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Efficacy and Safety of Erdafitinib in Adults With NSCLC and Prespecified Fibroblast Growth Factor Receptor Alterations in the Phase 2 Open-label, Single-arm RAGNAR Trial

Martin Schuler,[1] Josep Tabernero,[2] Omar Carranza,[3] Yohann Loriot,[4] Shubham Pant,[5] Dirk Arnold,[6] Gunnar Folprecht,[7] Daniel Palmer,[8] Hans Prenen,[9] Graziela Z. Dal Molin,[10] Iwona Ługowska,[11] Andrés Cervantes,[12] Hussein Sweiti,[13] Constance Hammond,[13] Saltanat Najmi,[13] Shibu Thomas,[13] Spyros Triantos,[13] Karen Xia,[13] Martin Gutierrez[14]

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Presented by: M Schuler; RAGNAR NSCLC at the 2024 ASCO Annual Meeting; May 31 – June 4, 2024; Chicago, IL, USA.

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CONCLUSIONS

- Erdafitinib demonstrated clinically meaningful activity in pretreated patients with NSCLC who had exhausted standard therapies and had prespecified *FGFR* alterations (ORR by IRC was 26.1%, mDOR was 4.6 months, and DCR was 73.9%)
- Responses were observed in patients with squamous and non-squamous NSCLC, with *FGFR*2 or *FGFR*3 alterations and with *FGFR* mutations or fusions
- Safety data were consistent with the known erdafitinib safety profile

DCR, disease control rate; *FGFR*, fibroblast growth factor receptor; IRC, independent review committee; mDOR, median duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate

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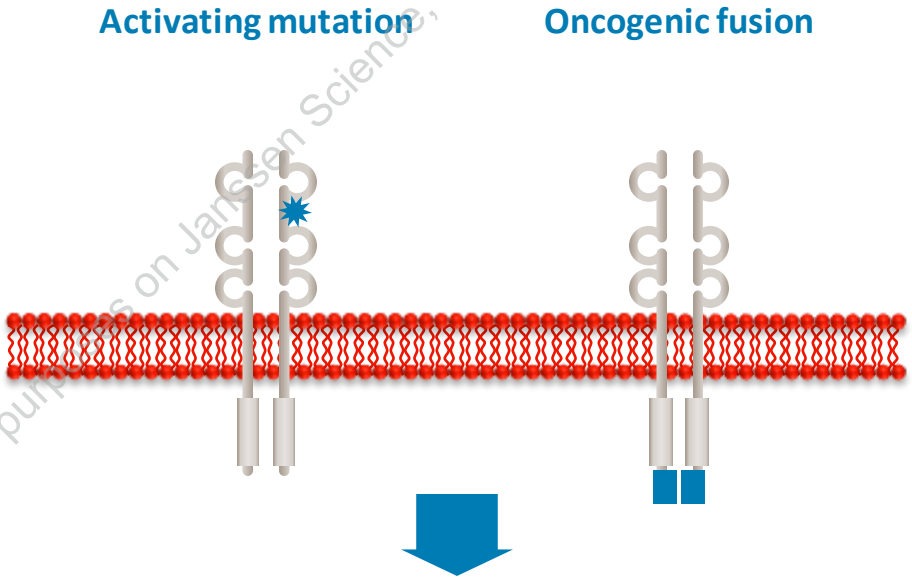
INTRODUCTION

- Erdafitinib is an oral selective pan-*FGFR* TKI approved by the FDA for the treatment of adults with locally advanced or metastatic urothelial carcinoma with susceptible *FGFR*3 alterations, who have progressed during or after ≥1 line of prior systemic therapy[1]
- The RAGNAR study (NCT04083976) showed tumor-agnostic efficacy of erdafitinib in patients with advanced solid tumors and predefined *FGFR* alterations[2]
  - ORR was 30% (95% CI, 24-36) and mDOR was 6.9 months (95% CI, 4.4-7.1)
- *FGFR* mutations and fusions have been reported in patients with NSCLC and may be implicated in oncogenesis and cancer progression[3]
- Here we report results on patients with NSCLC in the RAGNAR study



