Recognition under the NSW Office of Health & Medical Research Quality Recognition Scheme

How did we get there!

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Calvary Mater Newcastle

Pilot Program

- Nov 2023 pilot program
- Early Phase Trials
  - Application in redcap
  - Onsite visit
- Response from OHMR August 2024
  - Address all items that did not meet the criteria.
- Submission addressing outstanding items & site visit – March 2025
- Response to 4 minor findings- 16 April 2025
- Received recognition 13 May 2025

Background

- NCTGF working party – Oct 2022
  - Involvement of Quality Manager of CMN
  - Set up hospital wide SOP's (previously unit based only)
  - Trial Unit awareness of Hospital Wide Policies
- Well established in Phase 1b, 2 & 3 clinical Trials
- Started FIH in lower risk FIH trials in 2022

There were no major or critical findings identified during the Quality Recognition Scheme review that may impact on the safety of patients.

The site has been determined as working towards meeting Criteria 1 to 5 of the EPCT QRS standards.

Key areas for improvement:

- Opportunities for process improvement and documentation practice were found in the following areas:
  - Leadership succession planning
  - Quality issue management and CAPA follow-up
  - Clinical trial specific risk management planning during feasibility and ongoing through the trial life cycle
  - EPCT PI training requirements and resource management practice
  - Emergency training mock scenarios and testing

Team Approach- BIG THANK YOU

Standard (Criteria)	Working Party Lead	Team
Clinical and Medical Governance	Dr James Lynam	Dr Ralph Gourlay (DMS), Dr James Lynam & Dr Janine Lombard
Quality Process	Kerrie Cornall	Kirrilee Askew, Emily Munn, Dr Faisal Hayat & Saba Kugashiya
Risk Assessment and Management	Kim Adler	Catherine Johnson & Dr Girish Mallesara
Research Team	Dr Janine Lombard	Dr Tin Quah & Dr Matthew George
Facilities & Medical Emergency response. (EPCT Management & Medical Emergencies)	Casey Hutchinson	Gail Walker, Dr Lucy Corke & Marc Hodgson

What did we develop in response to the assessment - RISK

- Risk management assessment process for all EPCT
- Updated new protocol review checklist to include a detailed safety section for FIH trials
- Developed Phase 1/ FIH SOP
- Developed a Mentorship program for NEW EPCT staff

What did we develop in response to the pilot assessment - COMMUNICATION

- GP Letter for all participants on EPCT
- Emergency & ICU notification process
- Handover pack for Ward and DTC for all EPCT
  - Study summary
  - Potential risks
  - IP mode of action and administration
  - Administration equipment required
  - Blood sampling requirements

Calvary Mater Newcastle

MOR Clinical Trial Handover

General Overview

Protocol Title/Number	[redacted]
RGO Number	2024/STEC[redacted]
Sponsor	[redacted]
Principal Investigator (PI)	Howard Chan SD[redacted]
MOR Trials Team	Team 1
Primary Coordinator(s)	Kerrie Cornall Mob: 0[redacted]
Back up PI	Dr Faisal Hayat SD [redacted]

Study Phase: Phase 1 First in Human

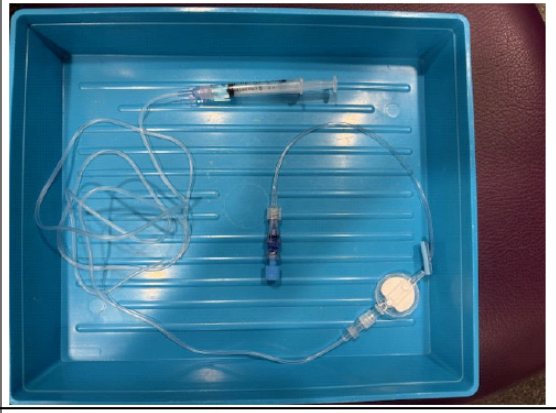
. To assess the safety and tolerability profile and determine the RP2D of [redacted] administered as monotherapy (Phase 1a)
. To assess the safety and tolerability profile and determine the RP2D of [redacted] administered as a combination therapy with a CPI (Phase 1b)
. To assess the PK profile of [redacted] as monotherapy (Phase 1a) and as a combination therapy with a CPI (Phase 1b)
. To assess the immunogenicity of [redacted] as monotherapy (Phase 1a) and as a combination therapy with a

