Just in Time (JiT) Activation Pre-Pilot: The PemOla Trial Information Sheet

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Introduction

The PemOla clinical trial is being used as a case study in the development of the Just in Time (JiT) activation scheme. The JiT site activation scheme is a project jointly developed by the NIHR Research Delivery Network (RDN), Health Research Authority (HRA), Health and Care Research Wales (HCRW), NHS Research Scotland (NRS), Health and Social Care Northern Ireland (HSCNI) and supported by UK Research and Development (UKRD). It aims to support the rapid set-up of sites for selected studies recruiting rare patient populations where the opportunity for the participant to be recruited would otherwise be lost if standard set-up timelines were followed. Site set-up for studies in the scheme commences when a potential participant is identified.

The scheme is in its developmental phase. The aim of this pre-pilot specifically is to assess the feasibility of initiating site set-up once a potential participant is identified, rather than the standard approach of setting up the trial in advance of patient identification.

The pre-pilot does not alter the delivery of the PemOla trial protocol as the scheme process only applies up to the point that the trial is open at site. We will use the experience from this pre-pilot to assess if and how we can extend the JiT scheme to more multicentre research studies involving rare patient populations through a formal pilot scheme.

This information sheet outlines the JiT activation pre-pilot and its implications for recruiting to the PemOla trial.

For further information about the PemOla trial, please contact cuh.pemola@nhs.net.

What are the benefits of the JiT Activation pre-pilot?

The JiT approach allows sites which are not already set up to recruit to a study to open quickly so that an identified patient can participate in a study. It is especially relevant for situations where trials are recruiting rare patient groups, and recruitment opportunities would be missed if standard site inclusion processes are followed.

Site set-up starts when a potential participant is identified rather than sites being identified and set up prior to patient identification. This reduces the amount of time and effort expended by NHS organisations and the Clinical Trial Units (CTU) in setting up sites that do not ultimately recruit any patients. It also means that patients with a rare condition do not miss the opportunity to participate in research.

Aims of the Pre-Pilot

We have adopted an iterative, co-production approach to developing this process. The pre-pilot aims to assess:

- the feasibility of the proposed site set-up timelines.
- the potential to initiate site set-up upon identifying a potential participant, with a view to reducing the time and resources required compared to standard procedures.

- any practical challenges or limitations including in the ways to communicate with NHS, along with potential solutions to address them.

This approach will help us evaluate its suitability for broader application across multiple studies.

If your site sets up through the JiT site activation pre-pilot, we will contact you to ask for feedback in due course.

Introducing the PemOla Trial

The PemOla Trial is a phase 2 single arm trial evaluating the role of immunotherapy in a subgroup of patients with metastatic pancreatic adenocarcinoma. PemOla is the first trial to utilise the JiT scheme. PemOla targets a rare patient population and involves the use of licensed drugs for an unlicensed indication. The assessment schedule is designed to align closely with the standard care these patients typically receive, eliminating the need for specialist research facilities. Patients are required to attend only on day 1 of each 3-week cycle, continuing until disease progression or for a maximum of two years.

The trial is recruiting only patients whose pancreatic tumours have a specific genetic profile (TMB ≥4 mutations/Mb or dMMR/MSI-H) which is found in about 5% of cases. Although around 15 UK sites will be opening the trial using standard trial set-up processes, given the rarity of this patient group, the JiT scheme allows for the opportunity for more sites across the country to recruit an eligible patient at short notice. The JiT process begins when a clinical team identifies a potential participant.

The main PemOla trial inclusion and exclusion criteria are summarised below:

To be **included** in the trial the participant must meet the following criteria:	The presence of any of the following will **exclude** participant inclusion:
✔ Have given written informed consent to participate. ✔ Aged ≥ 18 years old ✔ Histologically or cytologically confirmed PDA ✔ Confirmation that the PDA has TMB ≥4 mutations/Mb, or dMMR gene mutation,	✔ Patients with resectable or locally advanced PDA ✔ Other invasive malignancies diagnosed within the last 2 years which have not been treated with curative intent ✔ Prior CPIs or PARP inhibitors. This includes any prior therapy with an anti-PD-1, or

or MSI-H by IHC obtained from either tissue, or blood ✔ Radiologically confirmed stage 4 mPDA, with measurable disease ✔ Received no more than 1 prior systemic therapy regimen for unresectable (stage 3 or 4) PDA ✔ Received no more than 1 prior systemic therapy for metastatic disease ✔ Measurable disease which has not been irradiated in prior radiotherapy ✔ Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 ✔ Life expectancy >12 weeks from the date of screening assessment ✔ Adequate bone marrow function ✔ Adequate liver function ✔ Adequate renal function defined as a calculated creatinine clearance by Cockcroft-Gault of ≥50 mL/min	anti-PD-L1, or anti PD-L2 agent, or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g, CTLA-4, OX 40, CD137) ✔ Requirement for non-physiological dose of daily oral steroids, or regular use of any other immunosuppressive agents; prednisolone dose of ≤ 10mg (or equivalent steroid dose) is allowed. Use of inhaled or topical steroids is allowed. ✔ Significant acute or chronic medical or psychiatric condition, disease or laboratory abnormality, which in the judgment of the investigator would place the patient at undue risk or interfere with the trial. Concomitant use of known potent CYP3A4 inhibitors and inducers. Please consider wash-out periods. ✔ Has received prior systemic anti-cancer therapy including investigational agents within 4 weeks prior to screening.

