PVSRIPO With or Without Immune Checkpoint Blockade in Unresectable Anti-PD-1 Refractory Melanoma

LUMINOS-102

Authors

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Trial registration number: NCT04577807

Start date: November 17, 2020
Estimated completion date: May 2023

Objectives and Rationale

Primary objectives, to evaluate:
- Anti-tumor activity
- Safety and tolerability
- Effect on TME (injected/noninjected lesions)

Secondary objective:
- Evaluate survival and disease control outcomes

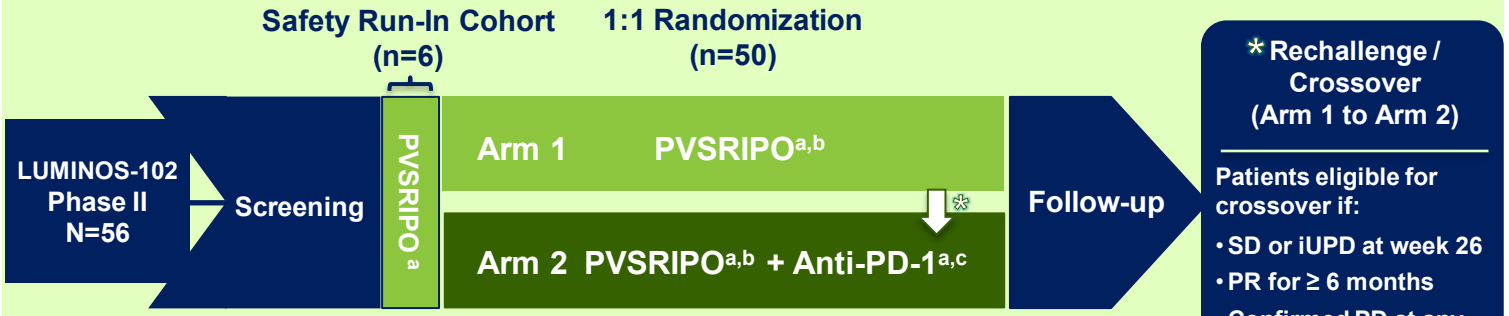
Key Eligibility Criteria

≥18 Age ≥18 years

ECOG PS 0 or 1

- Biopsy-confirmed, unresectable cutaneous, mucosal, or acral melanoma with confirmed disease progression (per iRECIST) after ≥6 weeks of approved anti-PD-1/L1 therapy
  - If known BRAF mutation, either failed or refused to receive BRAF-targeted therapy
  - Stable CNS metastases allowed
- ≥2 measurable melanoma lesions, with at least one lesion amenable to injection/biopsy (visible/palpable cutaneous, subcutaneous, or nodal lesion)
- Vaccination against PV and booster immunization within 1-6 weeks of PVSRIPO administration
- Within 4 weeks of PVSRIPO therapy, no previous systemic anti-cancer or potent immunosuppressive therapy or live vaccines
  - Exception: Anti-PD-1/L1 therapy allowed ≤4 weeks

Study Design



[a] Blood and tissue from injected/noninjected lesions & draining lymph nodes collected throughout study for translational analyses; [b] Dose up to $6x10^8$ $TCID_{50}$ into up to 6 lesions Q3W or Q4W; [c] IV pembrolizumab Q3W or Q6W or nivolumab Q2W or Q4W at PI discretion.

Study Endpoints

Primary endpoints:
- ORR per RECIST v1.1
- Safety and tolerability
- Changes in CD8+ TILs and PD-L1 expression

Secondary endpoints:
- OS and PFS, DOR, DCR, DCR-6mo, DRR per RECIST v1.1

Exploratory endpoints:
- Subgroup analyses of OS and PFS and anti-tumor response per iRECIST
- Identification/evaluation of biomarkers associated with MOA or response

Schedule of Events & Assessments

Day 1:	First PVSRIPO injection (single-lesion)
Day 10+:	-PVSRIPO injections (multiple-lesions; Q3-4W)
	-Anti-PD-1 infusion (Arm 2; Q2-6W)
Week 26:	Primary/secondary endpoint assessment
Month 24:	End of study

Interim Analysis

- To occur 3 months post-randomization of the first 20 patients
- Arm 1 will close if rate of cPD in Arm 1 ≥ 40% more than Arm 2 per DSMC recommendation; in this case, all ongoing patients in Arm 1 can crossover to Arm 2

CNS, central nervous system; cPD, confirmed PD; DCR, disease control rate; DCR-6mo, disease control rate-6 months; DOR, duration of response; DRR, durable response rate; DSMC, data and safety monitoring committee; ECOG, Eastern Cooperative Oncology Group; IPOL®, poliovirus vaccine inactivated; iRECIST, immune response evaluation criteria in solid tumors; iUPD, immune unconfirmed PD per iRECIST; IV, intravenous; MOA, mechanism of action; ORR, overall response rate; OS, overall survival; PD, progressive disease; PD-1, program death receptor-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PI, project investigator; PR, partial response; PS, performance status; PV, poliovirus; QXW, every X weeks; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TIL, tumor infiltrating lymphocytes; TME, tumor microenvironment

For more info. visit: Istarioncology.com, clinicaltrials.gov/ct2/show/NCT04577807 or Email: InfoLUMINOS-102@istarioncology.com