Efficacy of Erdafitinib in Adults with Advanced Solid Tumors and Non-prespecified Fibroblast Growth Factor Receptor Mutations in the Phase 2 RAGNAR Trial: Exploratory Cohort

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KEY TAKEAWAY

- In contrast to tumor-agnostic efficacy of erdafitinib reported in patients with predefined *FGFR* alterations (mutations or fusions), clinical activity was limited in tumors with *FGFR* mut not predefined as potentially susceptible

FGFR, fibroblast growth factor receptor; mut, mutation

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CONCLUSION

- These findings further validate the predictive FGFR biomarker panel studied in the RAGNAR Broad Panel Cohort in patients with advanced solid tumors and highlight the importance of careful *FGFR* mut selection for targeted FGFR inhibition

FGFR, fibroblast growth factor receptor; mut, mutation

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INTRODUCTION

- FGFR alterations may be associated with constitutive activation and tumor cell proliferation[1]
- Erdafitinib is an oral selective pan-FGFR TKI approved in the US for adult patients with locally advanced or metastatic urothelial carcinoma with susceptible *FGFR3* genetic alterations, as determined by an FDA approved companion diagnostic test, whose disease has progressed on or after ≥1 line of prior systemic therapy[2]
- Primary analysis of the RAGNAR study Broad Panel Cohort demonstrated tumor agnostic efficacy with an ORR of 30% in patients with solid tumors harboring predefined *FGFR* mutations or fusions[3]
- Here we report efficacy results from the RAGNAR exploratory cohort investigating erdafitinib in patients with **other *FGFR* mut that were not predefined as potentially susceptible alterations**

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1. USFDA. 2024. Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-erdafitinib-locally-advanced-or-metastatic-urothelial-carcinoma (Accessed on April 17, 2024).
2. Pant C, et al. *Lancet Oncol* 2023;24:925–35. 3. Friedlaender A, et al. Biomark Res. 2024;12(1):24.

FDA, Food & Drug Administration; FGFR, fibroblast growth factor receptor; mut, mutations; ORR, objective response rate; TKI, tyrosine kinase inhibitor; US, United States

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METHODS

- The exploratory cohort of the tumor agnostic, phase 2 RAGNAR study (NCT04083976) assessed efficacy and safety of **erdafitinib in patients with any advanced non -urothelial solid tumor with other non -prespecified *FGFR* mutations**

Patients

Key inclusion criteria

- Age ≥18 years
- Disease progression on ≥1 line of systemic therapy
- No alternative standard therapy available
- **Non-target FGFRmut (not included in Broad Panel Cohort)**

Key exclusion criteria

- Presence of *FGFR* gatekeeper, resistance mutations or FGFR fusions
- Patients with previous *FGFR* inhibitor treatment

Treatment

Erdafitinib 8 mg orally once daily for 21-day continuous cycle, with possible up-titration to 9 mg on the basis of day 14 serum phosphate concentrations

Assessments*

- Objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and clinical benefit rate (CBR), per Response Evaluation Criteria in Solid Tumors version 1.1 or Response Assessment in
- Neuro-Oncology as assessed by the investigator
- Progression-free survival (PFS) and overall survival (OS), assessed by the investigator and Independent Radiographic Review (IRR)
- Proportion of patients with treatment-emergent adverse events (TEAEs)

Statistical analysis

- Response rates: median was reported with the estimated 95% confidence interval (CI)
- Progression free survival (PFS) and overall survival (OS): median and 95% CI estimated using Kaplan–Meier methods

*ORR: Proportion of patients with a confirmed complete or partial response; DOR: Time of initial documentation of a response until the first documented evidence of progressive disease (or relapse for patients who had a complete response during the study) or death, whichever came first; DCR: Proportion of patients who achieved a best response of complete response, partial response, or stable disease; CBR: Proportion of patients with complete or partial response or durable stable disease (defined as a duration of at least 4 months); PFS: Time from the first dose of study drug until the first documented evidence of progressive disease (or relapse for patients who had a complete response during the study) or death, whichever came first; OS: Time from the first dose of study drug until death.

Pant C, et al. *Lancet Oncol* 2023; 24: 925–35.

CR, complete response; DCR, disease control rate; DOR, duration of response; *FGFR*, fibroblast growth factor receptor; mut, mutations; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease

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RESULTS

Baseline characteristics in the Exploratory Cohort

- At data cutoff of Dec 4, 2023, 53 patients received erdafitinib
  - Median age was 62 years (range 24-80)
  - 59% had ECOG performance score of 1
  - 94% of patients had visceral metastases
  - Patients had a median of 3 prior lines of systemic therapy

