

## Efficacy and safety of erdafitinib in pediatric patients with advanced solid tumors and FGFR alterations in the phase 2 RAGNAR trial.

Olaf Witt, Sameer Farouk Sait, Blanca D. Diez, Agustin Cardoso, David A. Reardon, Liam Welsh, Kent C. Shih, Capucine Baldini, Christophe Massard, Yohann Lorient, Shubham Pant, Hussein Sweiti, Shibu Thomas, Constance Hammond, Saltanat Najmi, Spyros Triantos, Lauren Crow, Birgit Georger; Hopp Children's Cancer Center Heidelberg (KiTZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ) and National Center for Tumor Diseases (NCT), Heidelberg, Germany; Memorial Sloan Kettering Cancer Center, New York, NY; FLENI, Buenos Aires, Argentina; Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, MA; The Royal Marsden NHS Foundation Trust, London, United Kingdom; Tennessee Oncology, Nashville, TN; Drug Development Department (DITEP), Gustave Roussy, Villejuif, France; Le Kremlin Bicêtre – France INSERM U1030, Molecular Radiotherapy, Université Paris-Saclay, Gustave Roussy, Villejuif, France; Department of Cancer Medicine, INSERM U981, Gustave Roussy, Université Paris-Saclay, Villejuif, France; Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX; Janssen Research & Development, Spring House, PA; Gustave Roussy Cancer Center, Department of Paediatric and Adolescent Oncology, INSERM U1015, Université Paris-Saclay, Villejuif, France

**Background:** Erdafitinib is an oral selective pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor approved in the US for adult patients (pts) 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  $\geq 1$  line of prior systemic therapy. Primary analysis of the RAGNAR study Broad Panel Cohort demonstrated tumor agnostic efficacy in pts with solid tumors harboring predefined *FGFR* mutations or fusions (Pant 2023). Here we report on Final Analysis of efficacy and safety results from the Pediatric Cohort of the RAGNAR study. **Methods:** Pediatric pts  $\geq 6$  years with advanced solid tumors and any *FGFR* mutation, fusion, or tandem duplication received oral erdafitinib. Starting doses were 8 mg, 5 mg, and 3 mg daily for ages  $> 15$  years, 12 to  $< 15$  years, and 6 to  $< 12$  years, respectively, in 21-day cycles with possible individualized up-titration based on serum phosphate and adverse events (AEs). The primary endpoint was objective response rate (ORR) (Response Evaluation Criteria in Solid Tumors [RECIST] 1.1 or Response Assessment in Neuro-Oncology [RANO]) by independent review committee (IRC). Secondary endpoints included ORR by investigator, duration of response (DOR), disease control rate (DCR), clinical benefit rate (CBR), progression-free survival (PFS), and overall survival (OS). **Results:** 11 pts (median age 13 years; range, 6–16; 64% female) received erdafitinib. Median follow-up was 9.7 months at data cutoff. Histologies included low-grade glioma (LGG–6 pts); high-grade glioma (HGG–3 pts); soft tissue sarcoma (1 pt), and temporal neurocytoma (TNEURO–1 pt). 7, 1, and 3 pts had *FGFR1*, *FGFR2*, and *FGFR3* alterations, respectively. 6, 4, and 1 pts had *FGFR* fusions, mutations, and tandem duplication, respectively. Pts had a median of 1 prior line of systemic treatment; 6 (55%) had prior radiotherapy. At data cutoff, 1 of 3 pts (33%) with HGG and an *FGFR1-TACC1* fusion achieved a partial response based on investigator assessment with a response duration of 19.8 months. Investigator-assessed objective responses were not observed in the other tumor types. DCR and CBR were 100% in pts with LGG and 67% in pts with HGG. Most common treatment-emergent adverse events (TEAEs) included hyperphosphatemia (64%), diarrhea (64%), pain in extremity (45%), alanine transaminase increased (36%), nausea (36%), and onycholysis (27%). No central serous retinopathy events occurred; related serious adverse events (SAEs) occurred in 4 (36%) pts, including 1 SAE of epiphysiolysis; there were no related TEAEs leading to death. **Conclusions:** In this small pediatric population comprising primarily refractory HGG and LGG with any *FGFR* alteration, erdafitinib demonstrated limited objective responses but promising disease control with acceptable safety. Clinical trial information: NCT04083976. Research Sponsor: None.