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FAVOUR: A phase 1b study of furmonertinib, an oral, brain penetrant, selective EGFR inhibitor, in patients with advanced NSCLC with EGFR Exon 20 insertions

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Background

- Epidermal growth factor receptor (*EGFR*) Exon 20 insertion (Exon20ins) mutations constitute approximately 9% of all the *EGFR* mutations (Robichaux et al. 2021) in non-small cell lung cancer (NSCLC).

- There are no EGFR targeted agents approved for first-line treatment of EGFR Ex20ins NSCLC. The current standard of care is platinum-based chemotherapy.

- Furmonertinib is an oral, highly brain penetrant, *EGFR* tyrosine kinase inhibitor (TKI) engineered for broad activity and selectivity across *EGFR* mutations including Exon20ins (Musib et al., NACLC 2022), and has an active metabolite with similar properties.

- Furmonertinib has previously been studied at doses up to 240 mg QD with good tolerability (Shi et al, JTO 2020) and higher furmonertinib doses are predicted to provide better efficacy against EGFR Exon20ins than the 80 mg dose approved in China for classical EGFR mutations.

- Previous FAVOUR study results in treatment naïve patients with NSCLC with EGFR Exon20ins showed an encouraging ORR of 60% by IRC (n = 10) (ESMO 2021, Abstract 1325). Here, we present the updated data for the FAVOUR study.

FAVOUR Study Design in NSCLC EGFR Exon 20 Insertion

Key Inclusion Criteria:

- Age ≥ 18 years
- Locally advanced or metastatic NSCLC
- Presence of EGFR Exon 20 insertion mutation
- ECOG PS 0-1
- ≥1 measurable lesions
- Asymptomatic stable CNS metastases are allowed

N=90

- Treatment naïve — Furmonertinib 240mg/day — n=30
- Previously treated — Furmonertinib 240mg/day — n=30
- Previously treated — Furmonertinib 160mg/day — n=30

Randomized 1:1

Follow up every 6 weeks

Treatment until:

- Disease progression
- Intolerable toxicity
- Death

Follow up :

- Until Disease progression: every 6 weeks （±3d）
- After Disease progression or Initiation of new therapy: every 12 weeks （±7d）

Endpoints

➢ **Primary**: ORR by IRC assessment; **Secondary**: DCR, DoR, PFS, OS, Depth of response, safety, quality of life

Interim results on data cutoff of June 15, 2023 are presented; 86 patients enrolled and 30 patients still on treatment

ORR: Objective Response Rate; IRC: Independent Review Committee; DoR: Duration of Response; DCR: Disease Control Rate; PFS: Progression-free survival; OS: overall survival

Demographics and Baseline Disease Characteristics

	Treatment Naïve 240 mg N=30	Previously Treated 240 mg N=28	Previously Treated 160 mg N=28
Age, median (min, max) (years)	61.5 (33, 73)	55.5 (33, 73)	58.5 (22, 77)
Male/Female, %	37% / 63%	43% / 57%	39% / 61%
ECOG 0/1, %	30% / 70%	7% / 93%	11% / 89%
Disease Stage IIIB/IV, %	7% / 93%	0 / 100%	4% / 96%
Brain Metastases*, %	17%	29%	39%
Non-smoker/Smoker/Former smoker, %	77% / 3% / 20%	82% / 0 / 18%	75% / 4% /21%
Number of Prior Systemic Anti-cancer Therapy, median, (min, max)	NA	1 (1, 4)	1 (1, 3)
Prior Treatment Type, % **Chemotherapy / Immunotherapy** **EGFR Targeted Therapy&**	 13% / 0 0	 96% / 39% 7%	 86% / 32% 14%

