Safety and Efficacy of BAY 2927088 in Patients with *HER2*-Mutant NSCLC: Expansion Cohort from the Phase I/II SOHO-01 Study

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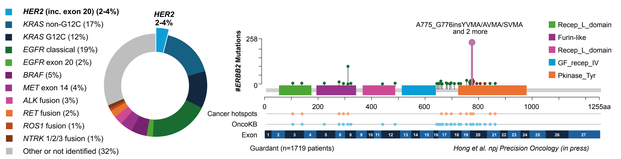
Background: HER2 mutations in lung cancer

***HER2* mutations are reported in 2-4% of NSCLC and are associated with poor prognosis**

***HER2* Y772_A775dup (YVMA) insertion represents 75% of all *HER2* mutant lung cancer**



Unmet needs in *HER2*-mutant NSCLC:

- Chemotherapy and ADCs are current options for patients with lung cancer harboring *HER2* mutations[1]
- However, there is a need for the development of oral, targeted small molecule therapies to achieve greater efficacy and safety for patients with *HER2*-mutant NSCLC

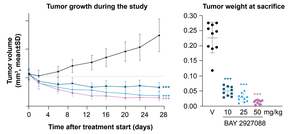
ADC, antibody-drug conjugates; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer

1. Riely GJ, et al. *J Natl Compr Canc Netw.* 2024;22(4):249-274.

Background: BAY 2927088

- BAY 2927088 is an oral, reversible tyrosine kinase inhibitor that potently inhibits activating *HER2* (*ERBB2*) mutations in preclinical models[1]
- BAY 2927088 has shown encouraging preliminary anti-tumor activity in patients' manageable safety and with advanced NSCLC harboring *HER2* mutations[2]
- The US FDA and Chinese NMPA have granted Breakthrough Therapy designations to BAY 2927088 for patients with unresectable or metastatic NSCLC with activating *HER2* mutations who have already received therapy[3,4]

***In vivo* antitumor efficacy of BAY 2927088 in the subcutaneous CTG-2543 (*HER2* YVMA) PDX model of NSCLC**

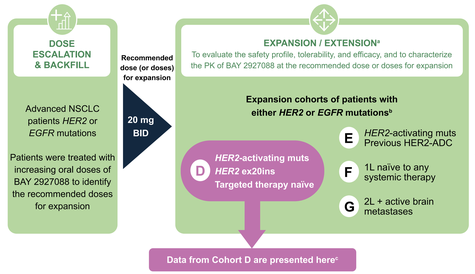


Here we report preliminary safety and efficacy of BAY 2927088 from the expansion phase of an ongoing open-label, first-in-human Phase I/II trial in patients with advanced *HER2*-mutant NSCLC naïve to HER2-targeted therapy

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

1. Siegel F et al. *Cancer Res* 2023; 83 (7 Suppl): 4035. 2. Girard N et al. *J Clin Oncol* 2024; 42 (17 Suppl): LBA8598. 3. 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. https://www.bayer.com/en/us/news-stories/fda-breakthrough-therapy-designation; 4. 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. 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

SOHO-01 study design (NCT05099172)



Primary endpoints:
Safety and tolerability
Pharmacokinetics

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

[a]Extension phase ongoing in selected cohorts. [b]EGFR cohorts not presented here. [c]July 1, 2024 data cut-off. Dose optimization cohort (D1) ongoing; not shown

BID, twice daily; DCR, disease control rate; DoR, duration of response; EGFR, epidermal growth factor receptor; ex20ins, exon 20 insertion mutations; muts, mutations; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival

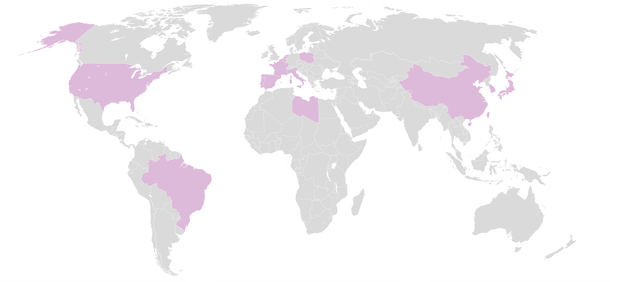
SOHO-01 Cohort D: demographics and disease characteristics

