

ATTC Network Helps Accelerate First-in-Human Cell Therapy Trial at The Christie

The Challenge

The Advanced Immunotherapy and Cell Therapy (AICT) team at The Christie NHS Foundation Trust delivers Advanced Therapy Medicinal Product (ATMP) clinical trials at this specialist cancer centre. The Christie is the lead site for iMATCH, a Manchester-born consortium of six sites which form one of the Advanced Therapy Treatment Centres (ATTCs) as part of the UK-wide ATTC network. The Cell and Gene Therapy Catapult (CGT Catapult) provide coordination of the network.

Sponsored by the biotechnology company Zelluna Immunotherapy ('Zelluna') based in Norway, ZIMA-101 is a complex first-in-human, first-in-class Phase I clinical trial evaluating ZI-MA4-1, an allogeneic TCR-NK cell therapy targeting MAGE-A4 positive solid tumours.

As Zelluna's first clinical trial and the first clinical translation of its TCR-NK platform, establishing ZIMA-101 presented several novel operational challenges. These included establishing the appropriate UK drug-supply and importation pathway for an off-the-shelf, cryopreserved cell therapy, and developing the pharmacy, storage, handling and clinical processes required to deliver multiple doses safely and effectively within an NHS research setting.

Unlike autologous cell therapies manufactured individually for each patient, ZI-MA4-1 is manufactured in advance and stored ready for use. This required the Sponsor and site teams to establish processes suited to the allogeneic, off-the-shelf nature of the product, including its use across different dose levels during the dose-escalation study.

Addressing these requirements at pace required close coordination between Zelluna, The Christie and the wider ATTC network. Through this collaborative approach, The Christie became the first site globally to open the ZIMA-101 clinical trial and consented the first patient 89 days after Health Research Authority (HRA) approval, and 126 days from application submission. This timeline comfortably met the UK Government's target for clinical trials to open and recruit their first participant within 150 days.

The following case study describes the key challenges encountered in establishing ZIMA-101 and the collaborative approach used to address them, providing learnings that can be applied across both the ATTC network and the wider field of advanced therapies.

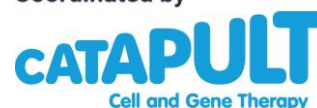
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The Solution

Connections built through the ATTC network

Zelluna is a clinical-stage biotechnology company developing T-cell receptor natural killer (TCR-NK) cell therapies for the treatment of solid cancers. The company has developed its lead programme, ZI-MA4-1, into a first-in-human clinical trial (ZIMA-101), evaluating an allogeneic TCR-NK cell therapy targeting MAGE-A4-positive solid tumours. Zelluna has also established a proprietary manufacturing process for this therapy, which enables multiple cryopreserved doses to be manufactured in advance and stored ready for use.

Zelluna identified The Christie as a potential lead site based on the site's experience in cell therapy and the delivery of first-in-human phase 1 studies across multiple cancer indications, engaging with Professor Fiona Thistlethwaite. As both the iMATCH ATTC Director and head of the AICT team at The Christie, Professor Thistlethwaite was able to understand the company's support needs and connect Zelluna with the CGT Catapult.

The CGT Catapult was then able to support Zelluna during preparation for ZIMA-101, Zelluna's first clinical trial, including development of the protocol and review of the briefing package prepared for scientific advice with the Medicines and Healthcare products Regulatory Agency (MHRA). The CGT Catapult also provided specific support on chemistry manufacturing and controls (CMC) considerations associated with the novel cell therapy product.

Agile clinical trial set up at site

Successful initiation of this clinical trial required early strategic alignment and collaborative expertise across multiple disciplines. As the investigational product was an off-the-shelf Advanced Therapy Investigational Medicinal Product (ATIMP), the requirements for handling, oversight and local implementation differed from those associated with conventional autologous ATIMPs. The Christie established a tailored investigational product pathway and supporting local processes to ensure the site was appropriately equipped to deliver the trial effectively.

To achieve the National Institute for Health and Care Research (NIHR) 150-day study set-up timelines, key preparatory activities were undertaken in parallel with regulatory review, allowing operational requirements, governance arrangements and documentation to be developed concurrently. Early and sustained engagement between the pharmacy, stem cell laboratory, clinical and sponsor teams enabled timely decision-making, proactive identification and management of potential risks, and effective resolution of trial-specific requirements.

This coordinated approach, supported by specialist AICT expertise, strong sponsor partnership and effective planning enabled The Christie to achieve efficient trial activation and first-patient recruitment within the required timeframe. The successful establishment of the ZIMA-101 trial

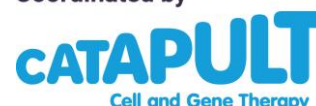
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highlights the importance of experienced multidisciplinary infrastructure in supporting the delivery of innovative early-phase clinical trials.

The Results

With Professor Thistlethwaite acting as the Global Chief Investigator, The Christie became the first research site worldwide to open the ZIMA-101 clinical trial and recruit a patient. Through the expertise and agility of the AICT team, the first global patient provided consent 126 days from submission of the regulatory approval application, demonstrating the capability of The Christie to support efficient delivery of complex ATMP clinical trials.

The key factors enabling this achievement included:

- Early engagement between Zelluna, as a new trial sponsor, and The Christie as the lead research site
- Establishment of a strong link between Zelluna and the ATTC network
- Targeted support provided to Zelluna through the CGT Catapult
- The highly specialist ATMP clinical trial expertise of the multidisciplinary AICT team at The Christie
- The AICT team's proactive patient pre-screening, enabling rapid identification and recruitment of eligible patients

Wider Impact

Early engagement between Zelluna and The Christie in turn enabled rapid connection to the ATTC network and the CGT Catapult, which was essential to progressing the novel operational aspects that were needed to initiate this first clinical trial for Zelluna. Through clear and efficient communication, Zelluna was supported to achieve key milestones in establishing and initiating the ZIMA-101 clinical trial.

Building these early connections ensured that the right clinical, regulatory and manufacturing expertise was accessed quickly. This powerful example of collaborative working demonstrates the ATTC network's mission: to make the UK the leading environment for ATMP clinical trials and to keep the UK as a location of choice for advanced therapy research.

"Collaborating with Prof Thistlethwaite and her talented team, with the support of the ATTC, has been instrumental in accelerating the translation of our novel TCR-NK platform into the clinic. The expertise of the group, combined with the ATTC's infrastructure and commitment to advanced therapies, aligns closely with Zelluna's mission to make next-generation, off-the-shelf cell

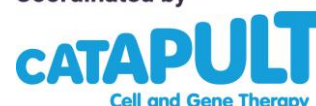
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therapies broadly accessible to patients with solid tumours who are in need of new treatment options.” [Quote from Namir Hassan, Zelluna CEO]

For further information and to hear from the first global patient on the ZIMA-101 clinical trial, please visit The Christie website: [First patient receives pioneering new cell therapy at The Christie.](#)

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