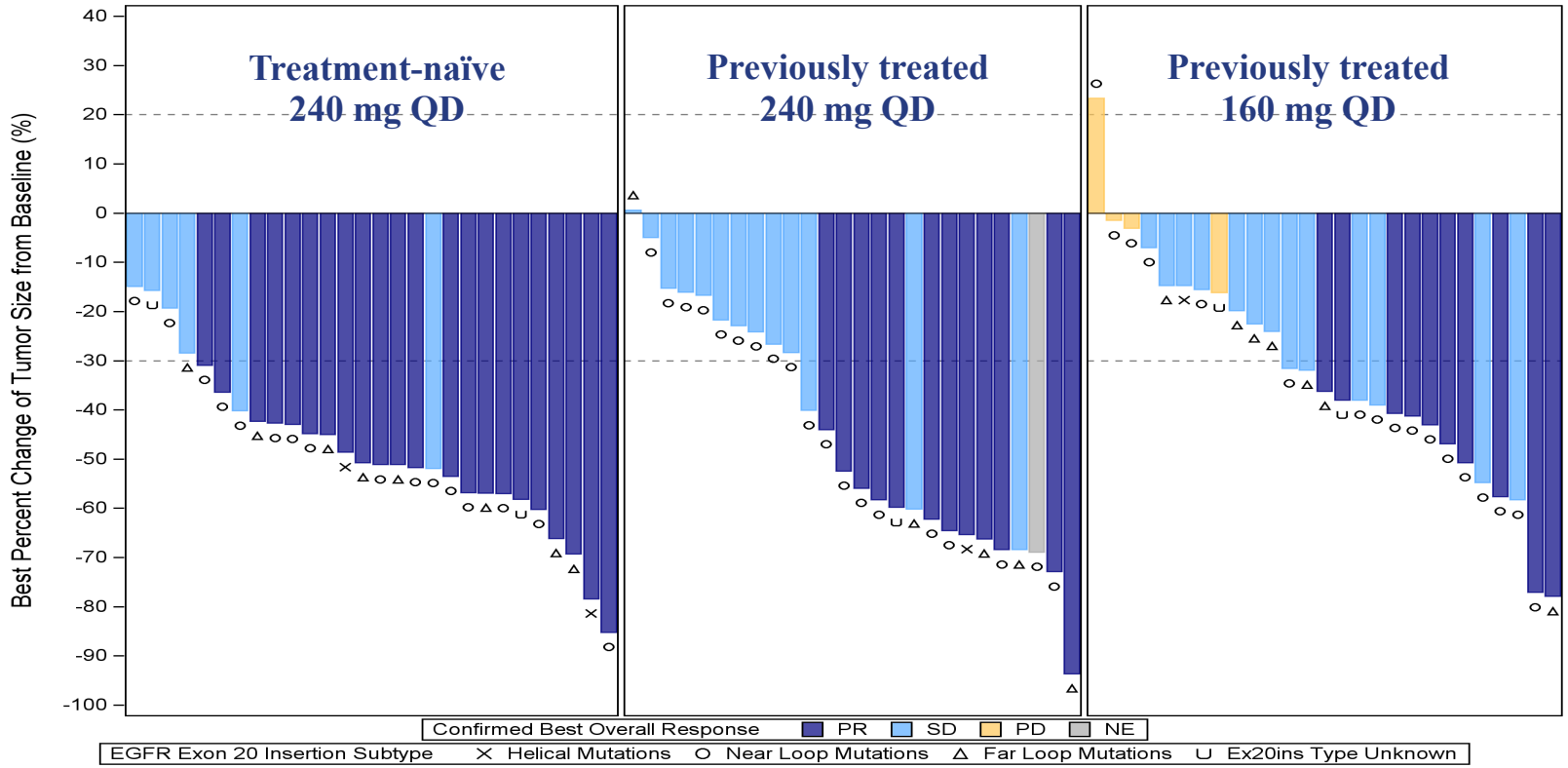
*History or presence of brain metastases
&EGFR targeted therapy includes: amivantamab, dacomitinib, poziotinib, erlotinib, and icotinib

Confirmed ORR by IRC by Cohort

Efficacy by IRC	Treatment Naïve 240mg N=28*	Previously Treated 240mg N= 26#	Previously Treated 160mg N= 26#
Confirmed ORR, % (95% CI)	78.6% (59.05%, 91.70%)	46.2% (26.59%, 66.63%)	38.5% (20.23%, 59.43%)
Best Response, n (%)			
Partial response (PR)	22 (78.6%)	12 (46.2%)	10 (38.5%)
Stable disease (SD)	6 (21.4%)	12 (46.2%)	12 (46.2%)
Progressive disease (PD)	0	0	4 (15.4%)
Not evaluable/Not done	0 / 0	1 (3.8%) / 1 (3.8%)	0 / 0
DoR, median (months) (95% CI)	15.2 (8.74, 24.84)	13.1 (5.62, 13.80)	9.7 (5.59, NA)
DCR (CR+PR+SD), % (95% CI)	100.0% (87.66%, 100.00%)	92.3% (74.87%, 99.05%)	84.6% (65.13%, 95.64%)

Analysis is based on EGFR exon 20ins patients who had measurable disease at baseline by IRC, had ≥ 2 tumor assessments, had PD/death, or discontinued from treatment.
* 2 patients: one patient had no measurable target lesion at baseline by IRC; another patient did not have an exon 20 insertion mutation.
# 26 of the 28 patients in 240 mg and 160 mg cohorts respectively had at least 2 tumor assessments by June 15, 2023.
IRC, independent review committee ; ORR, objective response rate; DoR, duration of response; DCR: Disease Control Rate; CI, confidence interval;

