

The UK training landscape in advanced therapies for the NHS

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1. Background

Advanced therapies have the potential to address significant and growing unmet healthcare needs. They offer the promise of treating and altering the course of diseases which cannot be addressed adequately by existing pharmaceuticals. The UK is at the leading edge of this disruptive field and there is an opportunity to build a large-scale industry delivering health and wealth to the country.

The UK is committed to allowing patients access to these novel treatments and was one of the first countries to approve the use of CAR-T treatments, with these being approved for use in England just 10 days after receiving EU marketing authorisation. Another show of government support to the sector of advanced therapies was through investment in the Advanced Therapy Treatment Centre (ATTC) programme, a network of centres designed to develop and test infrastructure to support the routine supply of advanced therapies by the NHS.

Not only is the UK leading in access to commissioned treatment, a large number of clinical trials in advanced therapies are now under way in NHS hospitals. According to the Cell and Gene Therapy Catapult annual review of advanced therapies there were 127 ongoing trials in the UK as of January 2020, representing 12% of global cell and gene therapy trials¹. The number of Advanced Therapy Medicinal Products (ATMPs) is expected to increase dramatically over the coming years as more trials recruit patients and treatments become approved by regulatory authorities.

There is a significant demand across the industry, both in the NHS and the private sector, to increase the knowledge and skills of the workforce in preparation for this expansion of capability demand. Across the ATTCs we are working to understand what training in advanced therapies is already available and what is required to ensure staff are equipped to understand these medicines and can answer questions from patients about their treatment. To this end we have undertaken an exercise to ascertain what training is currently on offer to healthcare professionals nationwide.

2. Currently available training in advanced therapies

2.1. Advanced therapies apprenticeships

The Advanced Therapies Apprenticeship Community (ATAC)² has been established to develop the first apprenticeship programme designed specifically to train and upskill individuals to develop and manufacture these innovative therapies at scale. A variety of programmes have been launched so far (Table 1), ranging from level 3 apprenticeships (equivalent to 2 A Level passes) to level 6 (equivalent to a Bachelor's degree or postgraduate diploma) and level 7 programmes (equivalent to Master's degree). In the UK alone, the ATMP manufacturing industry is expected to grow up to 112% by 2024³ and the ATAC scheme is designed to support this growth.

¹ <https://ct.catapult.org.uk/resources/cell-and-gene-therapy-catapult-uk-clinical-trials-database>

² www.advancedtherapiesapprenticeships.co.uk

³ <https://bit.ly/37HeIDq>

Course title	Level	Link
Science Manufacturing Technician	3	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/science-manufacturing-technician-for-atmps/
Laboratory Technician for ATMPs	3	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/laboratory-technician/
ATMP Technician Scientist Higher Apprenticeship	5	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/atmp-technician-scientist-higher-apprenticeship/
Modern Apprenticeship in Life Sciences (ATMP)	SCQF Level 7 HNC	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/modern-apprenticeship-in-life-sciences-atmp/
Clinical Trials Specialist	6	https://www.instituteforapprenticeships.org/apprenticeship-standards/clinical-trials-specialist-degree/
Regulatory Affairs Specialist ATMP	7	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/regulatory-affairs-specialist-for-advanced-therapies/
Senior Leader in Advanced Therapies	7	https://www.advancedtherapiesapprenticeships.co.uk/latest-news/programmes/senior-leader-in-advanced-therapies/

Table 1 UK apprenticeship programmes in advanced therapies. SCQF, Scottish Credit and Qualifications Framework; HNC, Higher National Certificate.

2.2. AToMIC

The Advanced Therapy Manufacturing Industry Consortium (AToMIC) is led by the Advanced therapy medicinal products Manufacturing Community⁴ (AMC) and comprises a group of cell and gene therapy organisations that are proactively working with the academic sector to develop industry ready students to meet their early career recruitment needs. Along with supporting the ATAC initiative, the AToMIC program also aims to support the development of relevant undergraduate and postgraduate degrees and to provide early career support for researchers in the ATMP community.

2.3. Post-graduate level courses in advanced therapies

The UK university sector has developed a number of MSc level courses to attract students that see advanced therapies as an emerging career opportunity. Many of these programmes are targeted towards the research

⁴ <https://atmpmanufacture.org/>

or manufacturing side of the advanced therapies industry or have adapted existing courses on stem cell medicine to include modules on advanced therapy. Some institutions are now reacting to the growth in the field to offer new MSc level courses focused on ATMPs, such as the MSc now offered at Manchester University as well as a Wellcome Trust funded MRes/PhD at King College London (Table 2).

