Background

There is an unmet clinical need for next-generation therapies with improved efficacy and tolerability for patients with metastatic urothelial carcinoma—15% of metastatic urothelial cancers harbor mutations or fusions in FGFR3. Erdafitinib is a pan-FGFR inhibitor that is FDA approved for the treatment of FGFR3- and FGFR2-altered metastatic urothelial carcinoma.

Results

**IN VITRO POTENCY**

TYRA-300 maintains potency against gatekeeper mutants V555M/L in enzymatic assays.

**IN VIVO POTENCY**

In vivo tumor efficacy in FGFR3 activating mutant, fusion, and gatekeeper-mutant bladder cancer xenograft models.

**SELECTIVITY**

TYRA-300 shows significant selectivity for FGFR3 over other FGFR isoforms. TYRA-300 is selective for FGFR3, while pan-FGFR TKIs are not.

**RESULTS**

TYRA-300 is potent in a CRISPR-engineered gatekeeper-mutant cell line.

TYRA-300 does not substantially elevate phosphate levels in rats.

References