	Cohort D (*N*=44)[a]
Female, *n* (%)	28 (63.6)
Race, *n* (%)	
White	10 (22.7)
Asian	30 (68.2)
Not reported	4 (9.1)
Median age, years (range)	62.0 (29-82)
Baseline ECOG PS, *n* (%)	
0	19 (43.2)
1	25 (56.8)
Smoking habits at informed consent, *n* (%)	
Never	31 (70.5)
Former	11 (25.0)
Current	2 (4.5)
NSCLC histology, *n* (%)	
Squamous cell carcinoma, not otherwise specified	2 (4.5)
Adenocarcinoma, mixed or not otherwise specified	42 (95.5)
Median time since initial diagnosis, months (range)[a]	16.0 (3.9-77.2)
Median time since most recent progression / relapse to first administration of study treatment, months (range)[a]	1.5 (0-14.4)

	Cohort D (*N*=44)[a]
***HER2* mutations**	
Y772_A775dup (YVMA) insertion	31 (70.5)
Point mutations[c]	3 (6.8)
Other	10 (22.7)
Brain metastases at baseline[d]	
Yes	8 (18.2)
No	36 (81.8)
Number of previous systemic anti-cancer treatments, *n* (%)	
1	20 (45.5)
2	10 (22.7)
≥3	14 (31.8)
Previous therapy[e]	
Previous platinum, no previous immunotherapy	17 (38.6)
Previous platinum and immunotherapy	25 (56.8)

[a]One patient excluded from efficacy analysis dataset due to withdrawal of consent prior to post-baseline tumor assessment

[b]Based on 44 patients with non-missing data; [c]Based on 38 patients with non-missing data; [c]L755S, S310F, V659E; [d]Previously treated and asymptomatic brain metastases at baseline; [e]1 patient only had received immunotherapy
ECOG PS, Eastern Cooperative Oncology Group performance status



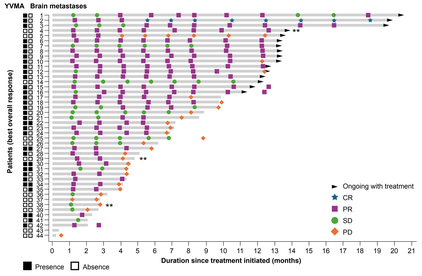
Europe
Belgium, France, Israel, Italy, Netherlands, Poland, Portugal, Spain

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

Americas
Brazil, USA

Countries participating in SOHO-01

Treatment duration and time of responses



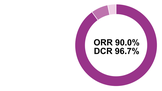
- Median follow-up was 10.9 months (range 0.9-20.2)
- 16 of 44 patients (36.4%) had ongoing treatment
- Treatment duration >12 months was observed in 14 patients (31.8%)
- Median duration of treatment was 7.1 months (range 0.2-20.2)

**HER2 point mutation:
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease

Subgroup analyses: *HER2* Y772_A775dup insertion

Subgroup		Patients,[a] *n*	ORR, *n* (%; 95% CI)
All evaluable patients in cohort D		43	31 (72.1; 56.3, 84.7)
***HER2* YVMA insertion**	Yes	30	27 (90.0; 73.5, 97.9)
	No	13	4 (30.8; 9.1, 61.4)
Brain metastases at baseline	Yes	8	5 (62.5; 24.5, 91.5)
	No	35	26 (74.3; 56.7, 87.5)
Previous therapy	Previous platinum, no previous immunotherapy	17	12 (70.6; 44.0, 89.7)
	Previous platinum and immunotherapy	25	18 (72.0; 50.6, 87.9)

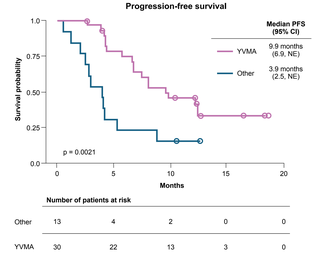
In patients with YVMA insertion (*n*=30)



Median DoR:
9.7 months (95% CI 5.5, NE)

Median PFS:
9.9 months (95% CI 6.9, NE)

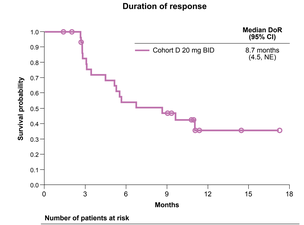
Progression-free survival



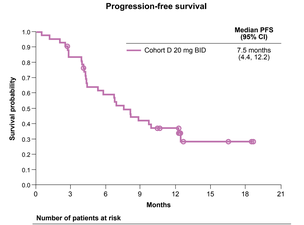
[a]All evaluable patients;
CI, confidence interval; DCR, disease control rate; DoR, duration of response; NE, not estimable; ORR, objective response rate; PFS, progression-free survival