Academic institution	Course title	Link
Aston University	MSc Stem Cells and Regenerative Medicines	https://www2.aston.ac.uk/study/courses/stem-cells-and-regenerative-medicine-msc
Bristol University	MSc Stem Cells and Regeneration	http://www.bristol.ac.uk/study/postgraduate/2020/health-sciences/msc-stem-cells-regeneration/
Imperial College London	MSc in Genes, Drugs and Stem cells – Novel Therapies	https://www.imperial.ac.uk/study/pg/medicine/genes-drugs-stem-cells/
Kings College London	Stem Cell & Regenerative Therapies: From Bench to Market	https://www.kcl.ac.uk/study/postgraduate/taught-courses/stem-cell-and-regenerative-therapies-from-bench-to-market-msc
Kings College London	Wellcome Trust Advanced Therapies for Regenerative Medicine	https://www.kcl.ac.uk/study/postgraduate/research-courses/wellcome-trust-advanced-therapies-for-regenerative-medicine-four-year-phd
Manchester University	MSc Advanced Therapy Medicinal Products	https://www.manchester.ac.uk/study/masters/courses/list/12672/msc-advanced-therapy-medicinal-products/
University College London	MSc Cell and Gene Therapy	https://www.ucl.ac.uk/prospective-students/graduate/taught-degrees/cell-gene-therapy-msc
University College London	Manufacture and Commercialisation of Stem Cell and Gene Therapies MSc	https://www.ucl.ac.uk/biochemical-engineering/study/postgraduate-taught/manufacture-and-commercialisation-stem-cell-and-gene-therapies-msc
University of Sheffield	Stem Cell and Regenerative medicine	https://www.sheffield.ac.uk/bms/study/masters/stem_cell
University of Southampton	Stem Cells, Development and Regenerative Medicine	https://www.southampton.ac.uk/medicine/postgraduate/research_degrees/degrees/mres-in-stem-cells-development-and-regenerative-medicine.page

Table 2 Examples of UK postgraduate level training in advanced therapies

2.4. Online training and resources

Some companies and charities have created educational videos about cell and gene therapies, making these publicly available through their own websites and platforms such as YouTube (Table 3). Whilst this content is welcome, commercially produced resources generally focus on the manufacturer's specific therapeutic product and do not necessarily present this material with the appropriate wider context. Standalone, uncoordinated resources do not provide the comprehensive syllabus needed by hospital staff to be able to gain a holistic understanding of these therapies needed to carry out their roles with confidence.

Video title	Organisation	Link
Introduction to ATMPs	NIHR	https://learn.nihr.ac.uk/course/view.php?id=411
SPEAR T-cells	Adaptimmune	https://www.adaptimmune.com/technology/overview
The science behind CAR-T therapy	Novartis	https://www.youtube.com/watch?v=PF6NnFVa1Sk
How Zolgensma works	AveXis	https://www.zolgensma.com/how-zolgensma-works
Gene therapy explained	Applied Genetic Technologies Corporation	https://www.youtube.com/watch?v=xOQFJJOBGM0
Gene therapy	UniQure	https://www.youtube.com/watch?v=f6UdOk9a--l
Gene Therapy Basics	American Society of Gene & Cell Therapy	https://www.youtube.com/watch?v=BxEoX6TkitY
Gene Therapy for Inherited Retinal Diseases		https://www.youtube.com/watch?v=JuEnCDByQQY
Gene Therapy for Blood Disorders		https://www.youtube.com/watch?v=zb3dlr20UV0
Duchenne Muscular Dystrophy and Gene Therapy		https://www.youtube.com/watch?v=Lf_cnJw9pZc
CAR T-Cell Therapy: How Does It Work?	Dana-Faber Cancer Institute	https://www.youtube.com/watch?v=OadAW99s4Ik&t=10s
How to biohack your cells to fight cancer	University College London	https://www.youtube.com/watch?v=Mt5C5fhuU_0

Table 3 Example online training resources in advanced therapies

3. Training needs analysis survey

In order to gain insight into the training needs of UK healthcare professionals involved in advanced therapy delivery, an online training needs analysis survey was devised and circulated across the ATTC network. The survey was also shared with the London Advanced Therapy (LAT) and UK Clinical Research Facility (CRF) networks. The specific aims were:

1. To understand what training resources are currently available or in development to support healthcare professionals working with advanced therapies;
2. To identify where there are gaps in current training provision;
3. To establish priorities for the development of new training resources;
4. To identify additional points of contact such as local education and training leads.

