Trials in Progress: Intrallesional PV-10 vs Systemic Chemotherapy for Treatment of Locally Advanced Cutaneous Melanoma

John F. Thompson1, Sanjiv S. Agarwala2, B. Mark Smithers3, Merrick L. Rosu4, Charles R. Soccigens5, Brendan J. Coventry6, Susan J. Neuhaus7, David R. Minor8, and Eric A. Wachter9

1Melanoma Institute Australia and the University of Sydney, Sydney, NSW 2000, 2.Duke University Hospital and Health Network and Temple University, Philadelphia, PA, 3.Queensland Melanoma Project, Prince Alfred Hospital, University of Queensland, Woolloongabba, QLD 4020, 4.M.D. Anderson Cancer Center, Houston, TX, USA; 5.University of Louisville, Louisville, KY 40202, USA; 6.University of Adelaide and Hope Adelina Hospital, Adelaide, SA 5000, USA; 7.California Pacific Medical Center, San Francisco, CA USA; and 8.Frisonio Biopharmaceuticals, Inc., Knoxville, TN, USA

Abstract

Study PV-10-MM-31 is an international multicenter, open-label, pivotal randomized controlled trial (RCT) of single-agent intrallesional (IL) PV-10 versus systemic chemotherapy with dacarbazine (DTIC) or temozolomide (TMZ) in patients with locally advanced cutaneous melanoma (ClinicalTrials.gov identifier NCT02288897). The primary endpoint of progression free survival (PFS) will be assessed according to RECIST 1.1 (based on blinded independent review of study photography and radiology data by an Independent Review Committee (IRC) to compare outcome in the study arms). A total of 225 eligible subjects are being randomized in a 2:1 ratio to the two treatment arms. Comprehensive disease assessments, including review of clinical photography of lesions and radiologic assessment for the presence of visceral and nodal metastases, are performed at screening and every 12 weeks thereafter, and at final follow-up by CT imaging. Clinical assessment of progression status will be performed at 28-day intervals during the treatment phase of the study. Patients must have locally advanced cutaneous melanoma (i.e., Stage IIIb or Stage IIC recurrent, satellite or in-transit cutaneous or subcutaneous melanoma) with at least 1 Target Lesion with longest diameter >10 mm; no lesion >30 mm in longest diameter; and no more than 20 total lesions at enrollment. Patients must have failed at least one immune checkpoint inhibitor or not otherwise be candidates for immune checkpoint inhibitors and must be BRAF wild-type.

Phase 2 Experience

Primary Ablation and Secondary Tumor-Specific Immune Response

- Intrallesional Injection
- Lysosomal Accumulation
- Lysosomal Disruption
- Autotytic Cell Death
- T-cell Activation
- Bystander Tumor Regression

Phase 3 Study in Locally Advanced Cutaneous Melanoma

- PV-10 vs DTIC or TMZ in 225 patients randomized 2:1
- Cross-over on documented progression
- Interim assessment

Patients

- Cutaneous and subcutaneous disease (Stage IIIb or IIC) with no active nodal disease
- Failed or not candidates for at least one immune checkpoint inhibitor
- BRAF wild-type
- Cutaneous only target disease [critical for photodocumentation and IRC review]
- All disease must be injectable on Day 1
- No lesion >3 cm, no more than 20 lesions at baseline
- 1-5 cutaneous target lesions at least 1 cm in longest diameter

Why Address Locoregional Disease with a Focal Treatment?

- Stepwise Progression (Locational Pattern)
- Shotgun Progression (Metastatic Pattern)

Demographics and Response Data for Recent Melanoma Immunotherapy Studies

Phase 3 Design

- Lesions Progression
- Interim Analysis

Systemic Chemotherapy

- Treatment Phase

- Response Follow-up Phase

- Primary EP

- Secondary

- Exploratory

- Change in Domain Scores on Skinex-16

- Change in Patient Reported Pain and Pain Medication Use
- Change in Investigator Assessed Lesion Blistering, Ulceration and Infection (CTCAE)

- Lesions

- Progression Free Survival by RECIST 1.1

- Clinical Assessment (CLIN)

- SD or PR

- Termination Visit and Survival Follow-up

- Randomized

- Clinical (CLIN)

- Follow-up (up to PO)

- COMP

- PO