Tumor Agnostic Efficacy and Safety of Erdafitinib in Patients With Advanced Solid Tumors With Prespecified Fibroblast Growth Factor Receptor Alterations (*FGFRalt*) in RAGNAR: Interim Analysis Results

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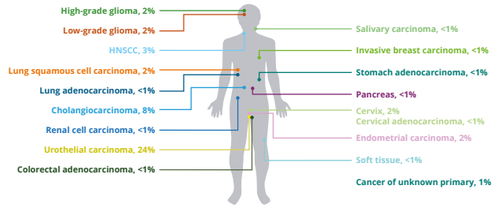
INTRODUCTION

- *FGFR* mutations and fusions may disrupt signaling and drive oncogenesis[1-3]
- A wide range of malignancies have *FGFRalts* at varying frequencies[1,2,4]
- FGFR inhibitors are approved for treatment of advanced or metastatic bladder cancer and cholangiocarcinoma with *FGFRalts*[5-7]
  - However, no FGFR targeted therapies have been approved for patients across tumor histologies
- Patients who have exhausted standard of care have a high unmet need
  - Targeted FGFR inhibition in patients with *FGFR* alterations warrants investigation

FIGURE 1: Estimated frequency of RAGNAR target *FGFRalts* by tumor location

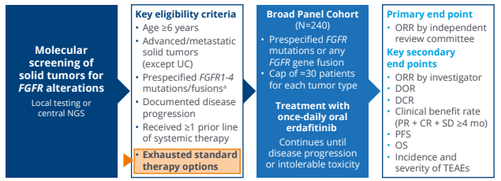


HNSCC, head and neck squamous cell carcinoma.
Based on searches of the GENIE database[a] for RAGNAR target *FGFR* alterations.

- Erdafitinib is an oral selective pan-FGFR tyrosine kinase inhibitor, the first and only approved to treat *FGFR*-altered urothelial carcinoma (UC)[5,8-10]
  - In the phase 2 BLC2001 study, erdafitinib showed an investigator-assessed objective response rate (ORR) of 40% and disease control rate (DCR) of 80%[9,10]
  - Erdafitinib is approved to treat advanced or metastatic UC in the United States[5] and 13 other countries
- Clinical activity of erdafitinib has also been investigated in other tumors, including cholangiocarcinoma, in phase 1/2 trials[11-13]
  - In the multicenter, single-arm phase 2a LUC2001 study in Asian patients with *FGFR*-altered cholangiocarcinoma, erdafitinib showed an ORR of 41% and a DCR of 82%[11]

METHODS

FIGURE 2: RAGNAR pivotal tumor agnostic phase 2 study design



- The RAGNAR study is ongoing at ≈160 sites globally
- Three additional cohorts are being investigated:
  - *Exploratory Cohort*: N≈40, other *FGFR* mutations
  - *Cholangiocarcinoma Expansion Cohort*: N≈30, prespecified *FGFR* mutations or any *FGFR* gene fusion
  - *Pediatric Cohort*[b]: N≈26, patients (ages 6-17 years) with *FGFR* mutation, fusion, or internal tandem duplication
- The primary analysis is planned at ≈200 response-evaluable patients in the Broad Panel Cohort
- There were 3 planned interim analyses
- Results of the 3rd interim analysis of the Broad Panel Cohort are reported here[c]

CR, complete response; NGS, next-generation sequencing; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event.
[a]Prespecified *FGFR1-4* mutations or any fusions were determined by bioinformatics and preclinical testing. [b]N≈20 patients with prior treatment + 6 newly diagnosed. [c]Data cutoff for interim analysis was October 26, 2021.

ADDITIONAL SOLID TUMORS

RESULTS

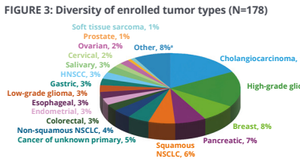
- The study population in this interim analysis includes 178 patients

TABLE 1: Baseline demographics and disease characteristics

Demographics	N=178
Age, median (range), years	56.5 (12-79)
Male, n (%)	96 (53.9)
Race, n (%)	
White	92 (51.7)
Asian	64 (25.8)
Black or African American	6 (3.4)
American Indian or Alaska Native	1 (0.6)
Not reported	31 (17.4)
FGFR alterations, n (%)	
Mutations	56 (31.5)
Fusions	122 (68.5)
FGFR gene with alteration, n (%)	
FGFR1	16 (9.0)
FGFR2	87 (48.9)
FGFR3	75 (42.1)
FGFR4	0
Disease characteristics	**N=178**
ECOG performance status, n (%)[a]	
0	52 (29.2)
1	123 (69.1)
2	1 (0.6)
Visceral metastasis, n (%)	129 (75.5)
Prior radiotherapy, n (%)	91 (51.1)
Prior cancer-related surgery, n (%)	121 (68.0)
Prior lines of anticancer therapies in the advanced/metastatic setting, n (%)	
1	45 (25.3)
2	59 (33.1)
≥3	74 (41.6)
Median, range	2 (1-12)
Response to last line of therapy, n (%)	16 (9.0)

ECOG, Eastern Cooperative Oncology Group.
[a]ECOG performance status was not available for 2 patients.

