Background: VSV-IFNβ-NIS (Voyager V1; VV1) is derived from VSV, a bullet-shaped, negative-sense RNA virus with low human seroprevalence; it is engineered to replicate selectively in and kill human cancer cells. VV1 encodes hIFNβ to increase antitumoral immune response and tumor specificity, plus the thyroidal sodium iodide symporter NIS to allow imaging of virus. VV1 is synergistic with different anti-PD-(L)1 antibodies in several tumor models. Three phase 1 clinical studies of VV1 are ongoing (IV and IT). The IT trial described here includes a monotherapy and a combination arm with an anti-PD-L1.

Trial design: The study uses two 2-part, open-label, phase 1, parallel, staggered escalations to determine safety, PK and tumor/biomarker response, after a single VV1 IT dose into 1 target lesion. VV1 is given alone in the 1st arm and in combination with IV anti-PD-L1 in the 2nd arm. Each arm has 2 parts: a single ascending VV1 dose escalation all comers (alone or in combination with anti-PD-L1 until PD) followed by a dose expansion at the RP2D in patients with metastatic colorectal cancer. Virus is injected under radiological guidance. The VV1 dose is escalated from 3 x 10^6 to 3 x 10^9 TCID₅₀ (dose infecting 50% of cells in culture). The primary objective is to identify MTD/RP2D alone and in combination.

Endpoints include PK by RT-PCR for viral genomes, serum hIFNβ levels, Tc-99m SPECT/CT imaging of virus infection in injected lesions, peripheral blood immunophenotyping with 11-color flow cytometry for activation markers on T cells, T-regs, NK cells, and MDSCs, and serial biopsies to assess the tumor microenvironment. IHC is performed on tumor biopsies for CD3, CD8, CD4, FoxP3, CD68, CD45, PD-1 and PD-L1 pre- and post-treatment (~day 29) in non-injected and injected lesions. All patients must have ≥1 measurable lesion per RECIST 1.1 amenable for a single IT injection and at least one patient per cohort is required to have ≥2 measurable lesions, one for injection and one to assess abscopal effects. The study started in 2017 and monotherapy escalation should be near completion, with combination underway, by October 2018.

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