Epi-R™ Technology Produces a Polyclonal TIL Product (LYL845) With a Greater Expansion Success Rate Across Hot and Cold Tumors, Improved Product Phenotype, and Reduced Impact of TCR Diversity

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Background

- Adoptive cell therapy (ACT) using tumor-infiltrating lymphocyte (TIL) therapy is a promising method for cancer treatment.
- TILs that are highly enriched with tumor-reactive T-cell clones have been shown to mediate treatment response in advanced cancer.4

Key Findings

- When compared with a control TIL product, LYL845 demonstrated successful TIL expansion with enrichment of CD8+ T-cells.
- Higher proportion of stem-like CD8+ T-cells and better expansion in products from samples with prior ICB.

Methods

- Epi-R® TIL Manufacturing Methodology
- LYL845 was produced at research scale using a total of 17 samples from immunologically hot (melanoma and lung) and cold (colorectal) tumors and was compared with control TIL products generated without Epi-R®.
- LYL845 was generated from five tumor samples, produced at large scale, and compared with corresponding research-scale products.

Results

- LYL845 Demonstrated Successful TIL Expansion Favoring Enrichment of CD8+ T-cells compared with the control product using a standard expansion protocol. Demonstration of research scale Epi-R TIL expansion protocol. The Epi-R TIL product (LYL845) has a higher proportion of stem-like CD8+ T-cells and better expansion in products from samples with prior ICB.

- These characteristics are maintained in large-scale production.

- **LYL845 Demonstrated Higher Frequency of Co-Stimulatory Markers Associated With Success and Steady Expansion Compared With Stem-like Cells**

- LYL845 had a higher proportion of stem-like CD8+ T-cells, compared with the control product.

- LYL845 and the control product were analyzed for the presence of CD8+ T cells in TIL products. The key attributes in research-scale products were reproduced in LYL845 large-scale products.

- **LYL845 Preserved High Clonal Diversity Relative to Source Tumor**

- Maintaining the polytymically of source TIL during the TIL expansion and production is correlated with effective tumor recognition and killing.

- LYL845 was enriched for genes associated with stem-like cells and enhanced metabolic fitness like TCF7, EM, and CD127, and showed a reduction in exhaustion-associated genes when compared with the control TIL product.

- **LYL845 From ICB-refractory Metastatic Melanoma Enriched For CD8+ T-cells With a Stem-like Phenotype Compared With ICB-refractory Control TIL Product**

- LYL845 produced using the Epi-R Protocol is an investigational autologous TIL product with a greater proportion of CD8+ stem-like T-cells, better metabolic fitness, and preserved polytymality when compared with a standard expansion protocol.

- LYL845 maintained stem-like CD8+ T-cell enrichment when manufactured from ICB-refractory melanoma.

- Results from LYL845 research and large-scale productions demonstrate that Epi-R technology is capable of enriching stem-like, metabolically fit TILs.

- These data support further development of LYL845, and an Investigational New Drug submission for LYL845 was accepted by the Food and Drug Administration in October 2022.

Conclusion

- LYL845, produced using the Epi-R Protocol, is an investigational autologous TIL product with a greater proportion of CD8+ stem-like T-cells, better metabolic fitness, and preserved polytymality when compared with a standard expansion protocol.

- LYL845 maintained stem-like CD8+ T-cell enrichment when manufactured from ICB-refractory melanoma.

- Results from LYL845 research and large-scale productions demonstrate that Epi-R technology is capable of enriching stem-like, metabolically fit TILs.

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