TRIAL IN PROGRESS

AXIOM

Stereotactic Body Radiotherapy plus Immunotherapy vs Immunotherapy Alone in 1–5 Extracranial Melanoma Oligometastases

Angela M. Hong[123*] · Tim Wang[124] · Matteo S. Carlino[15] · Serigne N. Lo[128] · Alexander M. Menzies[1267] · Inês Pires da Silva[128] · Georgina V. Long[12678]

1 Melanoma Institute Australia · 2 University of Sydney · 3 GenesisCare · 4,5 Westmead Hospital · 6 Royal North Shore Hospital · 7 Mater Hospital · 8 Charles Perkins Centre, University of Sydney

BACKGROUND

Immune checkpoint inhibitor therapy has transformed outcomes in metastatic melanoma, but there remains scope to further improve response rates and survival. Radiotherapy may convert immunologically "cold" tumours "warm" by increasing immunostimulatory cytokine production, recruiting antigen-presenting and immune effector cells, and upregulating antigen presentation and costimulatory signals.

SABR-COMET trial: 8-yr OS 27.2% vs 13.6%, SBRT vs standard of care (HR 0.50, 95% CI 0.30–0.84, P=0.008)

HYPOTHESIS

Upfront concurrent SBRT with immunotherapy is safe and prolongs survival through enhanced anti-tumour immunity, compared with immunotherapy alone.

OBJECTIVES

Primary objective: examine the efficacy of upfront SBRT with concurrent immunotherapy in patients with 1–5 extracranial melanoma oligometastases.

Secondary objectives: safety of upfront SBRT with immunotherapy; health-related quality of life (HR-QoL); translational investigation.

ENDPOINTS

Primary endpoint

- Overall survival (time from randomisation to death, any cause)

Secondary endpoints

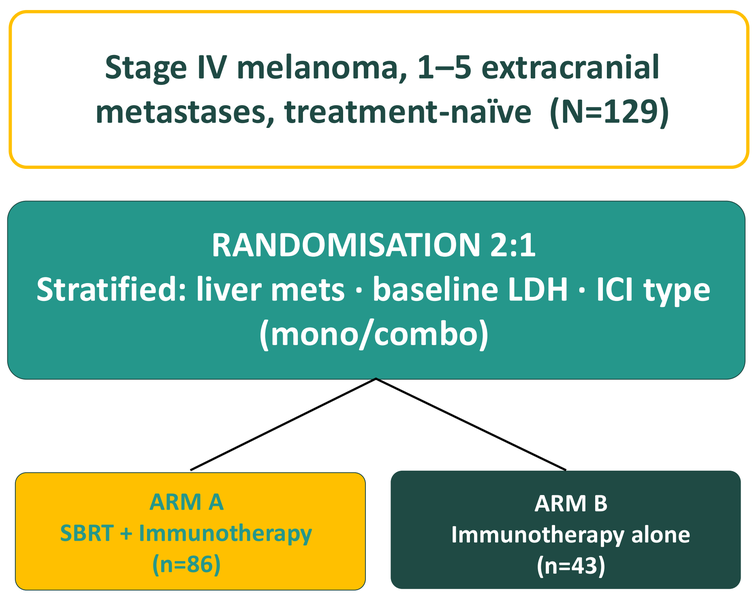
- Overall & new-disease progression-free survival (RECIST 1.1)
- Overall response rate; local control of baseline oligometastases
- Safety & tolerability (CTCAE v5.0)
- Salvage radiotherapy requirement in the ICI-alone arm
- Quality of life (EORTC QLQ-C30, EQ-5D-5L)

Exploratory / translational

- Predictive & prognostic biomarkers of response, resistance and toxicity from tissue, blood and stool

TRIAL DESIGN

Phase II, multicentre, open-label, two-arm parallel-group, randomised, non-comparative trial. Because ICI efficacy in this population is already established, the trial is powered as a single-arm design with a contemporary control arm to confirm historical assumptions. There is no formal between-arm comparison.



KEY ELIGIBILITY

Inclusion

- Age ≥18y; life expectancy >6 months; ECOG 0–2
- First presentation AJCC Stage IV, 1–5 extracranial oligometastases on CT + whole-body PET-CT
- ≥1 RECIST 1.1-measurable lesion; no cerebral metastases
- All metastases treatable with SBRT (BED ≥48 Gy_{10})

Exclusion

- Ocular or mucosal melanoma
- Definite/immediate indication for radiotherapy (e.g. cord compression)
- Inability to treat all disease sites with SBRT
- Prior systemic therapy for Stage IV melanoma

INTERVENTIONS

Arm A: SBRT (minimum BED 48 Gy_{10}, ≥30 Gy/5# to all disease sites) between ICI cycles 1–3, per UK 2022 OAR consensus constraints, plus standard of care immunotherapy

Arm B: standard of care immunotherapy

Immunotherapy options (both arms): anti-PD-1 monotherapy (nivolumab, pembrolizumab), or anti-PD-1 + anti-CTLA-4 (ipilimumab), or anti-PD-1 + anti-LAG-3 (relatlimab), per clinician choice.

STATISTICAL DESIGN

- N=129 (Arm A 86, Arm B 43); >80% power, 5% two-sided α, to detect 70% 3-yr OS in Arm A (15% absolute mortality reduction from historical 45%→30%)
- 6-year study; 3-year accrual; ≈46 deaths expected (26/20) after ≥2 years follow-up
- One interim analysis at 23 deaths (50%); independent DSMC reviews futility, Grade 4 CTCAE toxicity, recruitment, and emerging therapies

TRIAL STATUS

Recruiting across 5 sites in Australia and Canada

- Melanoma Institute Australia
- Westmead Hospital
- The Alfred Hospital
- Princess Alexandra Hospital
- Princess Maragret Hospital, Canada

CONCLUSION

AXIOM will provide the first prospective randomised data on adding SBRT to standard of care immunotherapy in extracranial oligometastatic melanoma.

TRIAL REGISTRATION
ClinicalTrials.gov: NCT06767306

Contact
Angela M. Hong
angela.hong@sydney.edu.au

FUNDING

Trial funding through the Varian Research Grants Program, supplied by Varian USA to GenesisCare Australia.