ATTC Advanced Therapy Treatment Centres

Northern Alliance Advanced Therapies Treatment Centre

Harmonised working: How NA-ATTC supports effective collaboration between NHS and Industry

Funded by

UK Research and Innovation

Coordinated by

CATAPULT Cell and Gene Therapy

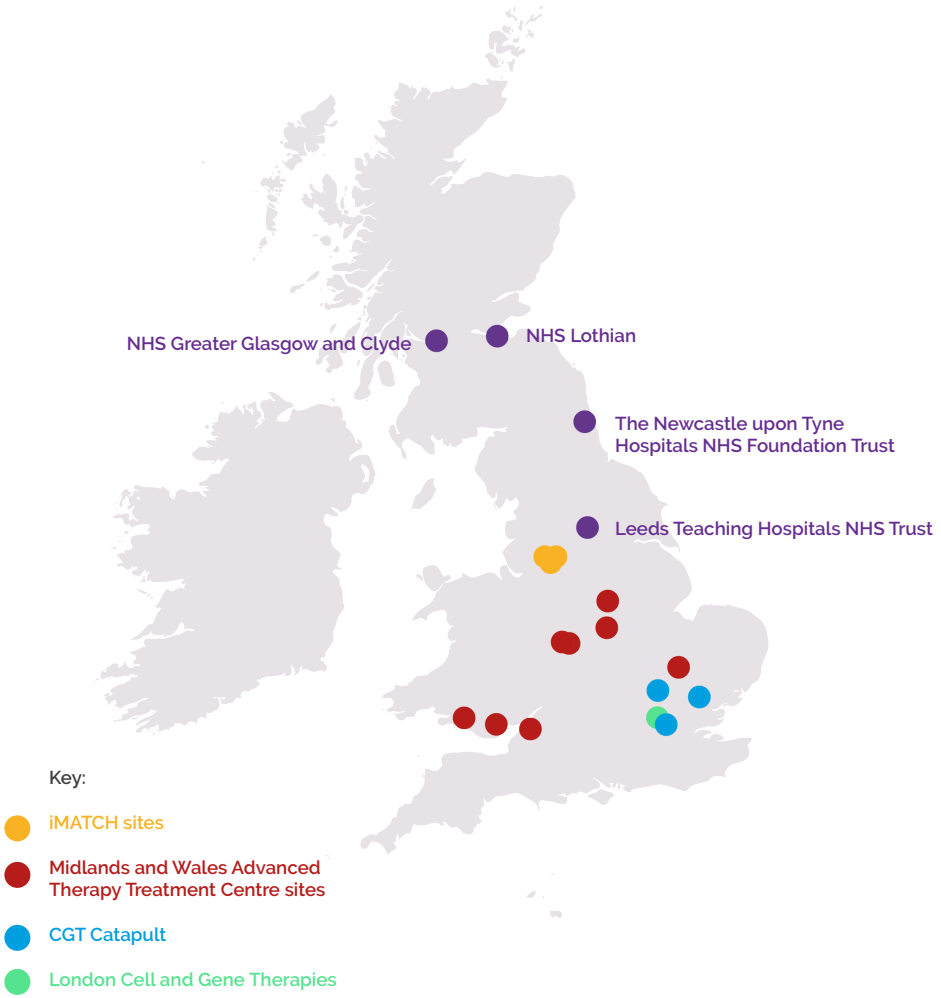
Who we are

The Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC) is a consortium of NHS trial sites and industry partners working in collaboration to improve patient access to Advanced Therapy Medicinal Products (ATMPs). NA-ATTC provides infrastructure, centralised resources and expertise to deliver these innovative medicines at scale to patients.
The geography of NA-ATTC clinical sites covers Northern England and Scotland.

The NA-ATTC is one of three centres in the ATTC Network which is funded by UKRI and co-ordinated by the Cell and Gene Therapy Catapult (CGT Catapult).

Our Approach

The alliance has taken an innovative pro-active approach to tackling the challenges associated with the development, set-up and delivery of complex trials across the NA-ATTC geography to ensure equitable access to patients.



