TPS3184 Poster Session

RYZ101 (^{225}Ac-DOTATATE) in patients with estrogen receptor-positive, human epidermal growth factor receptor 2–negative, locally advanced and unresectable, or metastatic breast cancer progressing after prior therapy: The phase 1b/2 TRACY-1 study.

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Background: RYZ101 (actinium-225 [^{225}Ac]-DOTATATE) is a radiolabeled somatostatin analog (SSA) for the treatment of patients with solid tumors expressing somatostatin receptor-type 2 (SSTR2). RYZ101 is composed of the alpha-emitting radioisotope ^{225}Ac, the chemical chelator DOTA (tetraxetan), and SSA octreotate (TATE). RYZ101 binds with high affinity to SSTR2 on the cell surface and is internalized, whereupon the alpha-particle emission of ^{225}Ac results in lethal double-strand DNA breaks. Although SSTR-directed therapy is widely used in patients with well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NETs), its relevance in non-GEP-NET SSTR-expressing neoplasms is still emerging. Clinical positron emission tomography (PET) imaging studies have reported SSTR expression in estrogen receptor (ER)-positive breast cancer. Available data support investigating the efficacy of RYZ101 in patients with ER-positive, HER2-negative, locally advanced and unresectable or metastatic breast cancer. **Methods:** TRACY-1 (NCT06590857) is a global, multicenter, open-label, two-part (dose escalation and expansion) phase 1b/2 study. Key inclusion criteria are: age ≥18 years; histologically confirmed, ER-positive, HER2-negative locally advanced and unresectable or metastatic breast cancer not amenable to curative-intent treatment; endocrine-refractory disease; documented progression (per RECIST v1.1) after ≥2 and ≤4 prior lines of chemotherapy and/or ADC (≥1 must be ADC if the patient is a candidate for ADCs and treatment is available); ≥1 RECIST-measurable SSTR−PET-positive lesion and ≥80% of RECIST-measurable lesions being SSTR−PET-positive on screening scan. Key exclusion criteria are: prior radiopharmaceutical therapy; prior anticancer therapy or external beam radiotherapy in past 4 weeks; anticancer hormonal treatments in past 2 weeks. Primary objectives are to determine the recommended phase 2 dose (R2PD) of RYZ101 (dose escalation; anticipated 6−24 patients), and the efficacy of RYZ101 at the RP2D defined as ORR as determined by BICR (dose expansion; approximately 100 patients). During dose escalation, patients will receive RYZ101 by IV infusion every 6 weeks for up to 6 cycles at a starting dose of 6.5 MBq (dose level [DL] 1), with escalation to DL 2 (8.3 MBq) and DL 3 (10.2 MBq), or dose de-escalation to 4.6 MBq if DL 1 is not tolerated, based on dose-limiting toxicity rates. In the expansion phase, patients will receive RYZ101 at the RP2D. Concomitant amino acid IV infusions (containing L-arginine and L-lysine) will be co-infused with RYZ101 for renal protection. The study is ongoing and enrolling patients in the USA. Clinical trial information: NCT06590857. Research Sponsor: RayzeBio.