LTHT/Cytiva Cell therapy Hub project – lessons learnt

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Background

In October 2019, the Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC) held a workshop to explore some of the logistical and tracking challenges of Advanced Therapies Medicinal Products (ATMPs). The resulting outputs, laid out in the document "The last 100m" (1), stated, "the management of [ATMPs] at scale within a healthcare provider is potentially highly complex - and making the management of logistics at site too complex will become a barrier to the adoption of these products. Therefore, ensuring that complexity is minimised should be a goal that therapy developers, logistics providers and healthcare organisations need be working on together."

In particular, it was identified that the delivery of ATMPs to clinical sites should be simplified by using "a designated drop-off point within a pharmacy department, to designated members of the pharmacy team who have been trained how to receive and check advanced therapy products."

The Cell Therapy Hub model

Cytiva has developed the concept of the 'Cell Therapy Hub' — a mobile/semi-mobile/modular/temporary facility that serves as a one-stop, manufacturer drop-off point for receipts of ATMPs. As such, it would enable the last few steps in the vein-to-vein delivery of cell therapies ("the last 100m"). These steps include receipt, final preparation steps (thawing of frozen products and/or any reconstitution activity) and issue where stability allows, or, receipt and issue prior to final preparation steps in the clinical area – handling the final product between courier and patient bedside.

Necessary equipment would be supplied to the Cell Therapy Hub for trained pharmacists to perform the receipt checklist of ATMPs, and for these pharmacists or operators skilled in handling cellular products to perform the final preparation steps of the therapy, depending on the classification and containment level of the product, as well as its available stability data. Equipment would for instance include desk, computer, internet, thawing device, isolator, etc., and be leased to LTHT. The Cell Therapy Hub could also serve to support the processing and logistics of patient starting materials (apheresis or tumour tissue). It would be operated by hospital staff, with regulatory, accreditation, and licensing extended from the host site.

With the potential of being fully mobile (via a container on a lorry), the unit would allow support for more than one hospital. Semi-mobile configuration would allow the container to be craned off anywhere on an outdoor space within the clinical site, with the possibility of being removed or moved elsewhere at a later point, if necessary. Alternatively, an existing space within the clinical site could also be refurbished into the Cell Therapy Hub for a more permanent solution.

Exploring the concept

LTHT performed an in-depth scoping exercise of the facility that would fulfill their needs. The exercise included looking into the possibility to have one facility for receipt and final preparation of *in vivo* (virus-based) and *ex vivo* (cell-based) gene therapy medicinal products (GTMPs). Such a facility should be able to process both GTMPs holding marketing authorizations, and clinical trials involving gene therapy investigational medicinal products (GTIMPs). Any such facility must comply with good manufacturing practice (GMP) requirements and other legislation in place. Depending on their classification and containment level, GTMPs/GTIMPs will require the most appropriate local aseptic

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facilities to be decided upon as described in the "Pan UK Pharmacy Working Group for ATMPs – Gene Therapy Medicinal Products – Governance and Preparation Requirements" (2).

To cover GTMPs that may be used in the future, the aseptic facility would have needed to be suitable for handling replication competent class 2 GTMPs/GTIMPs (since most GTIMPs that are in clinical trials or in development currently are class 1 or 2 genetically modified organisms). The all-encompassing facilities would have therefore been recommended to have a dedicated negative pressure isolator within a containment suite (negative sink or positive air bubble). Unfortunately, in addition to being over budget, this would have required more space than the Cell Therapy Hub model design allowed for, mainly due to the air filtration system necessary to achieve the level of cleanliness required. Furthermore, it would not have been feasible to deliver and evaluate a revised design specification within the NA-ATTC Runway project's timeframe.

However, the scoping exercise of a cell and gene therapy facility, and the learnings gathered from it, proved to be useful going forward.

Moving forward and next steps

According to LTHT, there is certainly a place for the original Hub model to work for GTIMPs – for LTHT, and for other NHS Trusts and Boards in the UK. In addition to the importance of a Cell and Gene Therapy Hub in the context of a global pandemic and the resulting strained health system, the main advantages of the Hub include that it:

- provides an opportunity to upscale
- does not require space within an existing building footprint
- avoids huge capital expenditure and refits

Therefore, it would be a lower-cost solution while providing interested researchers and clinicians more accessibility to infrastructure and equipment. The scoping exercise also demonstrated the Trust's and Aseptic Services acceptability of a mobile/semi-mobile/modular facility concept — should the specifications be met — as an easy-to-implement, relatively inexpensive way to increase capacity and revenue.

The 'gene therapy' roadblock to the Hub concept is more apparent for ATMPs in clinical trials. This is due to the fact that often, when marketing authorizations have been approved, the Summary of Product Characteristics (SMPC) has minimized the containment requirements because of experience gained in the clinical trial. This gene therapy clinical trial roadblock is considered by LTHT as a rate-limiting step to the adoption of such products in the UK. In order to solve it, a possible way forward has been identified: open discussions about facilities with the medicine regulator to agree on a pragmatic and deliverable way forward in collaboration with providers including Cytiva.

Implementation of any future recommendations will involve operationalizing by collaboration with the Specialist Pharmacy Service group, the Pan-UK Pharmacy Working Group for ATMPs.

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