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

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KEY TAKEAWAY

Erdafitinib exhibited clinical benefit in extensively treated breast cancer patients with predetermined *FGFR* alterations, who have exhausted other treatments

FGFR, fibroblast growth factor receptor

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CONCLUSIONS

- With an ORR of 31%, and DCR of 68.8%, clinically meaningful efficacy was observed with erdafitinib treatment in patients with breast cancer, who have limited therapeutic options available
- Breast cancer patients with either *FGFR2* fusions or *FGFR2/3* mutations exhibited positive responses to erdafitinib treatment
- Safety data were consistent with the known safety profile of erdafitinib

DCR, disease control rate; *FGFR*, fibroblast growth factor receptor; ORR, objective response rate

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INTRODUCTION

- Fibroblast growth factor receptor (*FGFR*) aberrations in patients with estrogen receptor–positive breast cancer are associated with aggressive disease and resistance to endocrine therapy and CDK4/6 inhibitors[1,2]
- Erdafitinib is an oral selective pan-*FGFR* inhibitor approved by the US FDA for the treatment of adults with locally advanced or metastatic urothelial carcinoma with susceptible *FGFR3* alterations who have progressed on or after ≥1 line of prior systemic therapy[3]
- The primary analysis of the RAGNAR study (NCT04083976; N=217) demonstrated tumor-agnostic efficacy with an overall response rate of 30% in advanced or metastatic solid tumors with predefined *FGFR* alterations, across 16 different tumor types[4]
- **Here, we present the findings from the RAGNAR study focusing on clinical responses in a subset of patients with breast cancer**

1. Santolla MF, et al. *Cancers (Basel)*. 2020 Oct;12(10):3029.
2. Sánchez-Guixé M, et al. *Clin Cancer Res*. 2022;28(1):137-149.
3. BALVERSA® (erdafitinib) [package insert]. Horsham, PA: Janssen Products, LP; 2024.
4. Pant S, et al. *Lancet Oncol*. 2023;24:925-935.

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METHODS

Study participants

- Patients with breast cancer, harboring predefined *FGFR1-4* alterations (mutations/fusions) with documented disease progression after ≥1 prior line of systemic therapy, and lacking alternative standard therapy
  - All patients received oral erdafitinib 8 mg daily with optional up-titration until disease progression or intolerable toxicity

FGFR, fibroblast growth factor receptor

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METHODS

RAGNAR study design (NCT04083976)

Molecular screening of solid tumors for *FGFR* alterations

Local testing or central NGS

Key eligibility criteria

- Age ≥ 12 years
- Advanced/metastatic solid tumors (except UC)
- Prespecified *FGFR1-4* mutations/fusions[a]
- Documented disease progression
- Received ≥ 1 prior line of systemic therapy
- **Exhausted standard therapy options**

Broad Panel Cohort (N≈240)

- Pathogenic *FGFR* mutations or any *FGFR* gene fusion
- Cap of ~30 patients for each tumor type

Treatment with once-daily erdafitinib

Continues until disease progression or intolerable toxicities

Primary endpoint

- ORR by IRC

Key secondary endpoints

- ORR by investigator
- DOR
- DCR
- CBR
- PFS
- OS
- TEAEs

Assessments

- Tumor assessments were performed every 6 weeks
- Primary endpoint was ORR assessed by an Independent Review Committee (IRC)
- Secondary included ORR by investigator, DOR, DCR, PFS, OS, and safety

CBR, clinical benefit rate (i.e., CR+PR+SD≥4 months); DCR, disease control rate (i.e., CR+PR+SD); DOR, duration of response; *FGFR*, fibroblast growth factor receptor; IRC, Independent Review Committee; NGS, next-generation sequencing; ORR, objective response rate; OS, overall survival; PFS, progression free survival; TEAEs, treatment-emergent adverse evets; UC, urothelial carcinoma

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RESULTS

Baseline demographics

- Sixteen patients with breast cancer were treated, with a median age of 54 years and the majority (62.5%) were white

Characteristics	N=16
Age, Median (range), years	54.0 (37–74)
Race	
Asian	2 (12.5)
Black or African American	1 (6.3)
White	10 (62.5)
Not reported	3 (18.8)
Ethnicity	
Not Hispanic or Latino	13 (81.3)
Not reported	3 (18.8)

Data are n (%) unless otherwise stated.

