A Basket Trial Evaluating the Safety and Efficacy of Lerapolturev Alone and Lerapolturev in Combination with Anti-PD-1/L1 Checkpoint Inhibitors in Patients with Bladder Cancer

istari ONCOLOGY

LUMINOS-103

Trial Information

Participating Study Centers

Duke University Medical Center, Duke Cancer Center, Durham, NC
New York University Langone Health, New York, NY
University of North Carolina Lineberger Cancer Center, Chapel Hill, NC
University of California San Francisco Medical Center, San Francisco, CA
Carolina Urologic Research Center, Myrtle Beach, SC
Henry Ford Health System, Detroit, MI

Trial Registration Number: NCT04690699
Start Date: June 2021
Estimated Completion Date: June 2025

Objectives

Primary objectives[a]:
- Evaluate safety and tolerability
- Evaluate anti-tumor response (phase 2)

Secondary objectives[a]:
- Evaluate anti-tumor activity
- Assess viral shedding

[a]*Unless specified, all objectives are for both phase 1 and 2 and cohorts A and B.*

Key Eligibility Criteria

Cohort A[a]

- Refused or ineligible for cisplatin-based therapy
- Stage T2-T4a, N0, M0 by MRI or CT urogram
- No prior systemic therapy for MIBC

Cohort B[b]

- Unresectable locally advanced or metastatic bladder cancer
  - T4b, any N
  - Any T, N 2-3
  - Any T, any N, M1
- ≤1 prior systemic therapy in the unresectable/ metastatic setting

Both Cohorts

- Histologically/cytologically confirmed urothelial carcinoma from lower urinary tract, and FFPE tumor specimen within 6 months of first lerapolturev dose
  - Pure non-urothelial histologies are excluded
- CrCl ≥45 mL/min (GFR is allowed)
- No antiplatelet or anticoagulant treatment within ±3 days of lerapolturev dose

[a]*Cisplatin-ineligible patients with resectable MIBC treated in the neoadjuvant setting;* [b]*Patients with unresectable locally advanced/metastatic bladder cancer treated in the first- or second-line setting.*

Bladder Cancer Study Design

LUMINOS-103 (Bladder Cancer)

Phase 1[a]

Lerapolturev[c]
Cohort A[d]
Cisplatin-ineligible patients with resectable MIBC

Safety Data Review
DSMC

Phase 2[b]

Cohort A[d] Lerapolturev[c] + Pembrolizumab[e]
Cisplatin-ineligible patients with resectable MIBC

Cohort B[d] Lerapolturev[c] + Pembrolizumab[e,f]
Patients with unresectable locally advanced/metastatic bladder cancer

[a]*Only enrolls patients from Cohort A;* [b]*Enrolls patients from Cohorts A and B in parallel; includes safety reviews by the DSMC after the first 6 and 12 patients are enrolled (either cohort) and have completed ≥21 days of combination therapy;* [c]*Patients receive up to 3 cycles of intratumoral administration of 2x10^9 TCID$_{50}$/injection of lerapolturev via cystoscopy;* [d]*Staggered enrollment of the first three patients by 21 days per patient;* [e]*Patients receive pembrolizumab IV 200 mg Q3W;* [f]*Continued pembrolizumab monotherapy is allowed after the third cycle; pembrolizumab 400 mg IV Q6W allowed after the sixth cycle.*

Study Endpoints[a,b]

Primary endpoints:
- Surgical complications (Cohort A)
- Proportion and timing of patients undergoing resection (Cohort A)
- Proportion of patients with pCR at cystectomy (phase 2, Cohort A)

Secondary endpoints:
- RFS; clinical to pathological TNM downstaging (Cohort A); proportion of patients with pCR at cystectomy (phase 1, Cohort A)
- Urine PV titers (Cohorts A and B)

[a]*In addition to those described in the master protocol;* [b]*Unless specified, all endpoints are for both phase 1 and 2.*

Schedule of Assessments

Screening Period: Patients receive IPOL® anti-PV booster vaccination

Cohort A[a]

Day 1:	Lerapolturev[b] intratumoral injection by cystoscopy (phase 1 only)
Day 1:	Lerapolturev[b] + pembrolizumab IV 200 mg Q3W (phase 2 only)
Week 9:	Cystectomy
Week 12:	End of treatment
Month 24:	End of study

Cohort B[a]

Day 1:	Lerapolturev[b] + pembrolizumab IV 200 mg Q3W
Day 14:	Tumor biopsy
Cycle 4 to 6:	Pembrolizumab IV 200 mg monotherapy
Cycle ≥6:	Pembrolizumab IV 200 mg Q3W or 400 mg Q6W
Month 24:	End of study

[a]*Continuous response endpoint assessments throughout study duration;* [b]*Lerapolturev intratumoral injection by cystoscopy x 3 cycles (21-day cycles).*

CNS, central nervous system; CrCl, creatinine clearance; CT, computed tomography; DSMC, data safety monitoring committee; FFPE, formalin-fixed paraffin-embedded; GFR, glomerular filtration rate; IPOL®, poliovirus vaccine inactivated IV, intravenous; MIBC, muscle-invasive bladder cancer; MRI, magnetic resonance imaging; pCR, pathologic complete response; PV, poliovirus; Q3W, every 3 weeks; Q6W, every 6 weeks; RFS, relapse-free survival; TCID, tissue culture infectious dose; TNM, Tumor-Nodes-Metastasis Classification of Malignant Tumors.

For more information, email LUMINOS-103@istarioncology.com **or visit** https://clinicaltrials.gov/ct2/show/NCT04690699.