Mode of action of investigational agent Administration

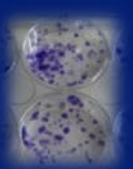
[redacted] is a novel synthetic, pegylated toll-like receptor (TLR) 2/6 agonist being developed by [redacted] hereafter, the Sponsor) for the treatment of solid tumors [redacted] is a potent and selective activator of the TLR2/6 receptor heterodimer complex, expressed across macrophages, dendritic cells, granulocytes, and subsets of natural killer cells and T-cells. [redacted] functions through a multicellular mechanism, including activation of the pro-inflammatory response, reduction in immunosuppressive macrophages at the tumor site, activation of dendritic cells, and release of chemokines to facilitate T-cell recruitment.
It is believed that [redacted] will elicit the innate immune system in a clinical setting in a similar fashion seen in nonclinical studies. Potential Risks Associated with [redacted] are as below:

- Joint inflammation
- Cytokine-associated symptoms (flu-like symptoms, fever, tachycardia, etc) or cytokine release syndrome)
- Hypotension
- Injection site reactions (localized redness, swelling, itching, and tenderness)
- Immune-related adverse events (irAEs)
- Embryofetal toxicities

Administration

IP	[redacted]
Dose	Refer to ARIA
Administration Guidelines	Micro- dosing. The administration line needs a pre saturation process. Pharmacy will provide a pre primed line attached with the IV line with dosing syringe. **1.** The IP dosing syringe can be loaded into the pump, then the administration line can then be attached to the patient's cannula. Refer to the Braun Perfusor Space Syringe driver cheat sheet for how to program the syringe driver. **2.** Select BD Plastipak syringe on pump - pump should display correct syringe size **3.** The pump can be programmed to prime the dead space in the cannula over 2 minutes: - **22G Blue cannula: Rate 2.1mL/hr over 2 minutes** **- 20G Pink Cannula: Rate 2.3mL/hr over 2 minutes** **- 20G Pink Cannula (1.88in Long U/S Cannula): Rate 2.5mL/hr over 2 minutes** **4.** Once the priming of the cannula has taken place the infusion pump will be programmed with the volume to be infused (VTBI), and time frame this will then automatically calculate the rate. Manually calculate rate to confirm. **5.** When the infusion is completed (**DON'T FLUSH THE LINE OR CANNULA**). The syringe and infusion line is disconnected from the drug cannula and the drug cannula is removed without flushing. This is to prevent a bolus dose of the trial drug that remains in the cannula. Please see picture below for saturation syringe set up. 
Infusion Line	Tuta mirco extension tube (will come pre primed from pharmacy)
Filter	Pall filter (will come pre primed from pharmacy)
Pump	BBraun perfusor space syringe pump (trials will supply pump)
Syringe	BD Plastipak (will come with correct dose from pharmacy)
Cannula	22g gauge blue, 20g gauge pink or 20g gauge U/S long pink



Trial Blood Samples Special instruction

Sample type	Blood	Blood tubes will be supplied for required time-points. **Collect from arm opposite to the Infusion.** Invert tube after collection. Call Primary coordinator to collect bloods to take to Medical Oncology lab for processing **Part A – Cycle 1 Day 1** • Pre-dose • 15 minutes post End of infusion (EOI) +/- 5 minutes • 30 minutes post EOI +/- 5 minutes • 1 hour post EOI +/- 15 minutes • 2 hour post EOI +/- 15 minutes • 4 hour post EOI +/- 15 minutes • 6 hour post EOI +/- 30 minutes • 8 hour post EOI +/- 30 minutes **Part B – Cycle 1 Day 1** • Pre-dose • 15 minutes post End of infusion (EOI) +/- 5 minutes • 30 minutes post EOI +/- 5 minutes • 1 hour post EOI +/- 15 minutes • 2 hour post EOI +/- 15 minutes • 4 hour post EOI +/- 15 minutes • 6 hour post EOI +/- 30 minutes

