Phase 1 Trial of LYL845, an Autologous Tumor-Infiltrating Lymphocyte (TIL) Therapy Enhanced With Epigenetic Reprogramming for the Treatment of Advanced Solid Tumors

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Figure 3: Dose-escalation and dose-expansion study design

Figure 4: Timeline of screening, treatment, and disease/safety assessments

Figure 5: LYL845-101 Design: NCT05573035

Figure 6: Figure 2: Epi-R produces products with a greater proportion of stem-like cells and a lower proportion of differentiated cells

LYL845-101 Design: NCT05573035

- Part A (dose escalation) will evaluate two planned dose level ranges of LYL845 using the modified toxicity prophylaxis interval-2, with a 28-day dose-escalating toxic period. Part B (dose expansion) will treat 15 – 30 patients in each disease cohort at the RP2DR determined in Part A (Figure 3)

- After TIL tissue collection and LYL845 manufacturing, enrolled patients receive lymphodepleting chemotherapy followed by LYL845 infusion at the assigned dose level. High-dose IL-2 is then administered every 8 hours for up to 6 doses as tolerated (Figure 4)

- Patient assessment and/or biopsy included before lymphodepletion, at days 1, 2, 3, 7, 14, and 28 post-LYL845 infusion, and at 60 days and 120 days after LYL845 treatment

LYL845 demonstrates enhanced T-cell function as indicated by increased activation and cytotoxicity

• LYL845-101 is an open-label, multi-center, dose-escalation study with expansion cohorts designed to evaluate the safety and antitumor activity of LYL845 in participants with R/R metastatic, locally advanced or unresectable melanoma, NSCLC, or CRC (Figure 3)

- Primary objectives
  - Evaluate safety and tolerability
  - Determine the RP2DR

- Secondary objectives
  - Evaluate antitumor activity

- Key Inclusion Criteria
  - Confirmed diagnosis of R/R metastatic or locally advanced or unresectable melanoma, NSCLC, or CRC
  - Measurable disease that includes a target lesion (≥10 mm) or lymph node (≥15 mm), plus one additional lesion ≤1.5 cm is not safely resectable
  - Two lesions may be combined to achieve this volume

- Subject Health
  - ≥18 years of age at time of informed consent
  - ECOG PS of 0 – 1
  - Adequate organ and marrow function per protocol

- Key Exclusion Criteria
  - Active CNV or retinopathy disease
  - Prior Treatment
    - No prior solid organ transplant or adoptive cell therapy
  - Subject Health
    - Uncontrolled pleural or pericardial effusion or ascites
    - HIV or active acute or chronic HBV or HCV
    - Other malignancy within 3 years prior to screening or TIL tissue collection surgery
    - Significant cardiovascular disease
    - Required chronic anticoagulation (stable regimen may be allowed)
    - Pregnant or lactating women

Participating Sites

- UCLA Medical Center, Los Angeles, CA
- Yale School of Medicine, Smilow Cancer Hospital, New Haven, CT
- Georgetown University, Washington, DC
- Massachusetts General Hospital, Boston, MA
- Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
- Hackensack Meridian Health, Hackensack, NJ
- Duke University Medical Center, Durham, NC
- The Ohio State University Medical Center, Columbus, OH
- Oregon Health Sciences University, Portland, OR
- Allegheny General Hospital, Pittsburgh, PA
- Huntsman Cancer Institute, Salt Lake City, UT
- Fred Hutchinson Cancer Center, Seattle, WA

Abbreviations
- GD: dose-determination
- CNS: central nervous system
- CRC: colorectal cancer
- cy: cyclophosphamide
- d: days
- ECOS PS: Eastern Cooperative Oncology Group performance status
- FU: follow up
- FL: fluorouracil
- HBV: hepatitis B virus
- HCV: hepatitis C virus
- IM: intramuscularly
- IV: intravenously
- IL-2: interleukin-2
- ICF: informed consent form
- IV: intravenous
- m: months
- n: number of patients
- NSCLC: non-small cell lung cancer
- RP2DR: recommended phase 2 dose range
- RPDR: recommended phase 2 dose range
- R/R: relapsed/refractory
- TIL: tumor-infiltrating lymphocyte

References

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