ANZUP Cancer Trials Group Limited

KEYPAD Trial News

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Welcome to our third KEYPAD newsletter

Congratulations and thanks to Fiona Stanley Hospital for randomising its first patient.

We'd also like to extend our thanks to the principle investigators, co-investigators, study co-ordinators and research teams at all the participating sites for your ongoing commitment and support to the study throughout the year.

SITES & RECRUITMENT UPDATE

Site *(in order of activation date)*	Activation date	Patients
Calvary Mater Newcastle	11/12/2017	3
St George Hospital	11/12/2017	3
Eastern Health / Box Hill	11/12/2017	0
Royal Brisbane & Women's Hospital	22/12/2017	2
Northern Cancer Institute	22/12/2017	0
Concord Repatriation General Hospital	24/01/2018	2
Flinders Medical Centre	16/02/2018	0
Icon Cancer Care	11/04/2018	1
Peter MacCallum Cancer Center	28/03/2018	1
Monash Health	23/05/2018	0
Ballarat Oncology	20/06/2018	1
Fiona Stanley Hospital	18/07/2018	1
Sunshine Coast University Hospital	Expected Q4 2018	-
Macquarie Hospital	Expected 2019	-
Total	14	14

Recruitment tip: Where possible, please utilise your hospital records to flag potential patients. These patients may not be eligble now but may be in the future.

If your site is experiencing specific barriers to recruitment, please contact us at: keypad@ctc.usyd.edu.au

Reminder: Please ensure all patients considered for study and found ineligible are documented on the Screening Log.

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Translational Research

REMINDER: Email all completed blood collection forms in real time to: keypad@ctc.usyd.edu.au AND autocheck@ctc.usyd.edu.au

AUTO-CHECK Study Update (as at 1-Nov-2018)

Trials/Cohorts activated	6/7
Hospital sites activated	62 (unique sites: 37)
Patients participating	164 (55% of target 300)
Real-time blood shipments (to Canberra)	270
IRAE blood samples collected	21 (13% of patients)

Data Management

CT imaging - Copies of de-identified reports of imaging for tumour assessments at baseline and at progression of disease are required to be forwarded to the CTC for central review. This is to confirm assessments of study endpoints by the KEYPAD clinical team. Imaging reports at other timepoints are not required to be forwarded however they should be retained for review if needed.

Annual Progress Report

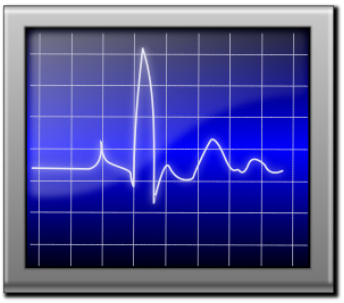
KEYPADs 2018 Annual Progress Report was recently submitted and approved by Lead HREC which was circulated to all sites on the 17th October 2018. Please ensure report and associated documents are forwarded to your site's RGO for acknowledgement and forward to the KEYPAD mailbox when recieved.

Updated Pembrolizumab Investigator Brochure (IB) version 16

MSD has released a new version of IB for Pembrolizumab. The changes were carefully reviewed by KEYPADs clinical team and no changes were required to the Protocol and PICF. Updated IN and associated documents were circulated 27th September 2018. Please ensure all documents are forwarded to your site's RGO for acknowledgement and forward to KEYPAD mailbox when received.

Monitoring visit

In line with KEYPADs protocol, monitoring visits will be conducted at recruiting sites for source verification, review of site study's site files and drug handling records. Please ensure study related documentations are up-to-date and filed correctly.



Supporting data

Ahern *et al.* have recently published an excellent review article in Nature Reviews: Clinical Oncology highlighting the roles of the RANKL–RANK axis in anti-tumour immunity[1]. In particular, it summarises the observational and preclinical evidence of RANKL–RANK interactions between immune cells in the tumour microenvironment. It also provides an elegant review of the data on RANKL inhibition in mouse models of cancer. KEYPAD is highlighted as one of the clinical trials assessing the immune anti-cancer effects of RANKL inhibition.

The publication can be accessed here: **https://www.nature.com/articles/s41571-018-0095-y**

Table 1: Trials assessing immune anticancer effects of RANKL inhibition. Abridged from Ahern et al. Nature Reviews Clinical Oncology 2018[1].

Trial	Indication	Intervention	Phase (treatment allocation)	Enrolment target (*n*)	Primary end points
Ongoing					
KEYPAD	Unresectable and/or metastatic clear cell renal cell carcinoma after progression on a VEGFR tyrosine kinase inhibitor	Denosumab plus pembrolizumab	II (single arm)	70	Objective response rate
CHARLI	Unresectable and/or metastatic melanoma in the first-line setting	Denosumab plus nivolumab with or without ipilimumab	Ib/II (randomized)	72	• Progression-free survival • Safety (select immune-related adverse events)
SPLENDOUR	Stage IV NSCLC (*EGFR* and *ALK* wild type) in the first-line setting	Standard chemotherapy[a] with or without denosumab	III (randomized)	1,000	Overall survival
Presurgical trial of denosumab in breast cancer	Operable breast cancer	Preoperative denosumab	0 (single arm)	35	Pharmacodynamic (RANK and RANKL protein expression)
Upcoming					
POPCORN	Resectable NSCLC	Preoperative nivolumab with or without denosumab	Ib/II (randomized)	30	Pharmacodynamic (including immune changes)
PERIDENO	HER2-negative breast cancer	Adjuvant chemotherapy with or without	II (randomized)	75	Pharmacodynamic (tumour immune

NSCLC, non-small-cell lung cancer; RANK, receptor activator of nuclear factor-κB; RANKL, RANK ligand. [a]Previous or concomitant treatment with immune-checkpoint inhibitors is allowed.

REFERENCES:

1. Ahern E, Smyth MJ, Dougall WC, Teng MWL. Roles of the RANKL-RANK axis in antitumour immunity - implications for therapy. *Nature reviews Clinical oncology* 2018;**15**: 676-93.

Thank you for all your support in 2018.
On behalf of ANZUP we wish you a happy and safe Christmas and New Year!

KEYPAD key contacts

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Trial pages: https://www.ctc.usyd.edu.au/our-research/clinical-trials/trial-pages-login.aspx
(log in required) here you will find downloadable copies of all study documents and tools.

ANZUP ClinTrial Refer app available for download from iTunes and Google Play