

FULL PROTOCOL TITLE

PALEO: Phase II clinical trial of chemoradioimmunotherapy for the ALleviation of oEsOphageal cancer complications

STUDY CHAIRS

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LINK TO STUDY

<https://gicancer.org.au/clinical-trial/paleo/>

TRIAL IDENTIFIER

ACTRN12619001371189

COORDINATING CENTRE

Calvary Mater Newcastle

FUNDING SOURCES

GI Cancer Institute; Varian Medical Systems;
Calvary Mater Newcastle; Hunter Medical
Research Institute

PRESENTER

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Flinders Medical Centre

FINANCIAL DISCLOSURE

Merck

AIM/S

The PALEO clinical trial enrolls patients with oligometastatic oesophageal cancer and dysphagia. The aim is to determine the activity of durvalumab given concurrently with chemoradiotherapy to the primary oesophageal cancer and stereotactic radiotherapy to a single metastasis.

BACKGROUND

The typical presentation of oesophageal cancer is with dysphagia. Our existing data shows that a 2-week chemoradiotherapy protocol (30Gy/10# with concurrent carboplatin and paclitaxel) is well tolerated and provides rapid dysphagia relief. We hypothesise that the radiotherapy interventions given in PALEO will be immune priming, and hence that multimodality treatment including checkpoint inhibition will enhance disease control at all tumour sites.

STUDY DESIGN

This is a multicentre, single arm phase II clinical trial. All participants receive 2 weeks of therapy with concurrent hypofractionated radiotherapy (30Gy/10#) to their primary tumour, weekly carboplatin AUC2, weekly paclitaxel 50mg/m² and q4weekly durvalumab, followed by durvalumab monotherapy continuing until disease progression or 24 months of therapy. A single metastasis is treated with stereotactic radiotherapy (24Gy/3#) 4 weeks after the completion of the chemoradiotherapy to the primary tumour.

ELIGIBILITY CRITERIA

KEY INCLUSION CRITERIA

- Biopsy proven adenocarcinoma or squamous cell carcinoma of the oesophagus or gastro-oesophageal junction
- Dysphagia (Mellow score >0)
- Oligometastatic (1-5 metastases on FDG-PET scan) or locoregionally advanced, unresectable disease
- ECOG performance status 0 – 2

KEY EXCLUSION CRITERIA

- Bulky or organ-threatening metastatic disease requiring upfront higher dose chemotherapy in the judgement of the treating clinician
- Known tumour HER2 positivity (IHC 2+ or more and HER2 gene amplification on in situ hybridisation)
- Contra-indications to carboplatin, paclitaxel or durvalumab
- Oesophageal stent in situ
- Previous systemic therapy for oesophageal or GOJ carcinoma
- Previous thoracic radiotherapy

STUDY UPDATE

PALEO is open at:

- Calvary Mater Newcastle
- Flinders Medical Centre, Adelaide
- Sir Charles Gairdner Hospital, Perth
- Peter MacCallum Cancer Centre, Melbourne
- Royal Brisbane Women's Hospital
- St Vincent's Hospital, Melbourne
- Auckland City Hospital, New Zealand.

Current recruitment is 9 participants of a planned 54 subjects by July 2025. The main barrier to recruitment has been trial conduct at only one site until 2023, with all other sites activating between February – July 2023. Recruitment is anticipated to increase in Q3-4 2023 and into 2024.

Participation in the PALEO trial is open to patients of all ethnic and cultural backgrounds. The use of a teletrial model for administration of durvalumab at satellite sites is under consideration, but may be limited by philanthropic funding constraints.

PUBLICATIONS

Day F, Sridharan S, Lynam J, Gedye C, Johnson C, Fraser A et al. Chemoradiotherapy with concurrent durvalumab for the palliative treatment of oligometastatic oesophageal and gastroesophageal carcinoma with dysphagia: A single arm phase II clinical trial (PALEO, sponsored by the Australasian Gastro-Intestinal Trials Group). *BMC Cancer*, ePub 17 December 2022

Day F, Sridharan S, Michael M, Christophersen L, Moore M, Eastgate M, et al. Chemoradiotherapy with concurrent durvalumab for the palliative treatment of oligometastatic esophageal and gastroesophageal carcinoma with dysphagia: A single arm phase 2 clinical trial, PALEO. *J Clin Oncol* 41, no. 16_suppl (June 01, 2023) TPS4172

Fiona Day, Swetha Sridharan, Michael Michael, Amitesh Roy, Louise Christophersen, Trevor Leong, Melissa Moore, Melissa Eastgate, Colin Tang, Stephen Thompson, Angela Mweempwa, Christopher Oldmeadow, Allison Fraser, Jarad Martin. "Chemoradiotherapy with concurrent durvalumab for the palliative treatment of oligometastatic esophageal and gastroesophageal carcinoma with dysphagia: A single arm phase 2 clinical trial, PALEO." Trial in Progress Poster Presentation at 2023 ASCO Annual Meeting.

TRANSLATIONAL RESEARCH

The study collects FFPE tumour tissue and serial blood samples at baseline, weeks 4, 9, 13, confirmed disease progression and in the event of any significant immune-related adverse event. Translational research in PALEO includes the measurement of T cell receptor diversity pre- and post-radiotherapy to the primary tumour and SBRT to a metastasis, for comparison between treatment responders and non-responders. Gene expression and proteomic analyses of blood samples will also be performed to determine changes in circulating biomarkers associated with tumour response to radiotherapy with checkpoint inhibition.

STUDY SCHEMA

Eligibility

Oligometastatic GOJ or oesophageal carcinoma
Dysphagia
ECOG 0-2
No prior therapy

Primary End Point

PFS rate at 6 months

Secondary End Points

Dysphagia relief
Nutritional status change
QOL
Response rate
Toxicity
Overall survival

2 weeks

4 weeks

Hypofractionated RT 30Gy/10#
to primary tumour

Stereotactic radiotherapy 24Gy/3#
to a single metastasis

Weekly in weeks 1 & 2: Carboplatin
AUC2Paclitaxel 50mg/m²

24 months

Durvalumab immunotherapy from week 1, continuing until disease progression, prohibitive toxicity or 24 months

N = 54 patients

Estimated study duration of 3 years plus 1 year additional minimum follow up