TPS4625 **Poster Session**

Updates to CORE-008: A phase 2 multi-arm, multi-cohort study to evaluate intravesical cretostimogene grenadenorepvec in patients with high-risk non-muscle invasive bladder cancer.

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Background: Treatment for High-Risk Non-Muscle Invasive Bladder Cancer (HR NMIBC) includes Transurethral Resection of Bladder Tumor (TURBT) followed by intravesical Bacillus Calmette–Guérin (BCG). Despite high initial response rates, over 50% of patients will recur and 20-40% are at risk for progression. Treatment of HR NMIBC is challenged by the ongoing BCG shortage, thus there exists a need for clinically effective, well-tolerated, and readily available treatment options. Cretostimogene grenadenorepvec is an oncolytic immunotherapy with a dual mechanism of action. It selectively replicates in and lyses bladder cancer cells with Retinoblastoma (Rb)-E2F pathway alterations. The subsequent release of virus- and tumor-specific antigens initiate antitumor immune activation which is further amplified by the GM-CSF transgene. Cretostimogene received Fast Track and Breakthrough Therapy Designations by the US FDA for HR BCG-Unresponsive NMIBC with CIS indication. Given the strength of these data, the CORE-008 clinical trial (NCT06567743) was developed as a Phase 2, multi-arm, multi-cohort trial to further evaluate the efficacy and safety of cretostimogene in patients with HR NMIBC. **Methods:** Eligibility criteria: pathologic confirmation of HR NMIBC, both CIS containing and papillary only, as defined by the American Urologic Association guideline. Cohort A (BCG-naive) includes patients who have not received prior BCG. Cohort B (BCG-exposed) consists of patients who have received prior BCG and recurred at the initial clinical evaluation or at a delayed timepoint. Cohort CX, recently added, will evaluate safety and High-Grade Event-Free Survival (HG-EFS) of cretostimogene in combination with intravesical gemcitabine, either concurrent (Arm 1) or sequential (Arm 2) in BCG-exposed and BCG-unresponsive patients. The combination is believed to leverage complementary mechanisms and potential immune modulating synergy to enhance outcomes. Intravesical cretostimogene will be instilled with n-dodecyl-β-D-maltoside (DDM), an excipient that enhances adenoviral delivery, for six weekly doses during the induction phase, followed by three weekly maintenance cycles quarterly through month 12, then every six months through month 36. Re-induction is permitted. The primary endpoint for CIS is Complete Response (CR) at any time and HG-EFS for papillary-only disease. Secondary endpoints will include Duration of Response, all-cause Event-Free Survival, Bladder Cancer Specific Survival, Cystectomy-Free Survival, safety, and tolerability. Exploratory outcome measures include Health-Related Quality of Life, Overall Survival, and biomarker assessments. All cohorts are open for enrollment. Cohort B has received collaborative support from the Society of Urologic Oncology-Clinical Trials Consortium (SUO-CTC). Clinical trial information: NCT06567743. Research Sponsor: CG Oncology.