, human epidermal growth factor receptor 2; mDoR, median duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; TRAE, treatment-related adverse event

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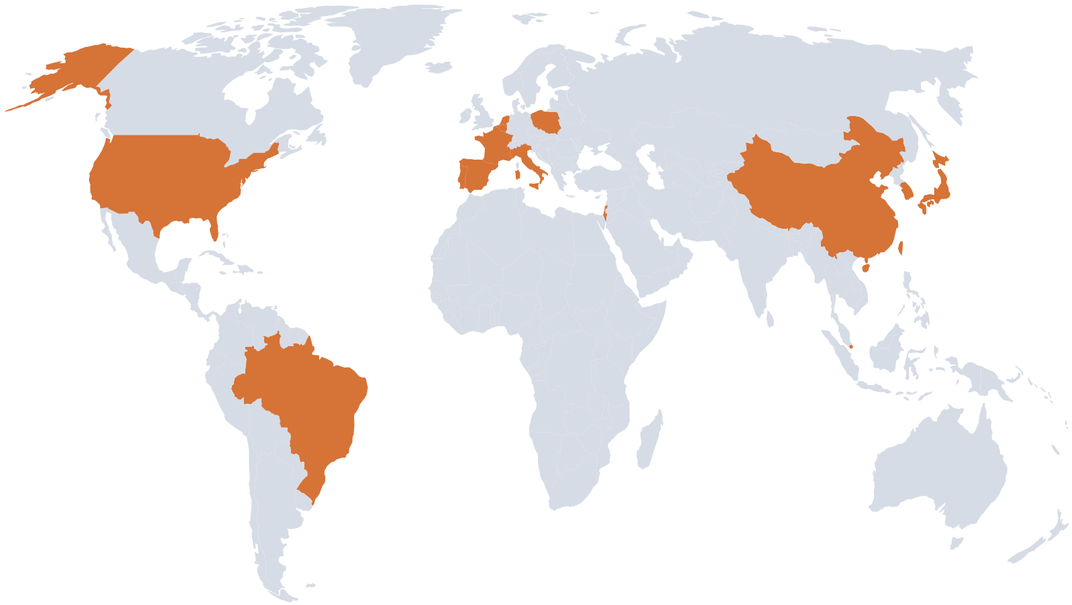

Participating centers in SOHO-01

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

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