3.1. Survey methodology

An online survey was constructed using the JISC Online Surveys tool⁵. A link to the survey was circulated to training leads across the ATTC/LAT/UKCRF networks.

3.2. Survey responses

In total 64 survey responses were received. The most responses were received from Birmingham, London and Manchester. It is important to note that some participants reported that they had completed the survey collectively with a team of colleagues; therefore the number of survey responses received underestimates the total number of participants (Figure 1).

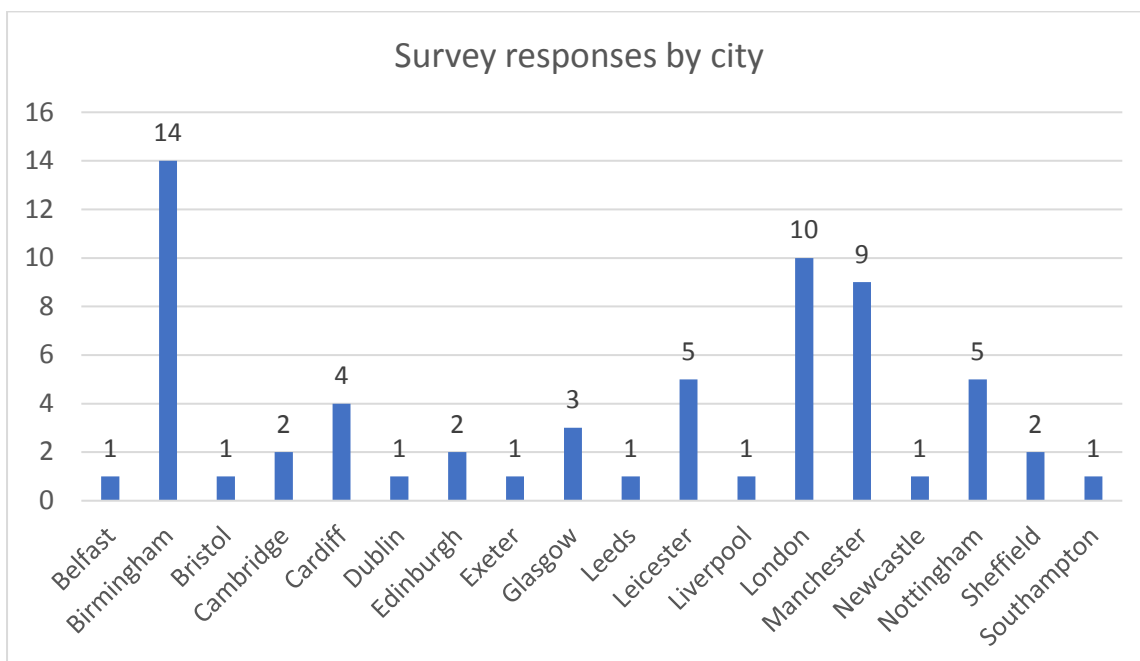


Figure 1 Survey responses by city

⁵ <https://www.onlinesurveys.ac.uk/>

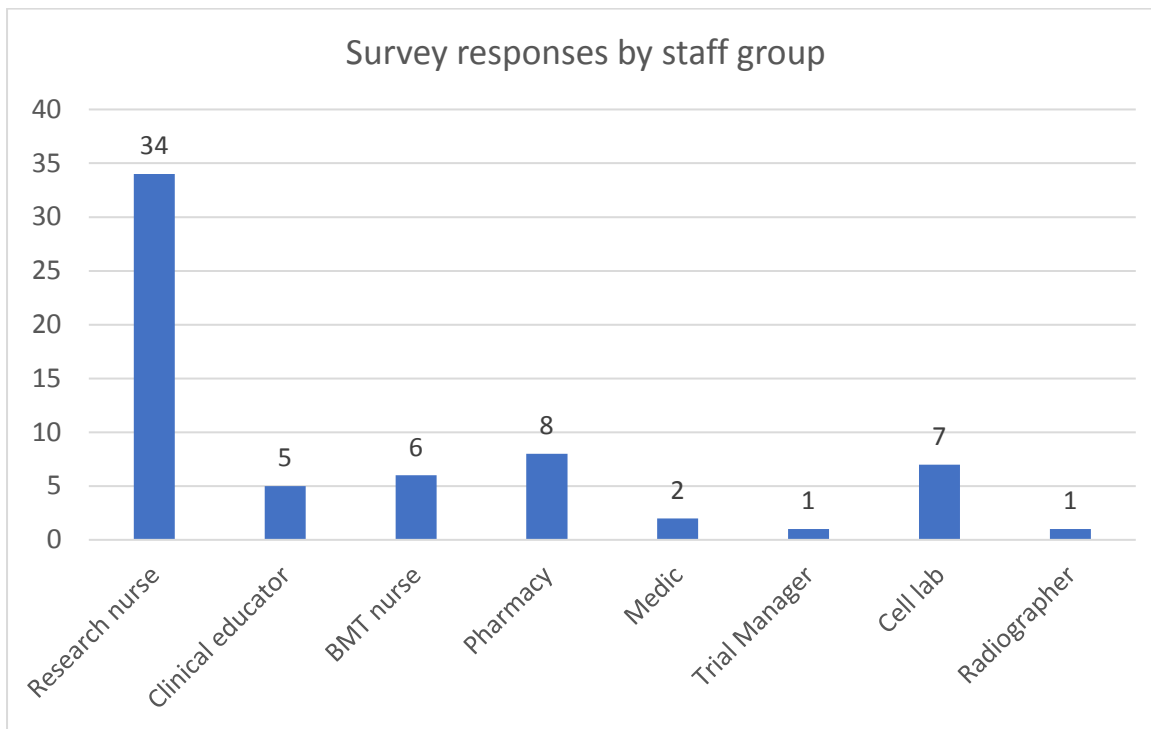


Figure 2 Survey responses by staff group

Most survey responses came from people working in research nurse roles (Figure 2), reflecting our understanding that nurses, particularly those working in clinical trials, should be considered a priority staff group for training in advanced therapy delivery. Focus group work across multiple hospitals has reinforced that educational resources are urgently needed to address the impact of ATMP adoption on nurses, stem cell laboratories and pharmacy.

Many of the respondents to the survey had very little or no experience with delivery of advanced therapies, but still engaged with the questionnaire (Figure 3). A number of hospitals who took part were preparing to start advanced therapy clinical trials, or to provide commissioned ATMPs, but had little experience of delivering these types of medicines. The survey indicated pockets of specialist experience around the country, but these were restricted to a few large teaching hospitals and generally limited to certain types of advanced therapy products (i.e. experience of delivering gene modified cells but not *in vivo* gene therapy, or *vice versa*).