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RESULTS

Baseline disease characteristics

- All 16 patients had visceral metastasis
- Overall, 37.5% had *FGFR* mutations and 62.5% had *FGFR* fusions across *FGFR1* (12.5%), *FGFR2* (75%), and *FGFR3* (12.5%) genes
- Co-alterations of *TP53* and *PIK3CA* were found in 6 patients
- Patients received a median of 5 lines of prior anti-cancer therapy and 12 had ≥3 prior lines; only 1 patient responded to their last line of therapy

Characteristics	N=16
Breast cancer subtypes	
ER/PR positive	10 (62.5)
ER/PR negative	6 (37.5)
FGFR Alterations	
Mutations	6 (37.5)
Fusion	10 (62.5)
Altered *FGFR* Gene	
FGFR1	2 (12.5)
FGFR2	12 (75)
FGFR3	2 (12.5)
FGFR4[a]	0
Baseline ECOG	
0	1 (6.3)
1	15 (93.8)
Time from progression/relapse on the last line of treatment to 1st dose, Mean (SD), months	1.83 (1.54)
Number of prior lines of anti-cancer therapies	
1	0
2	4 (25)
≥3	12 (75)
Number of metastatic sites	
1	0
2	4 (25)
≥3	12 (75)

Data are n (%) unless otherwise stated.
[a]No patients with *FGFR4* co-alterations were enrolled reflecting the low incidence of *FGFR4* in adult patients.
ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; *FGFR*, fibroblast growth factor receptor; PR, progesterone receptor; SD, standard deviation

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RESULTS

Exposure

- At the data-cut off date of December 4, 2023, the median treatment duration was 3.4 months
  - Reasons for treatment discontinuation: progressive disease (13 [81.3%]); study terminated by the sponsor, patient withdrawal, and other (1 patient each, [6%])

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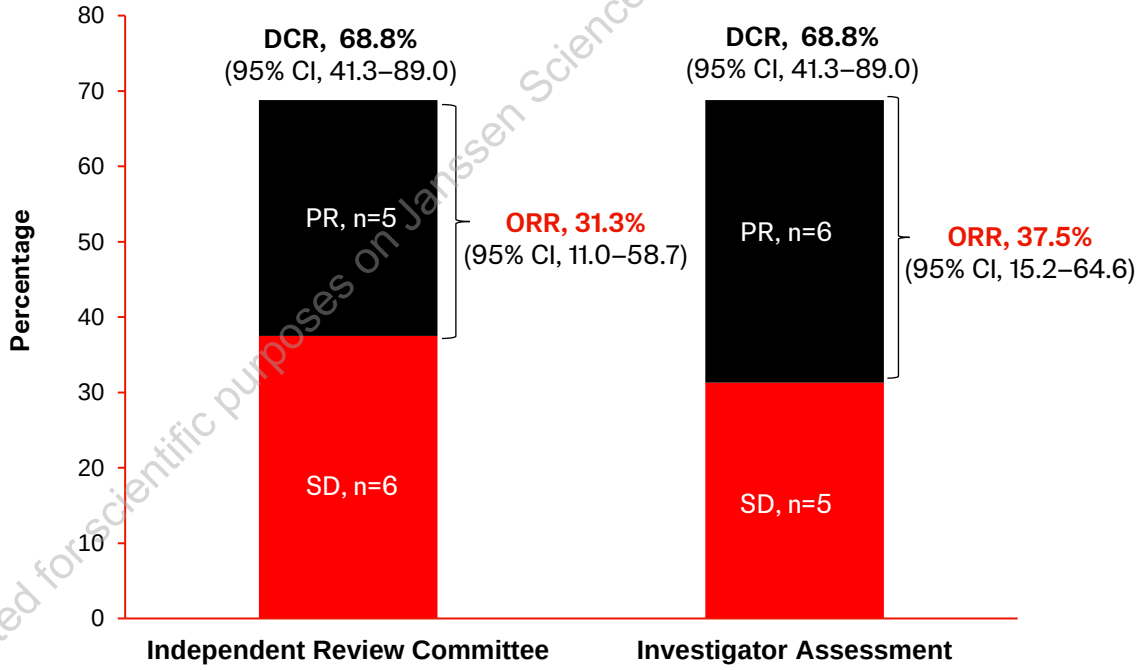
RESULTS

Tumor response (treated patients)

- The ORR per IRC was 31.3% (95% CI, 11.0–58.7) at a median efficacy follow-up of 14.1 months
  - All 6 patients with BOR of SD per IRC had durable SD ≥4 months
  - Of the 5 responders, the median time to response of 1.4 months
- The ORR per investigator assessment was 37.5% (95% CI, 15.2–64.6), at a median efficacy follow-up of 30.29 months



BOR, best overall response; DCR, disease control rate; ORR, objective response rate; IRC, Independent Review Committee; PR, partial response; SD, stable disease