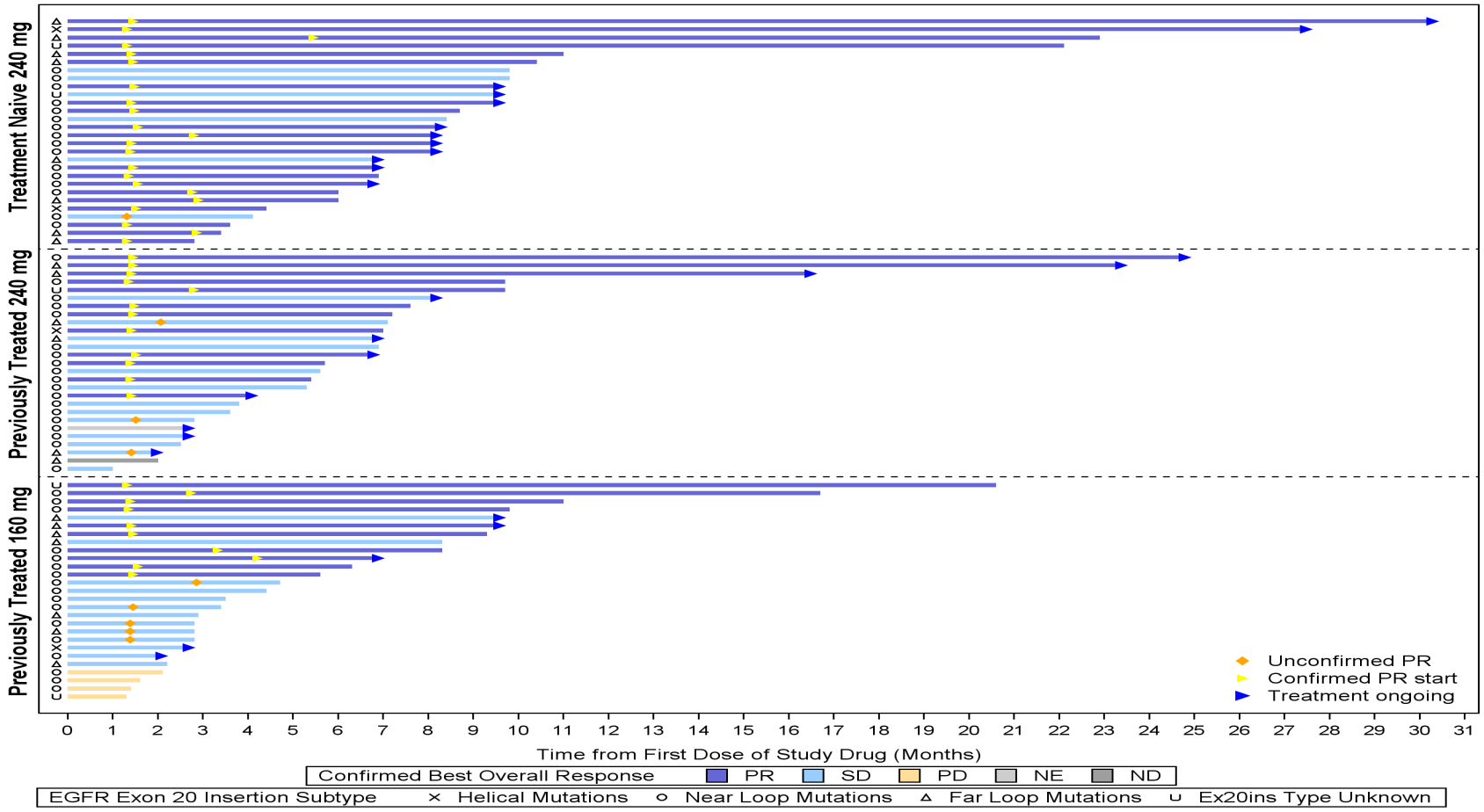
Depth of Response by Cohort and EGFR Exon20ins Mutation Subtype



- Responses observed across near-loop, far-loop and helical Exon20ins mutations
- Median maximum tumor reductions are 50.9% (Treatment-naïve), 54.2% (previously treated 240 mg) and 36.2% (previously treated 160 mg)

Waterfall plot was based on patients with at least one tumor assessment post baseline;
Near-loop region: A767-P772; far-loop region: H773-C775; Helical region: E762-M766

Time on Treatment and Time of Responses



The length of each bar represents the duration of the treatment for each subject.