Our Activities

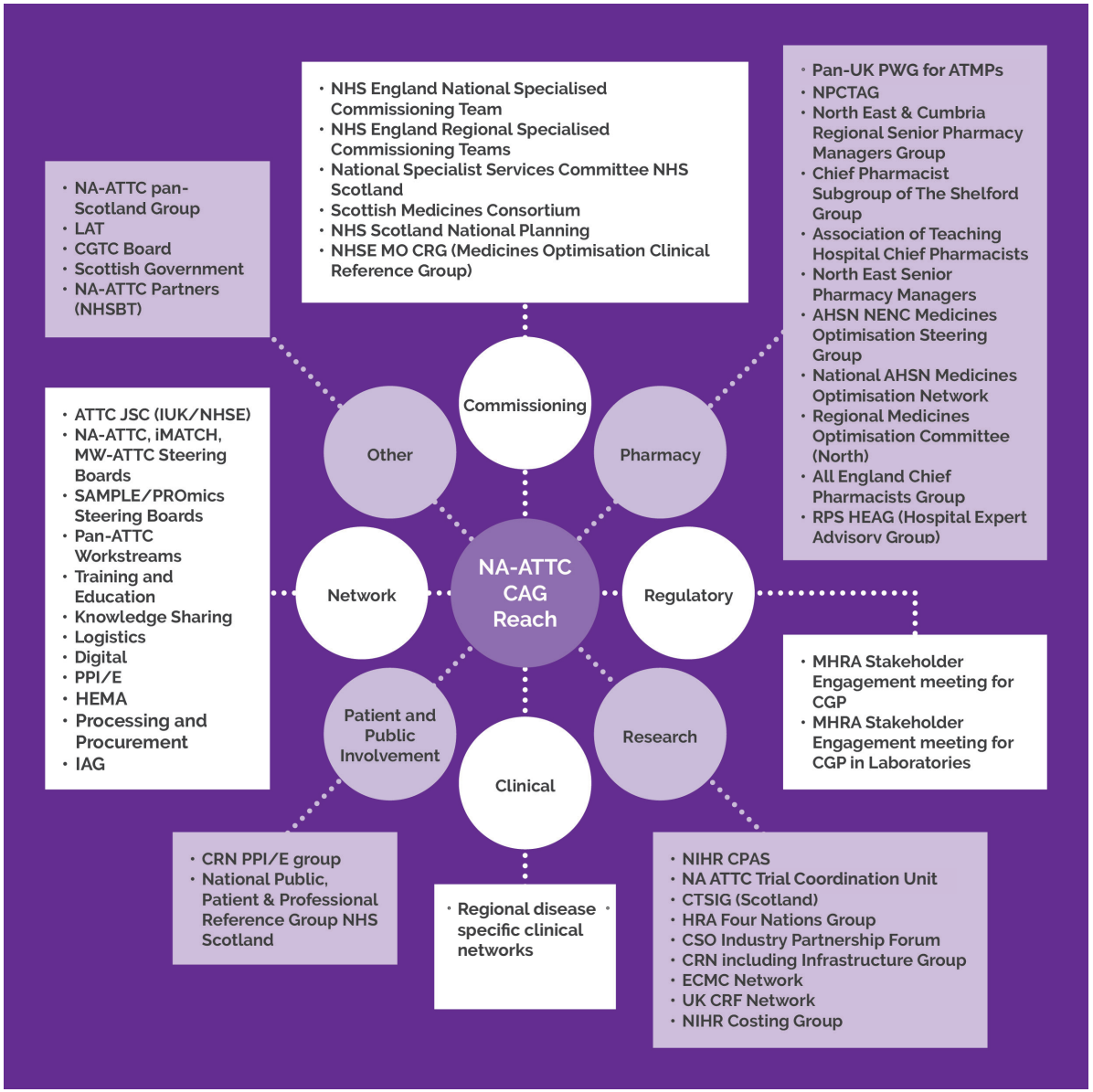
Clinical Advisory Group (CAG)

The NA-ATTC Clinical Advisory Group includes senior clinicians from each of the four core teaching hospitals in our area. Also represented on the Group are scientists and key stakeholders with clinical, academic, industry, commissioning and patient advocacy expertise. The CAG aims to accelerate implementation and successful completion of Advanced Therapy (AT) clinical trials and increase patient access to these products regionally and nationally by establishing and embedding cost-effective clinical delivery pathways which meet the needs of the providers of ATs, patients and multidisciplinary clinical teams.

