Purpose: PV-10 (10% rose bengal disodium for injection) is a small molecule investigational oncolytic immunotherapy that can yield high rates of complete response and durable local control in cutaneous metastatic melanoma. Ablation of injected tumors may elicit a tumor-specific T-cell response that can lead to regression of un.injected disease. A Phase 3 study to assess safety, pharmacokinetics, and preliminary efficacy of percutaneous PV-10 in patients with non-resectable hepatocellular carcinoma (HCC) or other cancer metastatic to the liver is underway (NCT00986661).

Materials and Methods: Subjects having at least one liver tumor ≥ 1 cm receive a single intraportal (IP) or intrasplenic injection of PV-10 at a designated Target Lesion at 0.25 or 0.50 mL per cm³ lesion volume. Plasma concentrations of PV-10 from 1 hour after IP injection are measured. Radiologic assessments are performed to determine response over initial 28- and longer-term 9-15 month follow-up intervals. Serum levels of potential liver injury biomarkers are measured, and adverse events recorded. Subjects with multiple tumors may receive sequential injection of additional tumors upon completion of the initial 28-day assessment.

Results: An initial 5 subjects received PV-10 in two sequential dose-escalation cohorts, with an additional 12 subjects receiving PV-10 at the higher dose level. Overall, 12 of 18 subjects had metastatic disease, including 5 with metastatic colorectal carcinoma (mCRC). Significant adverse events were observed in 4 of 18 subjects, consisting of single incidents of injection site reaction, phototoxicity reaction and lethargy that resolved without sequelae, while a single patient with an 8.9 cm HCC lesion experienced an apparent fatal thrombus. PV-10 levels in plasma decreased rapidly in a bi-exponential manner, and elevated liver enzyme levels observed immediately after injection subsided within a week. At last follow-up, 4 of 5 mCRC patients remained alive 9-73 months after receiving PV-10, including one having no evidence of disease at 73 months; the fifth, with multifocal disease, expired due to disease progression at 3 months.

Conclusions: Preliminary safety and efficacy endpoints for treatment of liver tumors were met. Toxicity was generally transient, and the investigational treatment had acceptable tolerability. The study is continuing to accrue 4 study centers in the USA in two expansion cohorts to extend assessment of safety and therapeutic activity in multiple hepatic tumor types.

Oncolytic Immunotherapy

Intraperitoneal Injection 
Lysosomal Accumulation 
Lysosomal Disruption 
Immunogenic Cell Death 
T-cell Priming and Activation 
Remote Tumor Regression

- Consistent response observed in multiple tumor models (e.g., melanoma, HCC, colon, breast, pancreatic)

Clinical Example – Subject 0006 / mCRC

Target Lesion: 2.5 cm, injected once with 4.1 mL PV-10

Byssolysis Lesions

- Clinical presentation of an oncolytic tumor response

- Rapid Primary Clearance of Extravasate

- Transient Elevation of ILs May Be Observed

Pharmacokinetics, Liver Enzymes and Long-Term Outcome

Rapid Primary Clearance of Extravasate

- Transient Elevation of ILs May Be Observed

Conclusions

INFRAHEPATIC ONCOLYTIC IMMUNOTHERAPY with PV-10

- Readily imaged drug delivery due to radiopacity of PV-10
- Immunogenic cell death and tumor-specific activation potential
- Intriguing long-term survival despite grim prognosis for metastatic colorectal cancer

This basket study is designed to demonstrate safety and relevance of PV-10 for design of future randomized studies.