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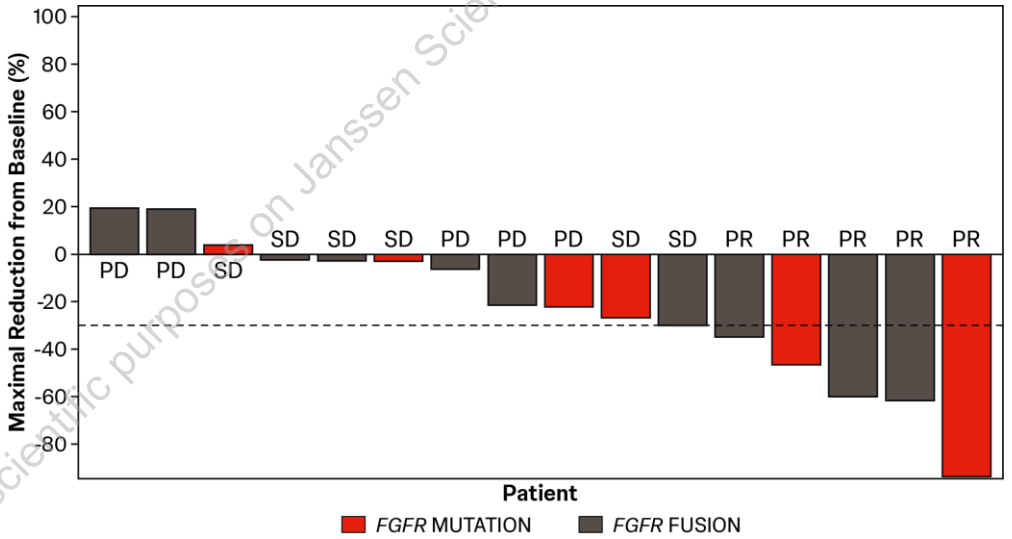
RESULTS

Duration of response and survival outcomes (treated patients)

Median (95% CI), months	Independent Review Committee (N=16)	Investigator Assessment (N=16)
DOR	6.93 (6.08–NE)	7.46 (5.59–NE)
PFS	5.73 (1.22–9.56)	4.17 (1.18–9.66)
OS		8.87 (4.86–11.76)



- DOR per IRC was 6.9 months (95% CI, 6.08–NE)
- Among responders, 3 patients had *FGFR2* fusions, 1 patient had a *FGFR2* mutation, and 1 patient had a *FGFR3* mutation

DCR, disease control rate; DOR, duration of response; *FGFR*, fibroblast growth factor receptor; IRC, Independent Review Committee; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression free survival; PD, progressive disease; PR, partial response; SD, stable disease

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RESULTS

Safety

- All 16 treated patients experienced drug-related TEAEs
- No TEAEs led to treatment discontinuation or death

TEAEs ≥20%	Erdafitinib (N=16)	
Overall		
Any TEAEs	16 (100)	
Grade ≥3 TEAEs	7 (43.8)	
Serious TEAEs	2 (12.5)	
TEAEs leading to dose reduction	11 (68.8)	
TEAEs leading to dose interruption	10 (62.5)	
TEAEs by preferred term in ≥20% of patients	**Any Grade**	**Grade ≥3**
Stomatitis	13 (81.3)	2 (12.5)
Hyperphosphatemia	11 (68.8)	0
Dry mouth	10 (62.5)	0
Diarrhea	10 (62.5)	1 (6.3)
Palmar-plantar erythrodysesthesia	7 (43.8)	0
Dry skin	6 (37.5)	2 (12.5)
Alopecia	4 (25.0)	0
Onycholysis	4 (25.0)	1 (6.3)
Asthenia	4 (25.0)	2 (12.5)

Data are n (%). Adverse events are coded using MedDRA Version 24.1.
Patients were counted only once for any given event, regardless of the number of times they actually experienced the event.
TEAEs, treatment-emergent adverse events

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DISCLOSURES

Omar Carranza has received consulting fees from Bayer US, LLC, and Janssen; honoraria from Bayer US, LLC, Janssen, Merck, Novartis, and Pfizer; and speakers' bureau fees from Merck and Pfizer. A complete list of author disclosures are available on the ASCO website.

ACKNOWLEDGMENTS:

Erdafitinib (JNJ-42756493) was discovered in collaboration with Astex Pharmaceuticals.

Shweta Pitre, MPH, CMPP (SIRO Clinpharm UK Limited) provided medical writing assistance and Jennifer Han, MS (Janssen Global Services) provided additional editorial support. Amit Kavle (SIRO Clinpharm Pvt. Ltd. India) provided graphic designing support.

FUNDING: This study was funded by Janssen Research & Development.

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