Efficacy of Single Administration of Tumor Infiltrating Lymphocytes (TIL) in Heavily Pre-Treated Metastatic Melanoma Patients Following Checkpoint Therapy

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ABSTRACT

Adoptive cell therapy (ACT) utilizing tumor infiltrating lymphocytes (TIL) has shown consistent overall response rates of >50% in metastatic melanoma patients at the National Cancer Institute (NCI) and other institutions globally.

Lion Biotechnologies aims to optimize and standardize the manufacturing of TIL as a central GMP facility to provide TIL therapy as a potentially curative option for patients with high tumor burden.

The objectives of the C144-01 clinical study are to assess the safety and efficacy of autologous TIL (LN 144) for the treatment of patients with metastatic melanoma. The study includes three cohorts evaluating two manufacturing processes for LN-144:

- Cohort 1: receiving fresh TIL, non-cryopreserved LN-144 product
- Cohort 2: receiving TIL manufactured through a more streamlined and rapid (∼3 week) process yielding a cryopreserved LN-144 product
- Cohort 3: all other patients (Cohort 1 or Cohort 2 patients)

This analysis presents primary data from the first 14 patients enrolled into Cohort 1 (non-cryopreserved LN-144 product) of this ongoing multicenter Phase 2 study of TIL for patients with metastatic melanoma.

RESULTS

- Retreatment with LN 144 Therapy
- Yield 10

METHODS

- Date of cut-off: 24 April 2017
- All patients included in analyses were treated under Cohort 1 (non-cryopreserved LN-144 product)
- Safety Set - 14 patients as of data cut-off, who received the NMA-LD non-mitigating pre-conditioning, lymphodepletion, cytopheraphic: 60 mg/kg IV 2 doses and fludarabine 25 mg/m2 (5 doses) to eliminate potentially suppressive tumor microenvironment
- Maximum engagement and potency of TIL therapy

TEAM STUDY DESIGN

Phase 2, Multicenter, 3-Cohort Study to Assess the Safety and Efficacy of Autologous Tumor Infiltrating Lymphocytes (LN-144) for Treatment of Patients with Metastatic Melanoma

Cohort 1: Non-Cryopreserved Therapy
- Cohort 2: Cryopreserved LN-144 product
- Cohort 3: Retreatment with LN-144 for patients without response or who progress after initial response

Figure 1. TIL Therapy Process

SHAPING THE FUTURE OF CANCER THERAPY

Figure 2: Efficacy of LN 144 Product

Figure 3: Time to Best Response and Duration

Figure 4: Percent Change in Sum of Diameters

Figure 5. CT Scan for Patient with CR

CONCLUSIONS

- This is the first time a company has manufactured TIL (LN-144) as central GMP facilities and treated patients in a multicenter clinical setting.
- Initial results indicate clinically-meaningful outcomes as assessed both by ORR and DoR in heavily pre-massed patients, all with prior PD-L1 and -100% with prior anti-CTLA-4 checkpoint inhibitors, including at least one durable complete response.
- Responses were observed in patients regardless of their BRAF mutational status.
- Initial clinical responses were rapid in the majority of patients with preliminary reduction in tumors observed at the first response assessment.
- Cultur 3 in this study will allow resection with second LN-144 infusion.
- An upcoming protocol amendment to this study will increase the number of patients with unresectable or metastatic melanoma who have progressed after immune checkpoint inhibitor therapy (e.g. anti-PD-L1) and if BRAF mutation-positive, after BRAF targeted therapy.