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Sunvozertinib for NSCLC Patients with EGFR Exon20 Insertion Mutations: Preliminary Analysis of the First Pivotal Study Results

Mengzhao Wang[1], Yun Fan[2], Meili Sun[3], Yongsheng Wang[4], Yanqiu Zhao[5], Bo Jin[6], Ying Hu[7], Zhigang Han[8], Xia Song[9], Anwen Liu[10], Kejing Tang[11], Cuimin Ding[12], Li Liang[13], Lin Wu[14], Junzhen Gao[15], Jianghong Wang[16], James Chih-Hsin Yang[17], Li Zheng[18], Pasi A. Jänne[19]

[1]Peking Union Medical College Hospital, CN; [2]Zhejiang Cancer Hospital, CN; [3]Jinan Central Hospital, CN; [4]West China Hospital of Sichuan University, CN; [5]Henan Cancer Hospital, CN; [6]The First Hospital of China Medical University, CN; [7]Beijing Chest Hospital, Capital Medical University, CN; [8]Xinjiang Cancer Hospital, CN; [9]Shanxi Provincial Cancer Hospital, CN; [10]The Second Affiliated Hospital of Nanchang University, CN; [11]The First Affiliated Hospital, Sun Yat-sen University, CN; [12]The Fourth Hospital of Hebei Medical University, CN; [13]Peking University Third Hospital, CN; [14]Hunan Cancer Hospital, CN; [15]The Affiliated Hospital of Inner Mongolia Medical University, CN; [16]Chongqing Cancer Hospital, CN; [17]National Taiwan University Hospital and National Taiwan University Cancer Center, TW; [18]Dizal Pharmaceuticals; [19]Dana-Farber Cancer Institute, US.

Background

- Sunvozertinib (DZD9008) is a rationally designed, irreversible EGFR inhibitor targeting EGFR mutations and with wild-type EGFR selectivity.
- Breakthrough Therapy Designation was granted by both U.S. FDA and China NMPA, based on previously reported data from WU-KONG1 (NCT03974022) and WU-KONG2 (CTR20192097) studies.
- Global pivotal studies are ongoing for ≥ 2nd line and 1st line treatment of NSCLC with EGFR exon20 insertion mutation (exon20ins).
- Here we presented preliminary results of WU-KONG6 (CTR20211009), the first pivotal study of sunvozertinib as a ≥ 2nd line treatment after platinum-based chemotherapy.

Methods

- WU-KONG6 is an open-label, single-arm, multicenter, phase 2 pivotal study conducted in 37 centers in China, with objective response rate (ORR) assessed by blinded independent central review (BICR) as the primary endpoint.
- The efficacy set comprised a total of 97 platinum-pretreated NSCLC patients with EGFR exon20ins from WU-KONG6 (Data cut-off date: 31 July, 2022).
- The safety analysis set comprised a total of 277 patients who received at least 1 dose of treatment from WU-KONG1, WU-KONG2, WU-KONG6 and WU-KONG15.

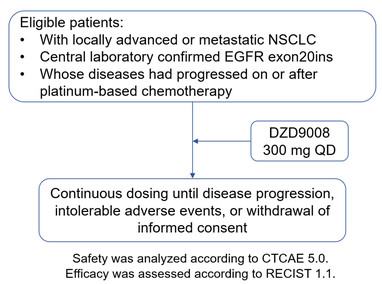

Figure 1. WU-KONG6 study design

Patient Demographics

Table 1. Patient demographics of the efficacy set

Characteristics	300 mg (N = 97)
Median age (range), year	58.0 (29, 79)
Female, n (%)	58 (59.8)
Race (Asian), n (%)	97 (100.0)
ECOG (0/≥ 1), n (%)	29 (29.9)/67 (69.0)#
Prior systemic anti-cancer treatment, n (%)	
One line/more than 1 lines	48 (49.5)/49 (50.5)
Platinum-based chemotherapy	97 (100.0)
PD-1/PD-L1	33 (34.0)
EGFR TKI	25 (25.8)
Baseline BM, n (%)	31 (32.0)

BM: brain metastasis. #: There is 1 (1.0%) missing data.

Results - Efficacy

- The confirmed ORR was 59.8% (58/97) by BICR. All confirmed responders had at least two post-treatment tumor assessments.
- The response rate for patients with baseline brain metastasis was 48.4% (15/31).
- Median duration of response (DoR) has not been reached. The longest DoR was > 9.7 months (patient still on treatment and responding).
- A total of 30 subtypes of EGFR exon20ins were enrolled. Anti-tumor activities were observed regardless of mutation subtypes and positions.