Observations and monitoring special instruction

Observations:

- Vital signs include systolic and diastolic blood pressure, respiratory rate, pulse rate, and body temperature (tympanic). At least 5 minutes of rest in either the sitting, semi supine or supine position in a quiet setting

- For all cycles, on Day 1, vital signs measurements will be performed:
  - Within 30 minutes before infusion, then every 15 min (+/- 5 min) until the EOI, and then at 30 minutes (+/- 10 min), 1 h (+/- 10 min), and 2 h (+/- 10 min) after EOI.
  - In addition, vital signs will be performed at 4 h (+/- 10 min) and 6 h (+/- 10 min) after EOI on **Cycle 1 Day 1**.
  - On other specified days, a single assessment will be performed.

ECGs:

For all cycles, on Day 1, ECG assessments will be performed within 60 minutes prior to dosing and again at 4 h (+/- 15 min) after EOI. At EOT/ET visit, a single assessment will be performed.

Single 12-lead ECGs will be obtained using an ECG machine. The 12-lead ECGs will be performed after the subject has rested in a supine position for at least 5 minutes. Wherever possible, ECG measurements must be taken using the same body position at subsequent visits and consistent methods between subjects. The ECGs may be repeated at the discretion of the Investigator to confirm errant readings.

LOCAL ECG MACHINE TO BE USED

Potential risks:

- First in Human study high level of monitoring

- Overdose from incorrect administration of drug – please seek guidance from Study team if unsure.

Infusion Reaction: see ARIA for Treatment management: Protocol guidelines: Yes – Located in patient handover folder.

Cytokine release syndrome protocol specific guidelines: Protocol guidelines: Yes – Located in patient handover folder

If you suspect CRS in this patient, **immediately contact:**

Dr Howard CHAN: [redacted]

If unavailable **contact: Dr Faisal HAYAT:** [redacted]

What did we develop in response to the pilot assessment – Ongoing Quality Audit Program

- Developed an Internal Quality Audit Program*
  - Target High risk studies
    1. Phase 1/ FIH
    2. Investigator Initiated
    3. Unmonitored studies

* *Adopted from A-CTEC Internal Audit Toolkit developed by Parkville Cancer Clinical Trials Unit (PCCTU) - V1 10 Dec 2024.*

Robust reporting to Executive:

- Clearer reporting lines to executive
  - Incorporated Risk assessment and EPCT New protocol review checklists into SSA submission process
  - Submit CAPA from internal audits
  - Notify RGO / Executive of all onsite audits- i.e sponsor audits & submit CAPA from the audit.

Key take home messages

- QRS is a big time commitment but worth it.
- Team approach essential
- Involve your quality manager and executive early in process
- There are lots of tools out there so look first

