**ABSTRACT**

**Background:** Intralesional rose bengal (PV-10, a sterile 50% solution in saline) can elicit selective ablation of solid tumors and acquired bystander response in experimental lesions. In phase I testing (Study PV-10-MM-02) 20 subjects with ACC Stage II-IV melanoma, a single injection of PV-10 into 1-3 lesions led to durable objective response (OR) in 24 weeks in 60% of subjects (20%/20/4% by modified RECIST and locoregional disease control (OR + PR = 50%) in 75% of subjects. Unmettled bystander lesions achieved OR in 10% of subjects, and all subjects with an OR of their regional lesions achieved disease control of their bystander lesions. PV-10 was well tolerated, with only one Grade 3 adverse event (gastrointestinal). The most common AEs were pain at the treatment site, localized inflammation/infection or pain.

**Methods:** Expanded phase 2 testing commenced in late 2007 in up to 80 subjects with measurable Stage I or II melanoma (Study PV-10-MM-04). After an initial treatment of 1-2 cutaneous, subcutaneous or nodal lesions, new or incompletely responsive lesions could be retreated at weeks 1, 2, 12 or 16, with follow-up to 52 weeks. An additional 2 to lesions, including eccrine sweat glands, remained unmet for assessment of bystander response. Seven centers in Australia and the USA enrolled subjects, with enrollment completed May 2009. A modified piping design allowed interim analysis of PV-10 on weeks 1 and 3, respectively, after treatment of the 20% and 60% subjects. The primary end point is OR of injected lesions in the interim trial population, secondary endpoints include OR of injected bystander lesions and PR.

**Results:** Preliminary data for the first 40 subjects treated is comparable with traditional local pain, with mild to moderate local pain, eczema or eczema-like symptoms. Grade 3 AEs have been seen in 4 subjects in 5 grade 4 (late onset) AEs. Overall efficacy of PV-10 is comparable with that of a phase 1 study is also comparable to that of a phase 1 study.

**Conclusion:** The efficacy and safety profile of interferon therapy with PV-10 compares favorably with available therapeutic options for the patient population.

**BACKGROUND**

**PV-10 is a sterile, non-lymphogenic solution of Rose Bengal disodium (2%) in saline: 2% is a fluorescent derivative attributed to Edwin in 1962.**

- Polyethylene glycol 1540
- I3-Heptadecane (1:2)
- Oleic acid: Sodium oleate and Monoolein

- Established Safety History
  - Metabolized, short half-life (ca. 30 minutes, excr cible)

- In-Noc-Efficient Testing PV-10 Targeted Hematic/Psoriasis
  - Mouse sarcoma Y1 sarcoma (Y1S) in companion animals
  - Protracted exposure in tumor
  - Reduced accumulation with lesion and chronic with acute necrosis
  - Minimal toxicity in normal tissue

- Selective chemokinesis of selectively tumor

- PV-10 May Elicit Bystander Effect in Non-Injected Tumors
  - Minimal tumor burden and immune response agents to host
  - Appropriate immune-mediated response
  - Positively systemic effects

- Phase 2 Clinical Testing
  - Single injection into 1-2 lesions in 20 subjects with ACC Stage II-IV melanoma
  - Intralesional dose at 50% of saline volume
  - 1-3 additional lesions untreated to assess bystander response

  - 12-18 weeks observation
  - OR by modified RECIST

- AEs generally mild to moderate—grade 3/4 locoregional

- Unmetted lesions achieved OR in 10% of subjects

- PV-10 is a 50% solution in saline

**EXAMPLE CLINICAL RESPONSE**

- Male, 70, Stage II (10a in transaxillary, axillae 1992, multiple 5a's since 2005.
  - Single treatment with 2 mL PV-10 to 10 lesions.
  - Unmetted bystander lesion.

- Male, 48, Stage III (MO in transaxillary) in 2000, 2a’s of 5m and 8m.
  - Single treatment with 3 mL PV-10 to 10 lesions.

**CONCLUSIONS**

PV-10 is well tolerated, eliciting a robust response in a majority of patients

- The safety and efficacy profile compare favorably with existing and emerging therapies.

- Likely to improve treatment of patients with partially responsive or new lesions to maximize OR and long-term outcome.

- Potentially systemic for locoregional disease control.

- Potential for systemic benefit via the bystander effect.

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**ABSTRACT**

**Phase 1 Overview**

- Study Design
  - Single injection into 1-2 lesions in 20 subjects with ACC Stage II-IV melanoma
  - Intralesional dose at 50% of saline volume
  - 1-3 additional lesions untreated to assess bystander response

- 12-18 weeks observation
  - OR by modified RECIST

- AEs generally mild to moderate—grade 3/4 locoregional

- Unmetted lesions achieved OR in 10% of subjects

**Adverse Events**

- Objective Response of Study Lesions
  - All subjects (N=40)

- Objective Response of Non-Study Lesions
  - All subjects (N=104).

- Objective Response of Bystander Lesions
  - Grouped according to Objective Response of Target Lesions
  - 9 subjects (Grade 0).