For a comprehensive list of the eligibility criteria and trial schedule of assessments, contact the PemOla trial team (cuh.pemola@nhs.net).

Why is the PemOla trial suitable to be set up "Just in Time"?

Setting up the PemOla trial should have a minimal impact on NHS organisations which set up through JiT after patient identification. Study delivery activities are considered to be straightforward, and do not require anything unusual to happen that organisations would not ordinarily be able to deliver as part of care. There are no special or specific arrangements required and no excess treatment costs. Sites utilising the JiT scheme are not expected to recruit many participants to the trial. The workload associated with the trial should not impact on the wider research, or clinical delivery at these sites.

There are several factors about the PemOla trial which we think makes it suitable for this pre-pilot:

- Research activities are usual care competence so should not require any additional staff training.
- The trial largely reflects standard of care pathways, so should not require special set-up activities or management.

- The trial activities have been allocated in the Schedule of Events Cost Attribution Template (SoECAT). It is expected that costs should not need to be negotiated because trial activities are minimal and there are no associated excess treatment costs.
- An unmodified model Non-Commercial Agreement (mNCA) will be used as the contract, meaning there is no contract negotiation.
- All study-specific training can be delivered remotely.
- The study has Pharmacy Assurance in place, which will help when setting up the pharmacy department.
- The study has Radiation Assurance in place, which will help when setting up the radiation department.
- Study drugs (IMPs) are licensed drugs being used in an unlicensed indication. They will be automatically ordered by the PemOla study team as soon as the site is activated with a delivery time of 3-5 working days.
- Similar prescription builds should be available to adapt easily at site, but the PemOla trial team can supply a prescription template if needed. The JiT scheme goal is for a patient to be treated within 2 weeks of site activation.
- There is no specialised tissue collection or processing needed; the collection of research blood, urine and stool samples are optional.
- Although a biomarker-specific trial, the biomarker is not part of the trial protocol and needs to be identified prior to trial recruitment through routine mechanisms.

How do sites set up PemOla using the Just in Time process?

1. If the clinician identifies a potentially eligible participant and is working in an any NHS organisation across the UK which is not yet set up as a PemOla trial site they contact the PemOla trial team (cuh.pemola@nhs.net), copying in their R&D department and the RRDN Study Support Services Team (or equivalent in Devolved Nations) to express their interest to recruit the patient via the JiT scheme.

   We recommend that this contact is made on the same day the clinician becomes aware of the potential participant and only if the potential participant has expressed an interest in joining the study.

2. Upon contact the PemOla trial coordination team will send the clinician the full protocol by email.

3. The clinician (who will act as site PI), PemOla trial coordination team and local trust R&D administrator confirm the following points either through a quick email exchange or ideally through a virtual meeting:

   a. Clinician makes a declaration confirming they have the skills and facilities required to manage this patient safely, in accordance with the protocol, and accepts responsibility

to do so including identifying which site personnel will be involved in managing the patient.
   b. The PemOla trial coordination team agrees to send any additional materials (e.g. a training video; Case Report Forms).
   c. The clinician's R&D department confirms the Trust / Health Board has capability.

4. Site PI and personnel undergo trial-specific training provided by the PemOla trial coordination team remotely.

5. All parties sign the trial contract (as in England/NI/Wales), or provision of NHS Management
   Permission in Scotland.

6. Following on from steps 1-5, site activation is confirmed by the PemOla trial coordination team, ideally within **3 working days of patient identification,** which is the rapid set-up time the JiT site activation pre-pilot scheme aims to achieve.

7. Once the site is activated the patient can be approached, given the Participant Information Sheet and arrangements made to seek consent. The PemOla Trial coordination team then dispatches a supply of the trial-specific investigational medicinal product on confirmation of patient consent. The JiT scheme goal is for a patient to be treated within 2 weeks of site activation.

What do you need to do now?

Please complete this short questionnaire to help us understand if it is feasible for you to set up the trial in the suggested timeframe and if not, why not, including any barriers and enablers to the set-up and delivery of the trial.

If you have a potentially eligible participant and have not undertaken the standard site set-up process and are interested in taking part, please contact the PemOla trial team (cuh.pemola@nhs.net), copying in your R&D department and the RRDN Study Support Services Team (or equivalent in Devolved Nations) for further information about the PemOla Trial.

Contacts

For any queries or feedback regarding the Just in Time scheme, contact catherine.fleetwood-walker@nihr.ac.uk.

For information and queries specific to the PemOla Trial, cuh.pemola@nhs.net.