Core functions of the CAG

- *Provides strategic oversight and facilitation of NA-ATTC clinical workstreams*
- *Identifies barriers to optimal and equitable patient access to ATs*
- *Fosters partnerships between stakeholder groups nationally / internationally*
- *Horizon-scanning to ensure institutional readiness for AT adoption and scale up of gene therapy clinical implementation*
- *Provides a single point of contact to enable an AT developer access to NHS organisations within the NA-ATTC.*

The reach of the NA-ATTC Clinical Advisory Group



Our Activities

Industry Advisory Group (IAG)

The IAG consists of industry representatives from both within and external to the NA-ATTC consortium. The main function of this group is to provide insight into matters of significant importance to industry partners in terms of clinical trials.

Core functions of the IAG

- *Horizon scanning for new Advanced Therapy products*
- *Engaging with companies outside of the NA-ATTC nationally and internationally*
- *Enabling early traction of new ATs by engagement with NA-ATTC*
- *Engaging agencies on areas of strategic importance*
- *Interacting with patient groups.*

Trial Coordination Unit (TCU)

The TCU provides an interactive forum for NA-ATTC NHS Clinical Centres to discuss and optimise operational delivery of AT Trials. The group was established to benefit from regional expertise and promote true collaboration throughout the NA-ATTC geography and accelerate trial delivery while establishing best practice and pathways for sustainable wider adoption / life-long follow up.

Core functions of the TCU

- *Development of published resources for training and upskilling of trial staff at NHS centres*
- *Sharing of best practice and knowledge exchange*
- *Contributing to and disseminating national health professional training initiatives*
- *Contribution to the development of national guidelines for set-up, delivery and governance of AT trials*
- *Establishment of cross site Multi-Disciplinary Teams to facilitate the implementation of AT trials.*

Knowledge Exchange / Lessons learned

Throughout the NA-ATTC project a strong emphasis has been placed on learning through experience. This has culminated in a formal 'Lessons Learned' audit being undertaken to better understand the experiences of NHS staff and industry partners when working together in real world clinical trial delivery.

The audit focused on three simple but fundamental themes:

- **What works well**
- **What can be improved**
- **What improvements could be suggested.**

The responses received have provided valuable insight into the set-up and delivery of trials within the NA-ATTC but we feel these experiences are likely to transcend the boundaries of the NA-ATTC region and that the lessons learned and recommendations will be applicable nationally.

Factors contributing to successful set-up and delivery

Communication: It was unanimously agreed among both NHS and Industry respondents that effective communication between trial sites and the sponsor organisation was a key factor in the successful delivery of a trial protocol. Although this would be expected in all study settings, the need for effective communication and training in the context of AT trials was seen as being particularly vital due to the additional complexities associated with these studies.

NHS Perspective: When giving examples of what effective communication means to them, the NHS respondents were keen to emphasise the importance of properly timed and comprehensive site selection discussions and site visits. Significance was placed on ensuring that study sponsors were fully aware of the capabilities and infrastructure at sites as early as possible. This was seen as particularly relevant for NHS organisations with facilities spread across multiple hospital sites.

Industry Perspective: When citing examples of effective communication it was clear that industry partners valued an increased level of engagement from investigators and close collaboration between the sponsor and the key stakeholders at site including nursing and pharmacy staff. It was noted that both NHS and Industry partners appreciated frequent and open discussions from initial feasibility through to patient recruitment and beyond.