- Most responses occur at the first tumor assessment for all 3 cohorts
- Longest DoR is > 26 months and treatment is still ongoing

Furmonertinib is Well Tolerated at Both 160 mg and 240 mg Dose Levels

	Treatment Naïve 240 mg N=30	Previously Treated 240 mg N =28	Previously Treated 160 mg N =28
Overview of Treatment Related AEs (TRAEs) (# of Patient, %)			
TRAE all grade	29 (97%)	28 (100%)	25 (89%)
TRAE Grade ≥ 3	4 (13%)	8 (29%)	5 (18%)
Treatment-related SAE	1 (3%)	5 (18%)	0
TRAE leading to fatal outcome	0	0	0
TRAE leading to dose interruption	7 (23%)	9 (32%)	4 (14%)
TRAE leading to dose reduction	4 (13%)	5 (18%)	3 (11%)
TRAE leading to treatment discontinuation	0	1 (4%)	1 (4%)
Treatment Duration (median)	8.4 months	5.7 months	4.0 months
Relative Dose Intensity %, mean (SD)	97.1% (8.0%)	94.9% (13.5%)	96.2% (9.4%)

- Low rates of dose reduction and discontinuation due to TRAE across all 3 cohorts, indicating acceptable tolerability for both 240mg and 160mg dose groups
- Overall safety and tolerability in 240mg treatment naïve group appeared better than 240mg previously treated group
- No death due to TRAE
- No treatment discontinuation due to TRAEs in 240mg treatment naïve group

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Most Frequent TRAEs (Incidence ≥ 20%)

Preferred Term, Number of Patient(s) (%)	Treatment-naive 240 mg (N = 30)		Previously Treated 240 mg (N = 28)		Previously Treated 160 mg (N = 28)	
	Total	Grade≥3	Total	Grade≥3	Total	Grade≥3
Diarrhea	22 (73%)	0	24 (86%)	0	9 (32%)	2 (7%)
Anemia	13 (43%)	0	7 (25%)	1 (4%)	4 (14%)	1 (4%)
Aspartate aminotransferase increased	8 (27%)	0	7 (25%)	0	10 (36%)	0
Alanine aminotransferase increased	7 (23%)	0	7 (25%)	1 (4%)	8 (29%)	0
Blood creatinine increased	6 (20%)	0	8 (29%)	0	7 (25%)	0
Mouth ulceration	9 (30%)	1 (3%)	4 (14%)	0	5 (18%)	0
Rash	7 (23%)	0	6 (21%)	0	4 (14%)	0
Electrocardiogram QT prolonged	8 (27%)	1 (3%)	4 (14%)	2 (7%)	2 (7%)	0
White blood cell count decreased	6 (20%)	1 (3%)	5 (18%)	0	6 (21%)	0
Decreased appetite	3 (10%)	0	8 (29%)	0	0	0
Weight decreased	3 (10%)	0	7 (25%)	1 (4%)	3 (11%)	0
Skin fissures	6 (20%)	0	3 (11%)	0	0	0
Paronychia	6 (20%)	0	2 (7%)	0	1 (4%)	0

Conclusion

- **Furmonertinib showed promising efficacy in both treatment naïve and previously treated patients with NSCLC with EGFR Exon20ins.**
  - In treatment naïve (first-line treatment) patients, the confirmed ORR was 78.6% with a preliminary median DOR of 15.2 months.
  - In previously treated patients both the 240 mg and 160 mg doses were active with confirmed ORR of 46.2% and 38.5% respectively.
  - Anti-tumor responses observed across near-loop, far-loop and helical Exon20ins mutations.
- **Furmonertinib showed a well-tolerated safety profile in patients with NSCLC harboring *EGFR* Exon20ins mutations. The most commonly observed TRAE at the 240mg dose was low-grade diarrhea. Safety profile was consistent with the 80 mg dose approved in China for classical EGFR mutations, and no new and unexpected safety signals were identified.**
- **Based on FAVOUR results, a global registrational Phase III study in first-line patients with locally advanced or metastatic NSCLC with EGFR Exon20ins mutations has been initiated (FURVENT/FURMO-004; NCT05607550) and is being presented at this conference as a Trials-in-Progress presentation.**
  - Title: FURVENT, Phase 3 trial testing furmonertinib vs chemotherapy as first-line treatment for advanced NSCLC with EGFR exon 20 insertions
  - Session P2.09-18. Monday, 11 September 2023 6:00 – 7:30.
- Furmonertinib is also being studied in an ongoing global phase 1b clinical trial in NSCLC patients with other uncommon EGFR activating or HER2 mutations (FURMO-002; NCT05364073).

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