Overall duration of response and progression-free survival

Duration of response



Progression-free survival



At-risk patient counts were calculated as the start of time point
BID, twice daily; CI, confidence interval; DoR, duration of response; NE, not estimable; PFS, progression-free survival

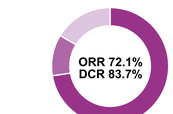
Safety and tolerability profile

n (%)	All grades (*N*=44)	Grade ≥3 (*N*=44)
Any TRAE	42 (95.5)	19 (43.2)
Most common TRAEs occurring in ≥10% of patients	38 (86.4)	11 (25.0)
Diarrhea	38 (86.4)	11 (25.0)
Rash	19 (43.2)	0
Paronychia	11 (25.0)	0
Nausea	11 (25.0)	1 (2.3)
Vomiting	9 (20.5)	2 (4.5)
Dermatitis acneiform	8 (18.2)	0
Stomatitis	8 (18.2)	1 (2.3)
Dry skin	7 (15.9)	0
Increased aspartate aminotransferase	6 (13.6)	1 (2.3)
Decreased appetite	6 (13.6)	2 (4.5)
Increased amylase	5 (11.4)	0
Anemia	5 (11.4)	0
Increased lipase	5 (11.4)	0
Decreased weight	5 (11.4)	0
Pruritis	5 (11.4)	1 (2.3)

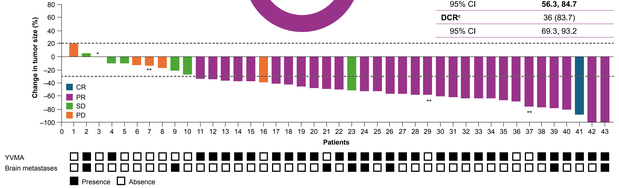
- Diarrhea was the most common TRAE, experienced by 38 patients (86.4%); principally grade 1 or 2
- 3 patients (6.8%) had TRAEs leading to treatment discontinuation
  - Included corneal epithelial microcysts (*n*=1), reduced visual acuity (*n*=1), abnormal hepatic function (*n*=1), and dyspnea (*n*=1)
- 14 patients (31.8%) had dose reductions due to TRAEs[a]
- 5 patients (11.4%) had serious TRAEs
  - Included diarrhea (*n*=1), duodenitis (*n*=1), vomiting (*n*=1), and abnormal hepatic function (*n*=2)
- There were no grade 4 TRAEs and 1 grade 5 event (dyspnea); no reports of ILD/pneumonitis

[a]≥2 patients: diarrhea (n=6), abnormal hepatic function (n=2), increased alanine aminotransferase (n=2), decreased appetite (n=2)
ILD, interstitial lung disease; TRAE, treatment-related adverse event

SOHO-01 Cohort D: ORR per investigator by RECIST v1.1



n (%)	Patients[a] (*n*=43)
CR	1 (2.3)
PR	30 (69.8)
SD[c]	7 (16.3)
PD	5 (11.6)
ORR[b]	**31 (72.1)**
95% CI	**56.3, 84.7**
DCR[b]	36 (83.7)
95% CI	69.3, 93.2



[a]All evaluable patients; [b]Patients with confirmed CR or PR; [c]Patients with confirmed CR or confirmed PR or SD for ≥12 weeks; *0%, SD; **HER2 point mutations
CI, confidence interval; CR, complete response; DCR, disease control rate; NR, no response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

Summary and conclusions

- **Treatment with BAY 2927088 led to rapid, substantial, and durable responses in patients with pretreated *HER2*-mutant NSCLC**
  - ORR was 72.1%, DCR of 83.7%, median DoR was 8.7 months, and median PFS was 7.5 months
  - In patients with *HER2* YVMA insertions, ORR was 90.0%, DCR was 96.7%, median DoR was 9.7 months, and median PFS was 9.9 months
- **The safety profile of BAY 2927088 was manageable and consistent with previous reports**
- **These data support the ongoing investigation of BAY 2927088 in patients with advanced NSCLC harboring *HER2* mutations**
  - Ongoing phase III SOHO-02 trial (see Goto *et al*., 2024 WCLC, EP.12H.08)

DCR, disease control rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival

Acknowledgments

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