FDA, Food & Drug Administration; *FGFR,* fibroblast growth factor receptor; mDOR, median duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; TKI, tyrosine kinase inhibitor

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

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METHODS

RAGNAR Study Design (Broad Panel Cohort; NCT04083976)

Patients

Inclusion criteria
- Age ≥12 years
- Advanced or metastatic squamous or non-squamous NSCLC with prespecified *FGFR*1-4 alterations (mutations/fusions)
- Documented disease progression after exhausting standard therapies
- Received ≥1 prior line of systemic therapy

Exclusion criteria
- Previous *FGFR* inhibitor treatment
- Other targetable alterations (e.g., *EGFR, ALK, ROS1*)

Intervention

Oral erdafitinib once-daily
- Given in continuous 21-day cycle until disease progression or intolerable toxicity as per pharmacodynamically guided up-titration:

Age ≥15 years:	Age 12-14 years:
8 mg to 9 mg	5 mg to 8 mg

Endpoints
by independent review committee

Primary*
- Objective response rate

Secondary
- DOR
- DCR#
- PFS
- OS
- Safety

Tumor assessment was done every 6 weeks

Data cut-off date: December 04, 2023

*Evaluated per Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1; #DCR: the proportion of patients with CR, PR, or SD
CR, complete response; DCR, disease control rate; DOR, duration of response; *FGFR*, fibroblast growth factor receptor; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease
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RESULTS

Baseline Characteristics

- Overall, 23 patients with NSCLC received erdafitinib
- 96% of patients had metastatic disease
- Patients were heavily pretreated
  - Only 2 (9%) patients had responded to their last therapy

Characteristics	Squamous (n=14)	Non-squamous (n=9)	Total (N=23)
Age, years, median (range)	60.0 (52.0-77.0)	63.0 (50.0-79.0)	63.0 (50.0-79.0)
Male, n (%)	11 (78.6)	6 (66.7)	17 (73.9)
Current/former smoker, n (%)	12 (85.7)	7 (77.8)	19 (82.6)
Metastasis, n (%)	14 (100)	8 (89)	22 (96)
***FGFR* gene, n (%)**			
*FGFR*2	2 (14.3)	5 (55.6)	7 (30.4)
*FGFR*3	12 (85.7)	4 (44.4)	16 (69.6)
***FGFR* alteration type, n (%)**			
Mutation	7 (50.0)	3 (33.3)	10 (43.5)
Fusion	7 (50.0)	6 (66.7)	13 (56.5)
Prior lines of therapies, median (range), n (%)	2.0 (1.0-6.0)	3.0 (1.0-7.0)	2.0 (1.0-7.0)
1	2 (14.3)	1 (11.1)	3 (13.0)
2	6 (42.9)	3 (33.3)	9 (39.1)
≥3	6 (42.9)	5 (55.6)	11 (47.8)
Response to last line of therapy, n (%)	2 (14.3)	0	2 (8.7)

