FULL PROTOCOL TITLE

Neo-CREATE: Neoadjuvant immune-chemo-radiotherapy in operable oesophageal and gastro-oesophageal junction adenocarcinoma cancers with carboplatin paclitaxel radiotherapy and avelumab

STUDY CHAIRS

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LINK TO STUDY

https://gicancer.org.au/clinical-trial/neo-create/

TRIAL IDENTIFIER

ACTRN12619000288123

COORDINATING CENTRE

Flinders Centre For Innovation In Cancer, Flinders Medical Centre

FUNDING SOURCES

Merck

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FINANCIAL DISCLOSURE

None to declare.

AIM/S

To evaluate preliminary efficacy in terms of pathological complete response (pCR), major histological response (MHR) with neoadjuvant chemo-radiotherapy plus avelumab (CRT-A) in operable oesophagus/ GOJ adenocarcinoma patients.

BACKGROUND

Oesophago-gastric (OG) cancers are a significant global health burden, representing the 8th most commonly diagnosed cancer. The incidence rates of distal oesophageal and gastro-oesophageal junction cancers are rising in western countries.

The purpose of this study is to assess the safety of adding avelumab (anti-PDL1) to chemo-radiation using two standard chemotherapy drugs, carboplatin, and paclitaxel (CROSS protocol), before surgery in patients with cancers of the oesophagus or gastro-oesophageal junction.

STUDY DESIGN

Neo-CREATE is an investigator initiated single arm, multi-centre phase II trial evaluating the safety and preliminary efficacy of avelumab, an anti-PD-L1 monoclonal antibody, with neoadjuvant carboplatin-paclitaxel CRT for patients with operable OG adenocarcinoma. Primary objective of Neo-CREATE is pCR rate and secondary objectives include safety, PFS, OS, QoL and correlative biomarker analysis. The recruitment target is 47 patients over 3-year period. All patients will be analyzed as per ITT regardless of whether they undergo surgery or not. The trial has a run-in phase of 10 patients to evaluate feasibility and safety and a planned futility analysis after 15 patients have undergone surgery. The trial will be stopped for further recruitment if › 2 of the 1st ten patients cannot undergo surgery or have significant perioperative complications due to avelumab-related toxicities.

Patients will receive 5 weeks of CRT plus intravenous avelumab (CRT-A) every two weeks (2 cycles concurrently with CRT and 2 cycles as monotherapy post completion of the CRT component). Surgery will be carried out 6-8 weeks post completion of CRT.

ELIGIBILITY CRITERIA

Patients with histologically confirmed and operable oesophageal or GOJ adenocarcinoma suitable for CROSS regimen will be recruited.

STUDY UPDATE

- Lead HREC approval occurred in May 2019 and the first site opened to recruitment in June 2019. A total of 7 Australian sites recruited to the study.
- The safety run in phase was done and the futility analysis on 15 patients that have had surgery has been completed.
- Enrolment to the study is now complete (total patients accrued: 48).
- Results to be presented at the 2023 AGITG Annual Scientific Meeting.

TRANSLATIONAL RESEARCH

- The trial has prospectively collected biopsy, surgical specimen, stool specimen and research blood samples at various time points to investigate candidate predictive/ prognostic biomarkers of treatment response.
- Current and future proposals (Biomarker work pending)
- Impact of cancer somatic mutation and neo-epitope load, tumour mutational burden on treatment responses.
- Correlation of pre-treatment PD-L1 and CPS expression as a predictor of response.
- Analysis of microbiome as biomarkers of response.
- ctDNA and serum small-RNAs (miRNAs, piRNAs) assessment pre-, during and post-therapy and correlation with outcome.
- HER2 expression and MMR and its correlation to outcomes

STUDY SCHEMA