Experience: Another area of unanimous agreement from both NHS and Industry perspectives focused on the significance of utilising experienced staff in the delivery of AT trials. It was recognised that ensuring both sponsor and site staff were suitably trained and knowledgeable led to more successful trial delivery. It was noted that the need for specialised staff went beyond those delivering the treatments and included clinical trial coordinators and R&D staff. Additionally it was noted that sponsor representatives with a good understanding of local NHS site process and national guidelines was a significant factor in determining success.

Consistency: When discussing the factors attributed to success, a key element which both NHS and industry partners valued was consistency. When discussing the issue of consistency there were a broad range of opinions relating to how this factor can affect success.

NHS Perspective: Respondents valued consistency in terms of specific sponsor training requirements and national guidelines, for example the acceptability of GCP training provision and the frequency at which this must be repeated. NHS partners also noted the benefits of consistency of sponsor staff and valued being able to build relationships with specific CRA's. NHS sites also valued a stable and structured approach to queries and requests for data and noted the difficulty in responding to frequent ad-hoc requests.

Industry Perspective: As with their NHS colleagues, industry responses also highlighted the value of consistency when working with NHS staff and the importance of relationship building. It was noted that sites which employ a coordinated approach to ensure consistency in their support department, Capacity and Capability and amendment approval process were greatly valued.

Working towards a truly synergistic harmonised co-production between Industry and the NHS

While it was clear that respondents had many positive experiences working together in the set-up and delivery of AT trials at NHS sites, both industry and NHS colleagues felt further improvements could be made in order to streamline process and accelerate trial delivery.

NHS Perspective:

Protocol Development: NHS trial sites noted that difficulties can arise when working with rigid trial protocols which do not often fit well with NHS or site level processes. This had been found to extend set-up times in order to develop solutions to avoid deviation.

It has been suggested that industry partners may wish to work more closely with NHS sites while developing protocols to utilise existing practice and NHS expertise. This feedback also extended into the use of specific equipment while administering the protocol. It was found that sites did not always use the same brand of equipment specified which had led to issues and delays, it was recommended that sponsors make allowances for this.

Standardised Documentation: NHS sites highlighted issues associated with running a number of AT trials with different sponsors and the variance in sponsor specific documents.

It was suggested that sponsors may wish to consider working with other sponsors and UK regulatory bodies to develop (where possible) a suite of standardised sponsor documents.

Standardised Wording: NHS sites also found that the need to complete a number of internal risk assessments (early phase committee, Genetic Modification Safety Committee (GMSC)) resulted in a considerable duplication of work to complete several forms requesting similar information.

It was accepted that NHS sites must work to reduce this burden on staff but it was also suggested that sponsors may be able to facilitate parts of the process via the provision of standard wording and part completion of any standardised cross-Trust / Board forms which may be developed.

Industry Perspective:

Coordinated Review Systems: Responses received from those directly involved in setting up NHS research sites highlighted the value in joined up internal systems such as a parallel R&D and support department review. It is suggested that sites consider setting up dedicated AT committees to ensure a coordinated approach to site level capacity and capability review. Additionally it was recommended that costing and contract finalisation be prioritised as this can often cause delays when taking place later in the process.

Improved IT Systems: Industry respondents also suggested that the NHS may wish to be more flexible and willing to utilise advances in technology to enable the sharing and access of site data for sponsors. Examples given included enabling remote access to study participant records and greater uptake in the use of file sharing platforms.

Proactive Communication & Feedback: Sponsor representatives would welcome increased dialogue with NHS sites throughout the set-up and delivery process. Including updates on significant internal changes to process, structures and key contacts. It was suggested that provisions should be made for an increase in the frequency of joint sponsor / NHS meetings throughout the trial lifecycle in order to share feedback and update information.

Outputs

Putting lessons learned into practise

Building confidence through training

In recognition of the importance of sharing knowledge to accelerate and improve processes, NA-ATTC partners have engaged in a number of initiatives which aim to enable activity and knowledge to be rolled out throughout the Alliance.