FGFR, fibroblast growth factor receptor; NSCLC, non-small cell lung cancer

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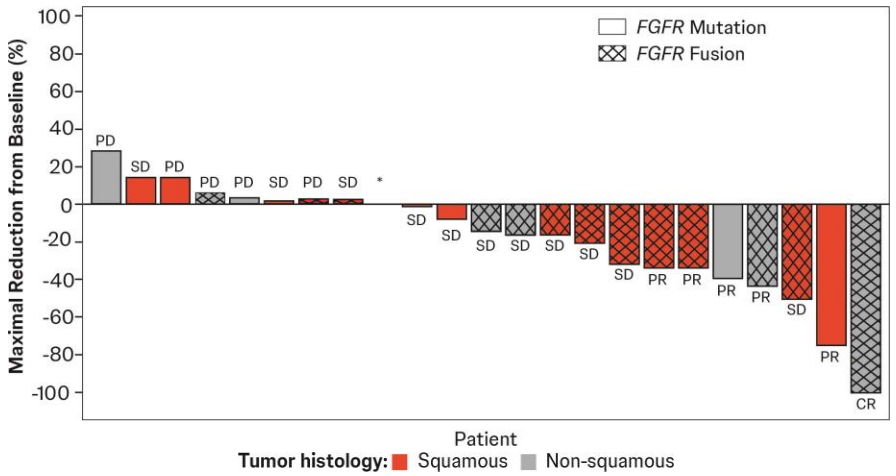
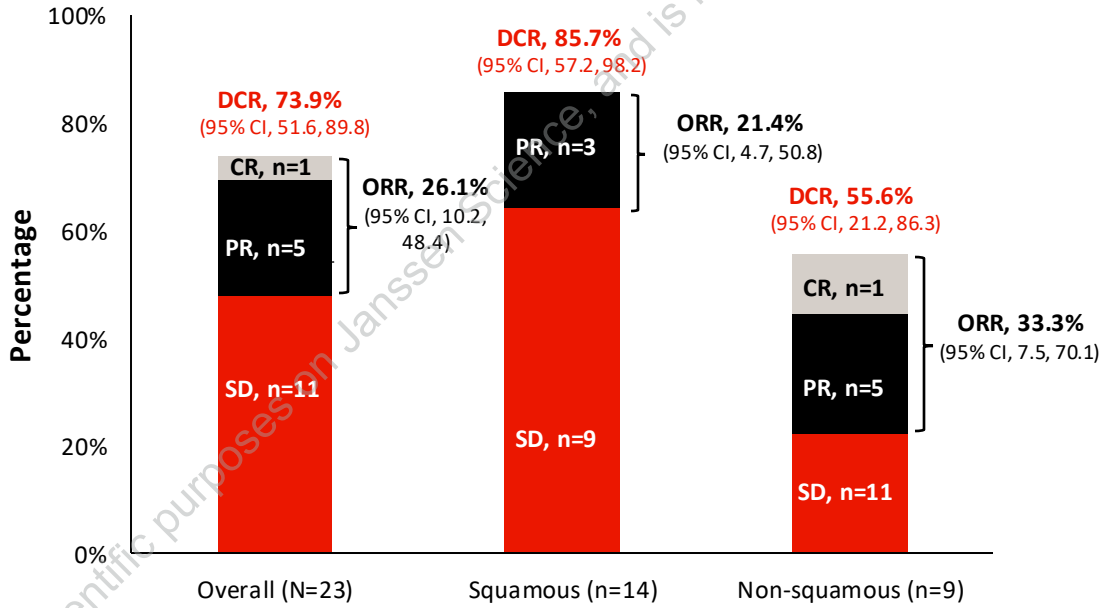
RESULTS

Tumor Response and Disease Control (per IRC)





- Median time to response was 1.5 (95% CI, 1.1-2.9) months
- ORR was 28.6% and 25.0% in patients with *FGFR2* and *FGFR3* gene alterations, respectively
- ORR was 30.8% and 20.0% in patients with *FGFR* fusions and mutations, respectively

*Squamous with *FGFR* mutation and non-CR/non-PD
CR, complete response; DCR, disease control rate; *FGFR*, fibroblast growth factor receptor; IRC, independent review committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

