TPS5117 **Poster Session**

A first-in-human, phase 1 dose escalation and expansion study evaluating the safety, tolerability, and anti-tumor activity of [225Ac]Ac-FL-020, an anti-PSMA radioconjugate, in patients with metastatic castration-resistant prostate cancer (mCRPC).

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Background: Prostate-specific membrane antigen (PSMA) targeted radioligand therapy is an emerging treatment modality for metastatic castration-resistant prostate cancer (mCRPC). Alpha emitting [^{225}Ac]Ac-FL-020 represents a new generation of PSMA-targeted radioconjugates (RDC) with potential improvements in pharmacokinetics and pharmacodynamics, aiming to enhance tumor uptake while minimizing healthy tissue exposure, including the salivary glands. This novel compound was discovered using our proprietary Clear-X technology platform. This Phase 1 study evaluates the safety, tolerability, and anti-tumor activity of [^{225}Ac]Ac-FL-020 in patients with mCRPC. **Methods:** This first-in-human, open-label, multicenter Phase 1 study consists of two parts: dose escalation (Part 1) and cohort expansion (Part 2). In Part 1, the study aims to establish the safety profile and maximum tolerated dose/recommended Phase 2 dose (MTD/RP2D) of [^{225}Ac]Ac-FL-020, guided by a Bayesian logistic regression model (BLRM) with overdose control. Eligible patients must show PSMA-positive lesions on a PSMA PET/CT scan, have histologically confirmed mCRPC with documented progression, and have received prior treatments including androgen receptor signaling inhibitors or CYP17 inhibitors, along with at least 1 previous taxane regimen. Exclusion criteria include patients with extensive PSMA-negative disease. The dose escalation follows cohorts starting with 1-3 patients, expanding to 3-6 patients, with provisional dose levels from 1 to 5 MBq. Part 2, the cohort expansion, will commence once the RP2D is established, enrolling an additional 18 patients to further evaluate safety and gather preliminary efficacy data. The primary objective is to establish the safety profile and determine the MTD/RP2D of [^{225}Ac]Ac-FL-020 in mCRPC patients. Secondary objectives include assessing pharmacokinetics, dosimetry, and anti-tumor activity, with the overarching goal of exploring the potential of this novel actinium RDC for improving outcomes in patients with mCRPC. The study is enrolling in Australia and US, with European sites planned to open later in 2025. Clinical trial information: NCT06492122. Research Sponsor: Full-Life Technologies GmbH.