A PHASE 1 STUDY OF ENADENOTUCIREV, AN ONCOLYTIC AD11/AD3 CHIMERIC GROUP B ADENOVIRUS, ADMINISTERED INTRAVENOUSLY - ANALYSIS OF DOSE EXPANSION AND REPEAT CYCLE COHORTS IN PATIENTS WITH METASTATIC COLORECTAL CANCER (MCRC)

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Aim: Enadenotucirev (EnAd) is an Ad11/Ad3 chimeric group B adenovirus, selective for killing cancer cells with little or no activity expected in normal tissues. EnAd shows a broad anti-tumour activity in preclinical models.

Methods: A 3 + 3 dose escalation design was used to determine a dose for Phase 2 (P2D) of EnAd delivered intravenously (IV) on Day (D) 1, 3 and 5. Once determined P2D was further evaluated in pts with mCRC as a single cycle (Exp cohort) or with up to 4 repeat cycles 21 D apart (RC cohort). Specific exploratory analyses conducted in the Exp cohort included metabolic response assessed by FDG-PET-CT at D 8 and 64, and tumour markers [CEA and circulating tumour cells (CTC)] at D 22 and 64. When tumour biopsies were available, replication of EnAd in tumour tissue was assessed.

Results: 34 pts were included in the Phase 1, with 6 pts treated in the RC and 9 pts in the Exp cohorts. One Exp cohort pt later switched to RC cohort. The recommended P2D is 6 x 10¹² vp over 40 min. Preliminary analysis of FDG-PET-CT scans for 9 Exp cohort pts showed increased metabolic activity in some tumour lesions at D 8 but no metabolic response at D 64. CTC analysis is ongoing. In the RC cohort, 3 cycles were delivered to all pts and 2 pts with no disease progression at week 9 received 4 cycles. Toxicities for RC were similar to single cycle administration, including mostly grade 1-2 symptoms. The most common EnAd related adverse events were flu like illness (all pts), thrombocytopenia, vomiting (3pts each), diarrhoea, asthenia, musculoskeletal pain, decreased albumin, hematuria and headache (2 pts each). No cumulative toxicity was observed. Biopsy of an inflammatory abdominal wall tumour taken on D 42 of RC administration showed delivery of EnAd in the nuclei of tumour cells using IHC staining of hexon protein.

Conclusions: An initial (D 8) increase in metabolic uptake is observed on FDG-PET-CT but no metabolic response is reported at day 64 in 9 pts with mCRC. Repeat cycle administration of EnAd is feasible and systemic delivery to cancer cells has been observed.

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