Endocrine and neuroendocrine tumours

470TIP AGITG NABNEC: A randomised phase II study of nab-paclitaxel in combination with carboplatin as first line treatment of gastrointestinal neuroendocrine carcinomas

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Background: Neuroendocrine carcinomas (NEC WHO grade 3) are aggressive cancers that are rapidly fatal. There have been no randomised trials to date to establish standard therapy for advanced gastrointestinal (GI) NECs. Etoposide and carboplatin are used by extrapolation from small cell lung cancer data. Paclitaxel is also active in NECs but there is no data on the role of nab-paclitaxel. This randomised study aims to establish if carboplatin and nab-paclitaxel combination is an effective and tolerable treatment for advanced GI NECs.

Trial design: NABNEC has commenced as a randomised phase II multicentre trial enrolling adults with advanced and/or metastatic non-resectable GI NECs. Patients are randomised to: Arm A (n = 47) IV nab-paclitaxel 100 mg/m² on Day 1 every week and IV carboplatin AUC = 5 on Day 1 every 3 weeks OR: Arm B (n = 23) IV etoposide 100mg/m² on Days 1-3 every 3 weeks and IV carboplatin AUC = 5 on Day 1 every 3 weeks. Treatment will continue until disease progression or unmanageable toxicity. The primary endpoint is objective response rate (RR) by RECIST 1.1. At 6 months, the RR in the intervention group would need to be at least 50% to justify further investigation. A total sample size of 70 patients with a 2:1 randomisation (intervention to control) will have 80% power with 95% confidence to rule out a 30% objective RR in favour of a more clinically relevant RR of 50% at 6 months. Secondary endpoints include progression free survival, overall survival, safety as measured by NCI-CTCAE V4.03, and quality of life using EORTC QLQ-C30 and QLQ-GINET21 questionnaires.

Translational research endpoints include (1) blood and tissue biomarkers (prognostic and/or predictive) correlated with clinical endpoints including (a) circulating tumour cells, (b) mutation profile by whole exome sequencing, (c) DNA methylation profile and (2) utility of 18-fluoro-deoxyglucose positron emission tomography (FDG-PET) imaging as an early predictor of response and association of SUV max with clinical end-points. NABNEC has opened to recruitment at 9 study sites and is currently enrolling
patients. The randomised NABNEC study will run at 20 sites in Australia and New Zealand. ANZCTR # 12616000958482.

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A multicentre, randomised, double-blind, parallel-group, placebo-controlled trial of apatinib in local progressive or metastatic radioactive iodine-refractory differentiated thyroid cancer

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Background: Radioactive iodine-refractory differentiated thyroid cancer (RAIR-DTC) is a big challenge in the management of thyroid cancer. Sorafenib and lenvatinib are the 2 FDA-approved tyrosine kinase inhibitors (TKIs), which might not be affordable for most of the Chinese patients (pts). Apatinib is an oral TKI targeting VEGFR-2, with a patient assistance program available in China. It achieved a quick Tg decline of 21% 2 weeks later and an objective response rate (ORR) of 90%, showing promising efficacy in RAIR-DTC (Lin et al, ATA 2016, Short Call Poster 65; Lin et al, Oncotarget, Epub Feb. 02, 2017). Thus, this study aimed to further evaluate the efficacy and safety of apatinib in treating RAIR-DTC.

Trial design: This study is a multicentre, randomised, double-blind, parallel-group, placebo-controlled, phase III trial in China. Adult pts with locally advanced or metastatic RAIR-DTC are eligible. The inclusion criteria include at least one measurable lesion; disease progression within the past 12 months; and ECOG PS 0–2. Pts are defined as RAIR-DTC if they have target lesion(s) without iodine uptake, received one RAI treatment (\(\geq 3.7 \text{ GBq}\) \(\geq 100 \text{ mCi}\)) but progressed within the past 12 months, received two RAI treatments or more with a time interval of less than 12 months and progressed at least 12 months later), or received cumulative RAI activity over 22.2 GBq \(\geq 600 \text{ mCi}\). Previous targeted therapy is not allowed. Enrolled patients will be randomly assigned to receive apatinib (500 mg qd) and placebo, respectively. Four weeks is defined as one cycle. Dose increase to 750 mg and dose reduction to 250 mg are allowed. The primary endpoint is progression free survival. The secondary endpoints include disease control rate, ORR, duration of response, changes in serum Tg and TgAb concentration, quality of life, and safety. A multiple Cox proportional hazards model is used to evaluate the hazard ratios after adjusting iodine uptake, metastatic lesion site, gender, and age. 118 pts will be recruited assuming a 106.9% increase in median PFS in the apatinib arm compared with the placebo arm. As of 2nd May 2017, 3 eligible patients have been enrolled.

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