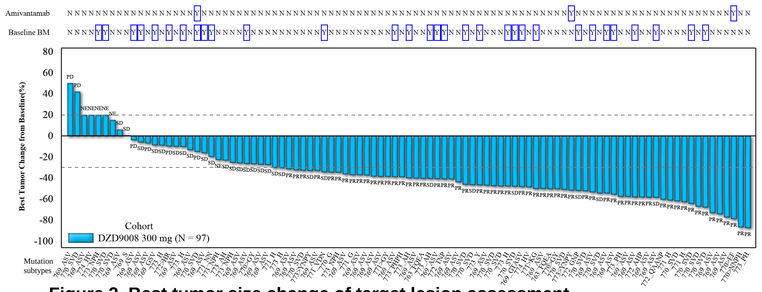

Figure 2. Best tumor size change of target lesion assessment
PR: partial response; SD: stable disease; PD: progressive disease; NE: not evaluable. BM: brain metastasis.

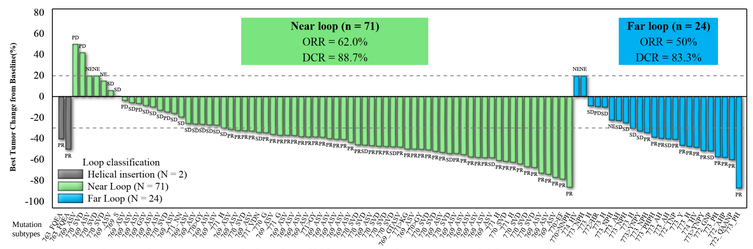

Figure 3. Anti-tumor activity in different EGFR exon20ins subtypes

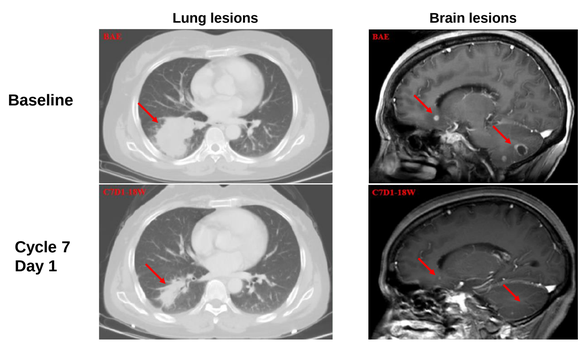

Figure 4. Anti-tumor activity in both extracranial and intracranial lesions

Results - Safety

Table 2. Summary of common (≥ 20%) drug-related TEAEs (≥ Grade 3)

AE summary, n(%)	300 mg (N = 178)	Total (N = 277)
Diarrhea	13 (7.3)	17 (6.1)
Rash	5 (2.8)	8 (2.9)
Blood CPK increased	24 (13.5)	31 (11.2)
Anemia	7 (3.9)	13 (4.7)
Stomatitis	4 (2.2)	5 (1.8)
Paronychia	3 (1.7)	4 (1.4)
Decreased appetite	3 (1.7)	7 (2.5)
Nausea	2 (1.1)	3 (1.1)
Vomiting	1 (0.6)	2 (0.7)

The severity of toxicities was graded according to CTCAE version 5.0; The causality was based upon investigator's assessment.

Table 3. Overview of TEAEs pooled analysis

Summary, n (%)	300 mg (N = 178)	Total (N = 277)
Drug-related AE leading to drug interruption	59 (33.1)	84 (30.3)
Drug-related AE leading to dose reduction	36 (20.2)	54 (19.5)
Drug-related AE leading to treatment discontinuation	14 (7.9)	17 (6.1)

- The most common drug-related TEAEs included diarrhea and rash, which were considered to be related to EGFR inhibition.
- Majority of the reported events were mild to moderate in severity, which could be monitored and managed in the clinics.
- After supportive care, these AEs were reversible and patients could recover.

Summary

- Sunvozertinib (DZD9008) demonstrated superior anti-tumor activities in advanced NSCLC patients with EGFR exon20ins, post platinum-based chemotherapy. The confirmed ORR at 300 mg was 59.8% by BICR.
- Patients with baseline brain metastasis showed significant response as well, with a confirmed ORR of 48.4%.
- Clinical activities were observed across a board range of EGFR exon20ins mutation subtypes and regardless of mutation positions.
- Sunvozertinib demonstrated a comparable safety profile to other EGFR TKIs.

Acknowledgments

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- We thank investigators and their team members at each study site.
- We thank staffs involved in WU-KONG1, WU-KONG2, WU-KONG6 and WU-KONG15 studies.

Dr. Mengzhao Wang has no conflict of interest to disclose.