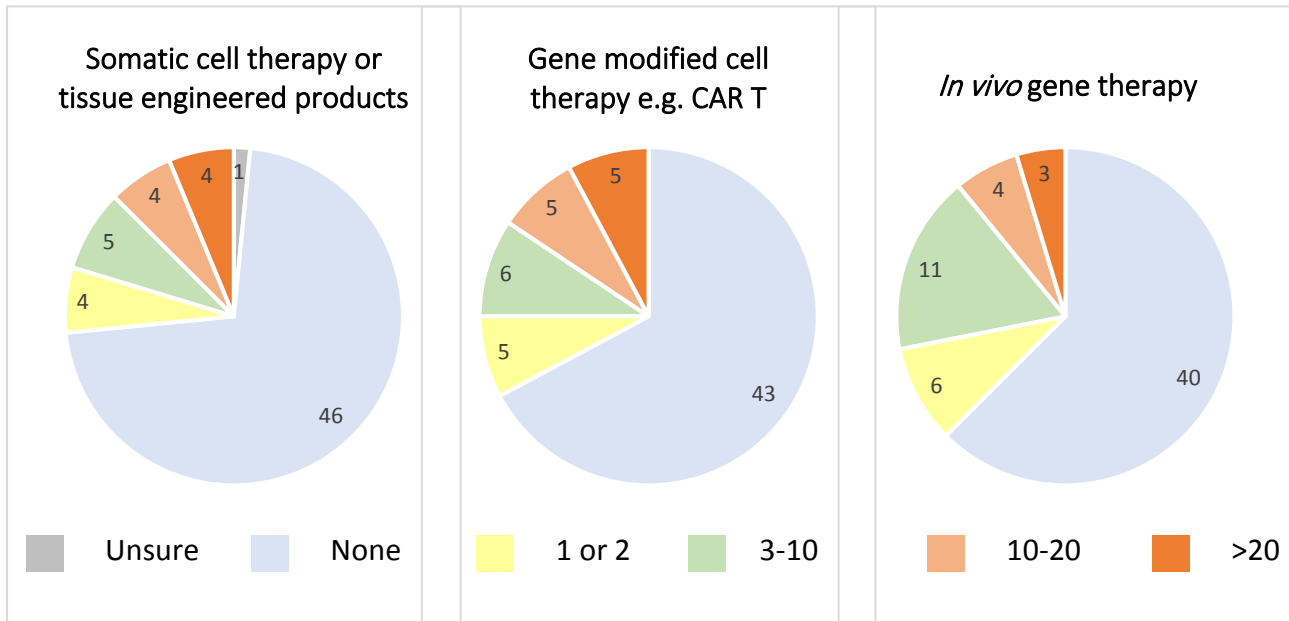


Figure 3 Number of patients that survey respondents have been directly involved in treating with somatic cell therapy/tissue engineered products, gene modified cell therapy or in vivo gene therapy.

Participants were asked to report on training resources that are already available or are being developed. For most topics specified, most survey respondents answered “no/don’t know” (Figure 4), indicating that these training resources are not yet widely available. Survey participants were also asked to provide further details of those training resources that are currently available or in the process of being developed. Findings from these free text responses are summarised in Table 4.

Just over half of respondents indicated that training materials are already available for thawing a cryopreserved cell-based product. Free text comments and follow up discussions indicated that these existing resources are largely limited to standard operating procedures (SOPs) that have been developed locally and/or by trial sponsors. The process of handling and thawing cryopreserved cells is unfamiliar to many healthcare professionals; careful training is required to ensure that staff are confident and competent to carry out this critical process correctly. Staff training to SOPs could be supported with more engaging resources utilising images and/or video footage. Although training resources are already available in some locations, 44% responded “no/don’t know” to this question, suggesting that there is a need to adapt product-specific training to produce more broadly applicable educational resources and/or to disseminate training materials more effectively.