PART 2: BROADER ASSESSMENT OF HAZARDS AND RISKS INVOLVED IN THE TRIAL

2. HAZARDS AND RISKS OF THE INTERVENTION (IMP) AND STUDY PROCEDURES

Hazard ID	Hazard	Concerns identified Provide details of trial-specific considerations / risk concerns	Hazard LIKELIHOOD of Occurrence 1 Rare 2 Unlikely 3 Possible 4 Likely 5 Almost certain	Hazard SEVERITY 1 Insignificant 2 Minor 3 Moderate 4 Serious 5 Catastrophic	RISK Low (1-8) Medium (9-12) High (15-25)	How will these risks be managed? Address all concerns identified	Monitoring strategies Discuss the impact on trial conduct monitoring and safety monitoring requirements
2.1 HAZARDS AND RISKS – PARTICIPANT							
2	**Expected hazards related to study intervention (i.e. Investigational Medicinal Product [IMP]) and/or its administration.**	*Include in this category (for example):* *IMP risks* • *side effects* • *Interactions with concomitant/permitted medications* • *Potential harm in reproduction* • *Precautions and impact on eligibility* *IMP administration risks* • *high risk dosing procedure e.g. cohort, maximum tolerated dose (MTD)* • *high level of treatment interception e.g. frequent PKs* *Other known or anticipated safety issues* ***Example text – customise*** *IMP & administration risks:* • *Minor side effects where the impact would be relatively non-substantial in this participant group: <insert where applicable>* • *Side-effects that could have a substantial impact in this group: <insert where applicable>* • *Risk of interactions of the IMPs causing harm to a foetus: <insert where applicable>*			0	*For example: Build into the protocol* • *Written documentation of Investigator's review of participant eligibility (to minimise ineligible participants being entered and exposed to the IMP).* • *Additional participant monitoring of <insert> (e.g. additional blood glucose monitoring for a product with hyperglycaemia as a hazard).* • *Exclusion of those taking medications with a known interaction to the IMP or other agents used in the trial.* • *Dose adjustment or stopping rules* • *Exclusion of women of child-bearing potential (WOCBP). Or, if included, build in (i) requirement for contraception plus (ii) pregnancy testing before, during and after (e.g. for XX half-lives after last dose) and (iii) follow up of any pregnancy (in participant or partner) until post-birth or otherwise (i.e. spontaneous termination) to allow information on the status of the mother and child to be reported to the sponsor pregnancy.*	***Example text – customise for your trial:*** *On-site monitoring of trial conduct:* • *Eligibility (inclusion/exclusion criteria) – verification will be performed for all/xx% of enrolled participants.* • *For those participants selected for monitoring, all safety events will be reviewed.* *Safety monitoring* • *Independent data and safety monitoring will be conducted by <insert> (e.g. an independent Medical Monitor or a Data Safety Monitoring Board)*

	2.1 HAZARDS AND RISKS – PARTICIPANT	Risk Rating
1	Expected hazards-Low Risk, related to Investigational Medicinal Product [IMP] (Toxicities)	High - Add Controls
2	Expected hazards-Moderate Risk, related to Investigational Medicinal Product [IMP] (Toxicities)	Medium - Add Controls
3	Expected hazards-High Risk, related to Investigational Medicinal Product [IMP] (Toxicities)	Medium - Add Controls
4	Expected hazards related to administration of IMP.	
5	Hazards related to study procedures/ investigations	
6	Non-compliance with consent process	
7	Serious breach of protocol, ethical requirements, confidentiality	
8	Hazards to participant well-being	
9	Hazards arising from complexity of study procedures	

	2.2 HAZARDS AND RISKS – TRIAL DESIGN, SYSTEMS, PERSONNEL & FACILITIES	Risk Rating
10	Inadequate Funding	
11	Recruitment target not met	
12	Outcomes not collected	
13	Protocol violation	
14	Data and samples	
15	Staff and skills	
16	Team cohesion	
17	Contracts and indemnity	
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	2.1 HAZARDS AND RISKS – PARTICIPANT
Total Risk: Low	0
Total Risk: Medium	2
Total Risk: High	1
Total Risk: Very High	0

	2.2 HAZARDS AND RISKS – TRIAL DESIGN, SYSTEMS, PERSONNEL & FACILITIES
Total Risk: Low	0
Total Risk: Medium	0
Total Risk: High	0
Total Risk: Very High	0

	Grand Total Overall Risk
Total Risk: Low	0
Total Risk: Medium	2
Total Risk: High	1
Total Risk: Very High	0