ReFocus: A Phase 1/2 study of the highly selective FGFR2 inhibitor RLY-4008 in patients with advanced solid tumors, including breast cancer

Suneel Kamath, David Tai, Irene Moreno, Hani Bakir, Zhaojun Jin, Changhoo Yoo, Fabien Ricard, Kai Yu Jen, Jim Coward, Lia Liu, Frans Opdam, Michael Millward, Mariano Ponz-Saavedra, Jeffrey Yachnin, Richard Kim, Joon Oh Park, Vivek Subbiah, Alison M. Schramm

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RANKONET FOR TGFR IN BREAST CANCER

- Breast cancer arises through a complex multistep process, gene fusions, and copy number amplifications and occurs across solid tumors (Figure 1).
- In public datasets, FGFR2 amplifications are reported in <7% of breast cancer patients overall with frequencies varying by age subgroup (driven by breast cancer subtypes).
- Amplification of FGFR2 in the breast cancer genome is associated with higher frequencies of FGFR2 amplifications across other solid tumors (Figure 1).
- Tumor models demonstrate the broad therapeutic potential of RLY-4008 across FGFR2-driven solid tumors, including breast cancer (Figure 2).
- FGFR2 inhibitors are a promising target for therapy and are being used in the clinic (Figure 3).

FGFR2 driver alterations in breast cancer

- FGFR2 inhibitor RLY-4008 is a highly selective, potent, irreversible FGFR2 inhibitor designed based on insights into the differences in conformational dynamics between FGFR2 and other FGFRs. This approach has allowed a degree of selectivity not previously achieved for FGFRs, with the aim to overcome the limitations of previous FGFR inhibitors.
- RLY-4008 has the first-known highly selective FGFR2 small-molecule inhibitor to reach the clinic (Figure 4).
- RLY-4008 is a high-affinity, potent, irreversible FGFR2 inhibitor designed based on insights into the differences in conformational dynamics between FGFR2 and other FGFRs. This approach has allowed a degree of selectivity not previously achieved for FGFRs, with the aim to overcome the limitations of previous FGFR inhibitors (Table 1).
- In vitro, RLY-4008 inhibited FGFR2 in breast cancer and other solid cancer cell lines with IC50 values in the low nanomolar range (Figure 5).
- In vivo, RLY-4008 inhibited FGFR2 in breast cancer, with tumor burden reductions ranging from 30-80% (Figure 6).

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