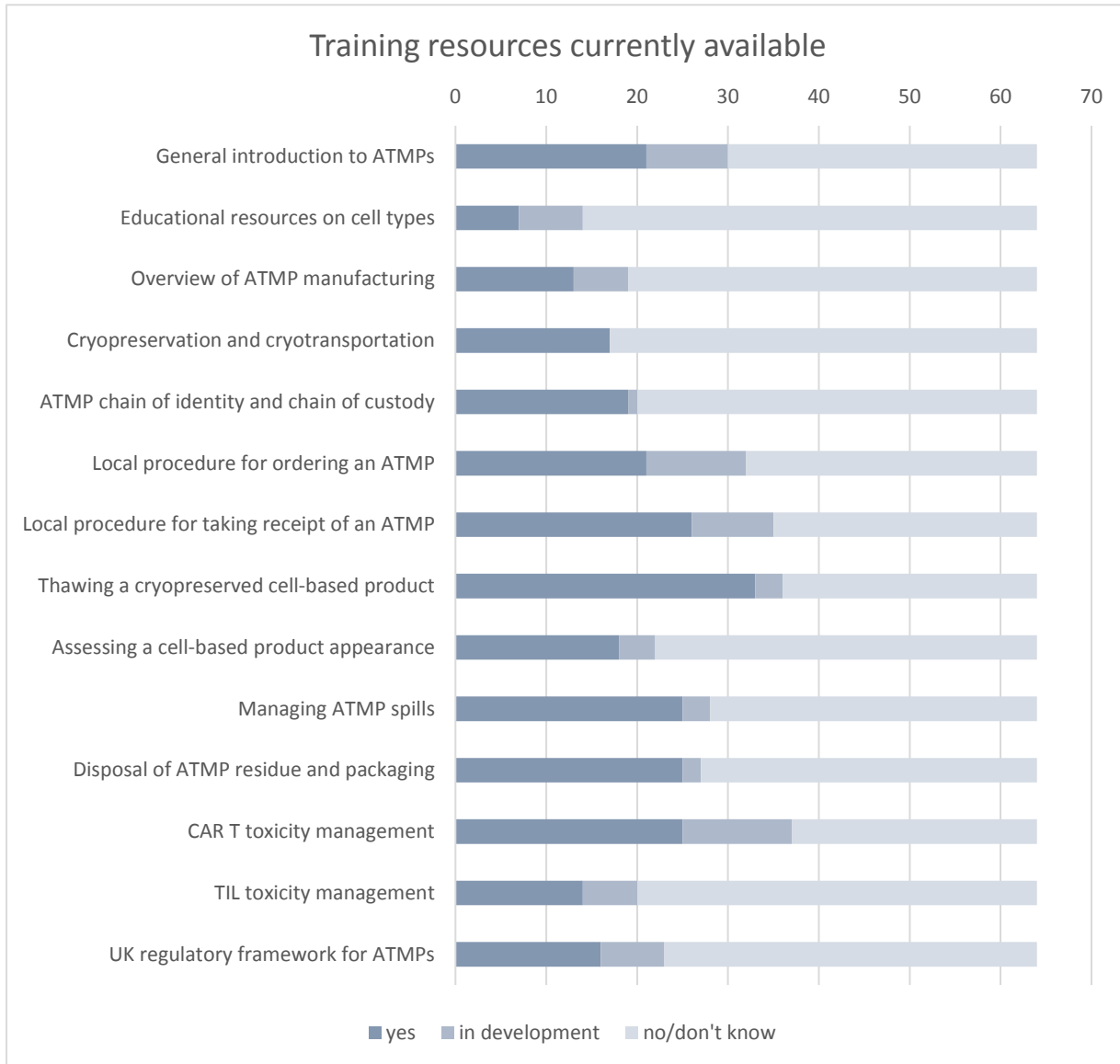


Figure 4 Survey findings on training resources currently available or in development

Training topic	TNA survey finding
<i>1. General introduction to ATMPs (overview of autologous/allogeneic pathways, ATMP classifications, example therapies)</i>	Limited introductory training available from National Institute for Health Research (NIHR), Aston University and the Clinical Research Network (CRN)
<i>2. Educational resources on individual cell types used in ATMPs (e.g. DCs, TILs, MSCs)</i>	Largely unmet training need
<i>3. A general overview of ATMP manufacturing, introducing processing concepts and terminology</i>	Largely unmet training need
<i>4. Principles of cryopreservation and cryotransportation</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>5. ATMP chain of identity and chain of custody</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>6. Local procedure for ordering ATMP X from manufacturer Y</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>7. Local procedure for taking receipt of an ATMP</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>8. Thawing a cryopreserved cell-based product</i>	Local/sponsor SOPs (study/CAR T-specific). Sometimes performed by cell therapy lab staff.
<i>9. Assessing the appearance of a cell-based product</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>10. Managing ATMP spills</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>11. Disposal of ATMP residue and packaging</i>	Local/sponsor SOPs (study/CAR T-specific)
<i>12. CAR T toxicity management</i>	Local documents and training
<i>13. TIL toxicity management</i>	Local documents and training
<i>14. UK regulatory framework for ATMPs</i>	Local pharmacist-led training
<i>15. General comments</i>	Majority of training is trial-specific from sponsors/locally developed or constitutes local documents and training focused on CAR T. No generic ATMP training is available and a national approach is required.

Table 4 Survey findings on existing ATMP training resources

Several respondents commented on their own inexperience and lack of currently available training resources around advanced therapy delivery:

“ **Minimal resources at present**, these all require development once we know what protocols will be implemented.

- Completely new to advanced therapies and need to implement all relevant training and protocols.
 - Haven't worked with ATMPs before.
 - I would welcome support with setting up advanced therapies.
 - I am new to oncology and ATMPs.
-

Helpful suggestions were made for key areas where training resources should be developed, and what people wished they'd known when they began working with advanced therapies:

“ **More education into how the cells work...** how to tell if they have been successful and **potential side effects**.

