A study of REOLYSIN® in combination with Pembrolizumab and chemotherapy in patients (pts) with relapsed metastatic adenocarcinoma of the pancreas (MAP)

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Background: REOLYSIN® is an immuno-oncology-reoviral agent that induces an inflamed tumor phenotype secondary to viral infection of cancer cells. In combination with chemotherapy, it achieves 1 & 2 year-survival rates of 46% & 24% in MAP pts, respectively. Tumor analysis from pts showed reovirus protein replication, T-cell infiltration and upregulation of PD-L1. Similarly, the combination of REOLYSIN® with anti-PD-1 antibody documented survival benefit in a pre-clinical model. We hypothesized that REOLYSIN® in combination with chemo and pembrolizumab in pts with MAP would be clinically efficacious.

Methods: A phase 2 study (NCT02620423) enrolled MAP pts who progressed after first line treatment. Pts received REOLYSIN® (4.5×10^{10} $TCID_{50}$ IV, D1 & D2), plus pembrolizumab (2mg/kg IV, D8) plus either 1)5-FU (LV (200 mg/m^2 /5-FU 200 mg /m^2 IV bolus, 5-FU 1200mg/m^2 continuous IV infusion D1) or 2) gemcitabine (1000 mg/m^2 IV, D1), or 3) irinotecan (125 mg/m^2 IV, D1) q3w, until disease progression or unacceptable toxicity. The primary endpoint was safety and secondary objectives included tumor response and tumor evaluation for reovirus replication/immune analysis. We report results of safety cohort analysis.

Results: 11 pts were enrolled with REOLYSIN®, pembrolizumab and gem (n=6), 5-FU (n=3), or iri (n=2). Grade 1 or 2 TEAEs occurred in all pts: fever (64%), headache (55%), chills (46%), fatigue (46%), dehydration (27%), and nausea (27%). In one pt (gem arm), transient Gr 2 increased transaminases was reported on two occasions. Grade 3 or 4 TEAEs occurred in 8 pts (73%): abdominal pain, anemia, arthralgias, biliary obstruction, chills, DVT, diarrhea, fever, hyperglycemia, leukopenia, myalgias, nausea, neutropenia, pulmonary emboli, vomiting. One pt withdrew consent due to Gr 3 “flu-like syndrome” after the first dose of the virus. Of the 5 efficacy evaluable pts, one had PR (6 m duration) and 2 SD (lasting 126 and 221 days). Seven died secondary to disease progression. On-treatment tumor biopsy show reovirus infection of cancer cells and immune infiltrates.

Conclusion: The combination therapy showed manageable safety profiles and antitumor activity in previously treated MAP pts. Further evaluation of anti-tumor activity of REOLYSIN® and anti-PD-1 antibody ± chemotherapy combos is planned.