Characteristics, n (%)	N=53
Age, years, mean (SD)	60 (11.7)
Female	32 (60.0)
Race	
White	25 (47.0)
Asian	24 (45.0)
Black or African American	4 (8.0)
ECOG	
0	22 (42.0)
1	31 (59.0)
Visceral metastasis[a], yes	44 (94.0)
Previous systemic therapy in advanced or metastatic setting	
Chemotherapy	51 (96.0)
Immunotherapy	13 (23.0)
Other systemic therapy	21 (40.0)
Number of previous lines of anticancer therapies, median (range)	3 (1-14)
1	11 (21.0)
2	14 (26.0)
≥3	28 (53.0)

[a]N=47
ECOG, Eastern Cooperative Oncology Group; SD, standard deviation

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RESULTS

Baseline characteristics in the Exploratory Cohort

- Common histologies were cholangiocarcinoma (n=10), breast cancer (n=7), endometrial cancer (n=6), squamous cell head and neck cancer (n=5), ovarian cancer (n=4), soft tissue sarcoma (n=4)
- Patients had mutations in *FGFR1* (17%), *FGFR2* (17%), *FGFR3* (30%), and *FGFR4* (38%)

Characteristics, n (%)	N=53
Tumor type	
Cholangiocarcinoma	10 (19.0)
Breast cancer	7 (13.0)
Endometrial cancer	6 (11.0)
Squamous cell head and neck cancer	5 (10.0)
Ovarian cancer	4 (8.0)
Soft tissue sarcoma	4 (8.0)
Colorectal cancer	3 (6.0)
High-grade glioma	3 (6.0)
Carcinoma of unknown primary	2 (4.0)
Esophageal cancer	2 (4.0)
Others[b]	7 (13.0)
FGFR gene alteration	
FGFR1	9 (17.0)
FGFR2	9 (17.0)
FGFR3	16 (30.0)
FGFR4	20 (38.0)
FGFR alteration type – mutation	53 (100)

[b]n=1 each: fallopian cancer, gastric cancer, hepatocellular cancer, malignant teratoma, non-squamous non-small cell lung cancer (NSCLC), squamous NSCLC, thymic cancer.
FGFR, fibroblast growth factor receptor

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RESULTS

Efficacy outcomes in Exploratory and Broad Panel Cohorts

- In the Exploratory Cohort objective response was seen in only 2 (4%) patients
  - 1 patient with breast cancer and *FGFR3* gene mutation had partial response for 2.79 months
  - 1 patient with carcinoma of unknown primary location and *FGFR4* gene mutation had partial response for 3.02 months

	Exploratory Cohort (N=53)	Broad Panel Cohort [1] (N=217)
ORR, % (95% CI)	4 (1, 13)	30 (24, 36)
DOR, months, median (95% CI)	NE	6.9 (4.4, 7.1)
PFS, months, median (95% CI)	0.94 (0.49, NE)	4.2 (4.1, 5.5)
OS, months, median (95% CI)	1.79 (0.92, NE)	10.7 (8.7, 12.1)

- In comparison, ORR was 30% in the Broad Panel Cohort
- ORR, DOR, PFS and OS outcomes in the Broad Panel Cohort (with target FGFR alterations) were better than in the Exploratory (with non-target FGFR alterations)

1. Pant C, et al. *Lancet Oncol.* 2023;24:925–35.

CI, confidence interval; DOR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression free survival; NE, not evaluable

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RESULTS

Safety in the Exploratory Cohort

- All 53 (100%) erdafitinib-treated patients had at least one TEAE; 96% were drug-related
  - Grade 3 or higher TEAEs occurred in 39 (74%) patients, of which 24 (45%) were erdafitinib-related
- The most common (>20%) TEAEs were hyperphosphatemia, diarrhea, dry mouth, stomatitis), decreased appetite, fatigue, and increased alanine transaminase levels
- No treatment-related deaths occurred
- Safety data were consistent with the known safety profile of erdafitinib

TEAE, n (%)	N=53	
Overall		
Any TEAEs	53 (100)	
Drug-related TEAEs	51 (96.0)	
Grade ≥3 TEAEs	39 (74.0)	
Serious TEAEs	26 (49.0)	
TEAEs leading to dose reduction	19 (36.0)	
TEAEs leading to dose interruption	29 (55.0)	
TEAEs leading to treatment discontinuation	7 (13.0)	
TEAEs leading to death*	1 (2.0)	
Drug-related TEAEs by preferred term (≥20% of patients)	**Any grade**	**Grade ≥3**
Hyperphosphatemia	42 (79.0)	--
Dry mouth	24 (45.0)	--
Diarrhea	23 (43.0)	2 (4.0)
Stomatitis	21 (40.0)	7 (13.0)
Decreased appetite	14 (26.0)	2 (4.0)
Alanine aminotransferase increased	12 (23.0)	4 (8.0)

*Respiratory failure was the cause of death, which was not drug-related.
TEAE, treatment-emergent adverse event

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2. USFDA. 2024. Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-erdafitinib-locally-advanced-or-metastatic-urothelial-carcinoma (Accessed on April 17, 2024).
3. BALVERSA®(erdafitinib) [package insert]. Horsham, PA: Janssen Products, LP; 2024.
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