- I think there needs to be some education into the importance of team working, early communication and detailed plans as to who needs to be made aware of the patient and at what stage. For example, what notice do staff need to give to couriers, pharmacists and cell manufacturers, wards, ITU etc.
 - As a unit we would want to have generic training for all clinical staff and more in-depth training for staff working on ATMP studies.
 - Principles of cryopreservation and cryotransportation should include safety aspects of handling LN2 or LN2 vapour phase shippers and transporting around hospital sites.
 - Need better cross training among pharmacists, scientists, nurses and doctors - even if not performing tasks it is important to understand it.
 - Practised scenarios for things like Level 3 escalation and management of patients. Clear and agreed levels of responsibility and action. Trust Board level support.
-

Several comments were made around a need for targeted training on the regulatory aspects of advanced therapy delivery:

“ *From discussions held with managers, delivery staff are always well educated and have SOPs in place before starting a trial procedure with the products. There is more of a need to educate teams in the regulatory aspects of ATIMPs / GMSC requirements and the managerial responsibility of this work.*

- *Knowledge on tissue engineered products and regulatory requirements. Procedure for ordering locally and visual inspection are covered at SIV / induction level and generic training material may not be required.*
 - *Starting material requirements - e.g. consent, HTA licence requirements.*
 - *UK regulatory framework for cellular medicines when not managed through pharmacy.*
-

The need to streamline and standardise both processes and training was highlighted:

“ *Need for consistency in standard of training.*

- *A joint framework from all manufacturers rather than a different process for each CAR-T provider. Makes training cumbersome and difficult to manage in small teams.*
 - *National approach to CAR-T handling and storage required. Each company requires a different storage temperature, no double bagging, variable labelling etc.*
-

Survey respondents provided insightful comments around methods of training delivery:

“ *More interactive methods of teaching would be more helpful as the access of SOPs is self-driven and relies on the nurse looking out the information. Training videos or e-learning modules would be helpful.*

- *What would be useful is a recording / e-learning so that those staff including medics unable to attend the training due to shift work etc are able to access it – have a resource to reflect on.*
 - *Training videos will be valuable.*
-

Participants also indicated that they would welcome opportunities to learn from a wider network of colleagues delivering advanced therapies:



*We would welcome some **basic training/discussion forums** at regional multi-disciplinary meetings where **information/best practice can be shared** so that we are better equipped.*

- *I'd welcome any opportunity to meet with teams delivering ATMP, shadow or observe in order to establish the benchmark for training in this organisation. If you have any contacts you could share I would be very grateful.*
 - *Any other education training details / study days for ATMP please pass on.*
-

Respondents were also asked to report how many members of staff from their teams will be involved in various processes necessary for ATMP delivery (figure 5). Across the pathway, 15-23% of respondents were unable to say how many members of their team are or will be involved, whereas approximately half of survey respondents (42-63%) indicated that between 1-10 of their direct colleagues will participate. This indicates that while there is uncertainty around the practicalities of delivering these therapies to patients, it may initially be the responsibility of small numbers of clinical staff to oversee or conduct these novel processes. The safe delivery of ATMPs to patients involves a wide variety of skilled professionals and when taken together, even for a medium sized hospital, the number of staff who require some level of training on advanced therapies could soon reach into the hundreds.