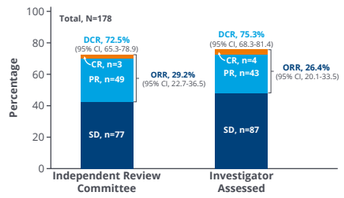
FIGURE 3: Diversity of enrolled tumor types (N=178)



- RAGNAR enrolled patients with prespecified *FGFRalts* across >20 tumor types

NSCLC, non-small cell lung cancer. [a]1 patient each (0.6%) was enrolled with the following malignancies: adenoid cystic carcinoma, anal adenocarcinoma, basal cell carcinoma, conjunctival epidermoid carcinoma, duodenal cancer, gallbladder carcinoma, gastrointestinal stromal tumor, germ cell tumor, malignant small round cell tumor, mesothelioma, parathyroid carcinoma, testicular cancer, thymic cancer, and thyroid carcinoma.

FIGURE 4: Efficacy of erdafitinib in the tumor agnostic population



- The clinical benefit rate was 48.9%[a]
- Median DOR was 7.1 months (95% CI, 5.5-9.3)[a]
- Median PFS was 5.2 months (95% CI, 4.0-5.6)[a]
- Median OS was 10.9 months (95% CI, 7.9-14.3)[a]
- Median follow-up time is limited to 11 months
- 51% of responses are ongoing[a]
- ORR in patients with *FGFR* mutations versus fusions was comparable (26.8% vs 27.0%, respectively)[a]

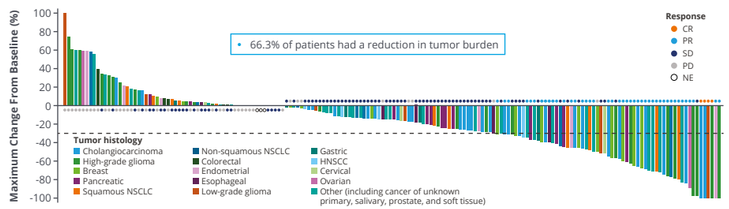
[a]Investigator assessment data are shown. Results for these end points were similar by independent review committee.

TABLE 2: Summary of TEAEs

TEAE by preferred term in ≥30% of patients, n (%)	N=178	
	Any grade	Grade ≥3
Hyperphosphatemia	122 (68.5)	10 (5.6)
Diarrhea	103 (57.9)	8 (4.5)
Stomatitis	94 (52.8)	16 (9.0)
Dry mouth	86 (48.3)	1 (0.6)
Dry skin	60 (33.7)	3 (1.7)
Palmar-plantar erythrodysesthesia	57 (32.0)	11 (6.2)
Constipation	54 (30.3)	2 (1.1)

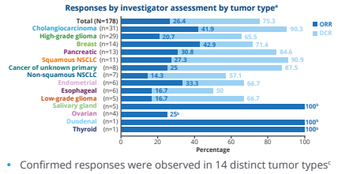
- Drug-related TEAEs of grade ≥3 occurred in 44.9% of patients and were manageable with supportive care and treatment interruptions or reductions
  - 7.3% of patients had serious drug-related TEAEs
  - 7.3% of patients discontinued due to drug-related TEAEs
  - 1 death (pulmonary embolism) was reported as drug related by the investigator; subsequently reassessed as not related
- Central serous retinopathy events were reported in 14.6% of patients; no grade 3-4 events
  - 7.9% had dose interruptions; 9.6% had dose reductions; no discontinuations

FIGURE 5: Investigator-assessed change in tumor target lesion



NE, not estimable; PD, progressive disease.

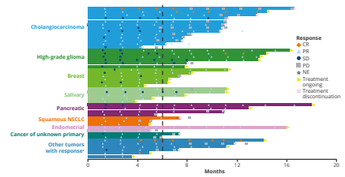
FIGURE 6: Confirmed responses across tumor types and *FGFRalts*



- Confirmed responses were observed in 14 distinct tumor types[c]
- No responses were observed to date in patients with colorectal, gastric, or cervical cancer[d]
- CRs and PRs were observed in patients with *FGFR1-3alts* across multiple tumor types

[a]Only tumor types with ≥1 CR or PR are shown. [b]ORR and DCR were equivalent for this tumor type. [c]Responses by independent review committee were observed in 15 distinct tumor types. [d]Based on investigator assessment and independent review committee in tumor types with ≥4 patients enrolled.

FIGURE 7: Swim lane plot[a] for treatment duration and response[b]



- Median follow-up duration was 11 months
- Median DOR (investigator assessed) was 7.1 months
- 24 of 47 responders (51.1%) have ongoing responses as of the interim analysis data cutoff

[a]Swim lane plot shows only patients with CR or PR. [b]Investigator assessed.
[c]Tumor types with 1 responder each (top to bottom): low-grade glioma, ovarian, non-squamous NSCLC, esophageal, thyroid, and duodenal.

KEY TAKEAWAYS

- RAGNAR is the largest tumor agnostic trial reported of a targeted therapy to date (N=178 in this analysis)
- In this planned interim analysis, erdafitinib demonstrated an ORR of 29.2% and a DCR of 72.5% in patients with *FGFR*-altered advanced solid tumors (excluding UC) with no alternative treatment options
- Safety data were consistent with the known safety profile of erdafitinib in UC

CONCLUSIONS

- Durable investigator-assessed responses were observed in patients with 14 different tumor types with *FGFR1-3* mutations and fusions
- Toxicities were generally manageable with supportive care and dose modification
- These interim analysis results from RAGNAR suggest that erdafitinib has a broad role in patients with *FGFR*-altered malignancies, with mutations and with fusions

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DISCLOSURES

Y. Loriot has received consulting fees from Janssen, Astellas Pharma, Roche, AstraZeneca, MSD Oncology, Clovis Oncology, Seattle Genetics, and Bristol Myers Squibb; and has been reimbursed for accommodations or expenses from Astellas Pharma, Janssen Oncology, Roche, AstraZeneca, MSD Oncology, Clovis Oncology, Seattle Genetics, and Bristol Myers Squibb.

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