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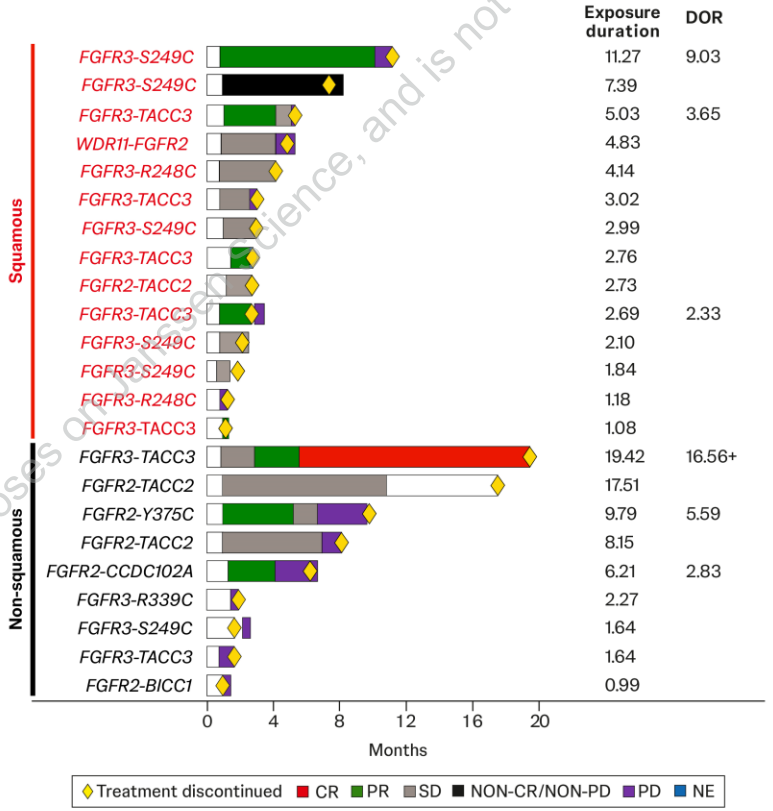
RESULTS

DOR, PFS and OS

Median (95% CI)	Overall (N=23)	Squamous (n=14)	Non-squamous (n=9)
DOR	4.6 (2.3-NE)	3.7 (2.3-NE)	5.6 (2.8-NE)
PFS	4.1 (2.4-6.9)	4.1 (2.4-NE)	4.1 (1.4-NE)
OS	10.5 (4.4-14.8)	10.5 (2.4-14.5)	9.9 (2.4-NE)



DOR, duration of response; CR, complete response; NE, not evaluable; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease

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RESULTS

Response by *FGFR* Co-Alterations (co-Alts)

- 78% (11/14) of squamous and 78% (7/9) of non-squamous patients had co-alts
- *TP53* co-alts were most prevalent in squamous (71% [10/14]), and *PIK3CA* co-alts (27% [3/9]) were most prevalent in non-squamous
- Responses were observed in patients with *TP53, PIK3CA, PTEN, CDKN2A*, and *RB1* co-alterations

	Squamous		Non-squamous	
	N	ORR , n (%)	N	ORR, n (%)
Overall*	14	3 (21.4)	9	3 (33.3)
TP53	10	3 (30.0)	2	1 (50.0)
PIK3CA	5	2 (40.0)	3	0
PTEN	3	2 (66.7)	0	NE
CDKN2A	1	1 (100)	3	2 (66.7)
RB1	2	1 (50.0)	0	NE
MTAP	0	NE	2	1 (50.0)

*Included only co-alterations with at least 2 patients in either squamous or non-squamous subgroups
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Safety

- 91.3% erdafitinib-treated patients had at least 1 drug-related TEAE
- Drug-related TEAEs of grade ≥3 occurred in 39.1% of patients and were manageable with supportive care and treatment interruptions or reductions
- 8.7% of patients discontinued due to drug-related TEAEs
- 8.7% of patients had serious drug-related TEAEs
- 56.5% of patients had dose reduction due to drug-related TEAEs
- 78.3% of patients had dose interruption due to drug-related TEAEs
- No treatment-related deaths were observed

TEAE by preferred term in ≥30% of patients, n (%)	N=23	
	Any grade	Grade ≥3
Hyperphosphatemia	15 (65.2)	0
Diarrhea	13 (56.5)	1 (4.3)
Stomatitis	13 (56.5)	3 (13.0)
Dry mouth	10 (43.5)	1 (4.3)
Nail disorder	8 (34.8)	1 (4.3)
Dry skin	7 (30.4)	0
Palmar-plantar erythrodysesthesia syndrome	7 (30.4)	2 (8.7)

TEAE, treatment-emergent adverse event
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APPENDIX

REFERENCES:

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)
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DISCLOSURES:

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