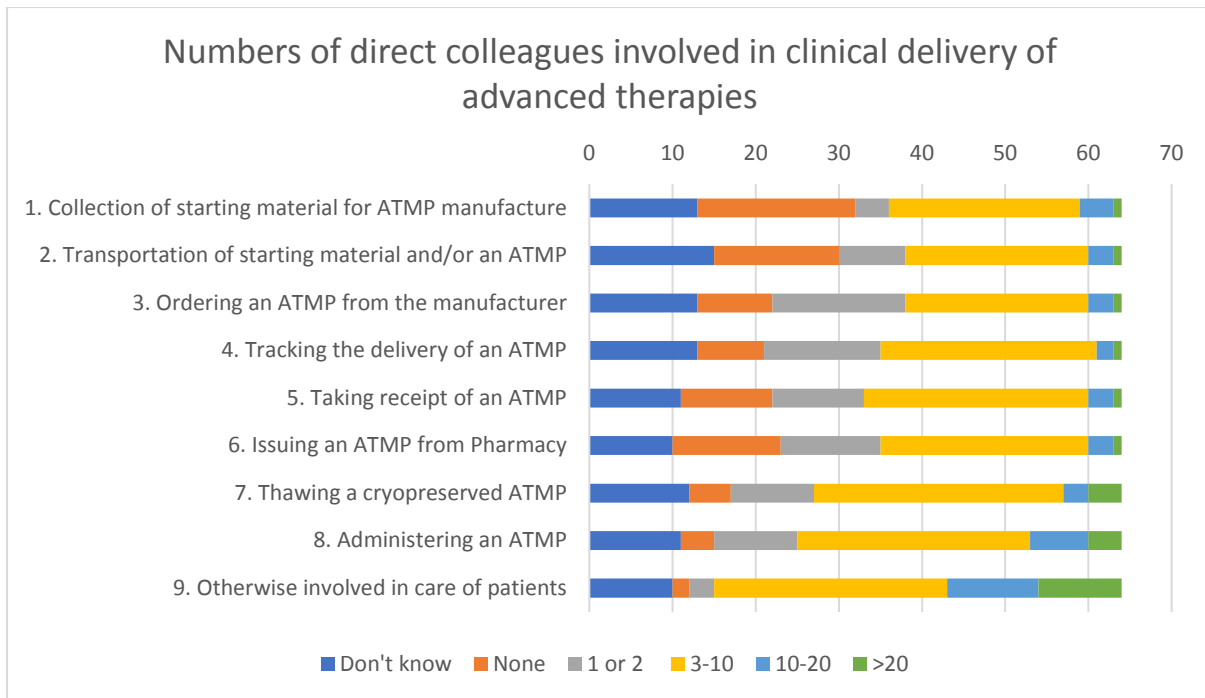


Figure 5 Numbers of direct colleagues involved with ATMP delivery. Survey respondents were asked how many staff from their team will be involved in processes along the ATMP pathway.

4. Conclusion

Advanced therapies are rapidly coming to the fore, both in a clinical trial setting and in commissioned services; the US regulatory authorities are expecting between 10 and 20 applications for marketing authorisation per year in the coming 5 years⁶. These treatments pose a significant number of changes to the current treatment paradigm, involving new ways of working for multiple professionals involved. Current training for NHS professionals largely consists of locally developed materials and therapy-specific information provided by product manufacturers. Such training is predominantly procedurally-driven and is delivered with variable levels of educational support to provide staff with essential underpinning knowledge, potentially leading to inconsistencies and knowledge gaps across the NHS workforce.

While the need for therapy-specific training must continue to be delivered locally in close partnership with product manufacturers and trial sponsors, it is not sustainable for hospital clinical education teams – who may be themselves require subject matter training – to locally generate, maintain and grow core education resources in such a rapidly evolving and expanding field of medicine. It will also be increasingly important to reach NHS staff working in primary care and secondary referring centres, who may not currently have access to specialist educational materials on the therapies that their patients are or will soon be receiving.

⁶ FDA Press release, Jan 15 2019; <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics>

There is a clear need and opportunity to create high quality training materials that will be scalable and accessible to anyone within the NHS involved in the care and treatment of patients with advanced therapies. The requirement for a standardised, national approach to the development of generic educational resources, that will equip NHS staff with theoretical knowledge and awareness to complement their practical training in the workplace, is evident from this report. The workforce has requested a blended approach, featuring a combination of regional/national meetings that can bring together specialist staff working in small clinical teams, but also the provision of a suite of high quality, relevant and engaging e-learning materials to cater for the needs of different workforce groups. This will require several iterations of development, beginning with the generation of training content of broad interest across the workforce. Once this overarching educational material is developed, more bespoke training packages should be produced to support particular staff groups in their specific role around advanced therapy delivery.

5. Recommendation

From the evidence presented in this report, there is a role for the health education authorities to take the lead and support the development of a suite of e-learning resources that cater for the different needs of the professionals involved in the delivery of advanced therapies to patients. As this is an emerging field, it is an opportunity to create the education standard across the country, being hosted on a reputable source that is widely accessible to the healthcare workforce. The introductory modules giving staff the knowledge of what these treatments are and how they work should be created immediately, along with resources covering the challenges involved in the logistics of these treatments. Finally, more detailed modules detailing individual therapies, their challenges and side effects could be created in a flexible manner as the need arises.

The UK is successfully positioning itself as the European centre for advanced therapies and having an educated and fully prepared workforce is a key element of this strategy. The development of training materials to support NHS staff in their treatment of patients can only benefit this approach.

6. Acknowledgements

The authors would like to thank all those who participated in the training needs analysis survey. We are particularly grateful to the ATTC network and the UK Clinical Research Facility Network for helping to reach a wider audience.