To facilitate the roll-out of CAR-T trials in multiple NA-ATTC centres, The Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) hosted a knowledge sharing event for 50 NA-ATTC delegates. The event was organised and coordinated by Autolus Therapeutics.

The event provided a forum to enable Autolus and NHS colleagues to share the practical lessons learned from working collaboratively in the set-up and delivery of CAR-T clinical trials in Newcastle. The day featured sessions providing perspectives from the sponsor and the clinical site sharing experience of delivering CAR-T trials, given by Apheresis, Cellular Therapies Facility, Pharmacy, Research Nurses and Trial Administrators. Workshop sessions also took place in which delegates engaged in activities designed to help assess institutional readiness to deliver CAR-T trials.

Advanced Therapies Clinical Trials Toolbox

The Trial Coordination Unit have developed, and implemented throughout the NA-ATTC region, the AT Clinical trials Toolbox. The Toolbox specifically addressing the unique complexities associated with AT trials by providing information and guidelines to assist NHS Trusts and Boards, clinical leads and industry and academic partners to better understand the diverse and specialised processes involved in the set-up and delivery of AT trials and to streamline trial set-up within the NA-ATTC View toolbox **https://www.theattcnetwork.co.uk/wp-content/uploads/2020/02/NAATTC-WP3-external-toolbox.pdf**

Establishing disease specific clinical networks

The NA-ATTC recognises the important role clinical networks can play in disseminating knowledge, learning and best practice, supporting professional development and driving improvement.

We are working to develop cross-organisational clinical networks to serve as a mechanism to support in the preparation and delivery of AT trials and provide a foundation to enable potential regional hubs to be created allowing for studies to run in multiple NA-ATTC centres or provide preferential pathways for patients which ensure fair and equitable access to these sought after therapies.

To date the NA-ATTC has successfully aided in the development of several clinical networks and facilitated the set-up and delivery of AT trials in multiple NA-ATTC centres and have supported other sites nationally.

Case Study: Macrophage (MATCH Trial)

Liver disease is the third leading cause of premature death in the UK, with deaths increasing by 400% since 1970. Currently the only curative option for end-stage liver disease is liver transplantation. Two partners within the NA-ATTC (University of Edinburgh and Scottish National Blood Transfusion Service) have been developing a new macrophage cell therapy for liver cirrhosis. Clinical trials commenced in 2016 within the MATCH (Macrophage therapy for Liver Cirrhosis) study.

In 2018 the MATCH study (EudraCT Number: 2015-000963-15) successfully completed phase I trials and was moving into phase II. The study was able to expand to multiple clinical sites quickly due to the network within the NA-ATTC. Not only has this aided in meeting recruitment numbers but also has allowed the exploration into stable transportation of the starting material and therapy, expanding into potential technology transfer. Provision of this therapy on a national scale will need to involve close collaboration between partners, as shown within the NA-ATTC and further afield in the ATTC Network.

Outputs

Implementing harmonised processes within NA-ATTC centres

In recognition of the feedback received from NHS and industry partners, relating to the need for consistency of process. NA-ATTC stakeholders have been leading on initiatives nationally and within the consortium aimed at developing and refining processes to ensure simplified and consistent pathways exist within centres to accelerate AT trial set-up.

Working groups have been set-up and facilitated through the TCU to ensure consistent mechanisms are in place at sites to support investigators and AT developers in the set-up and delivery of trials; this has included the scoping of dedicated AT committees, shared document sets within NA-ATTC centres and mechanisms for the collection and dissemination of AT trial metrics data within the alliance.

Case Study: DMD Hub – efforts towards harmonisation of Risk Assessment reviews (to accelerate access to trials).

The DMD Hub **https://dmdhub.org/** is a network of trial sites with trained staff which are funded to carry out clinical trials for Duchenne Muscular Dystrophy and have worked closely with the NA-ATTC.

A key recommendation from DMD Hub forums was to 'Consider how the DMD Hub can accelerate R&D process and regulatory reviews for gene therapy trials including exploring the idea of centralised gene therapy ethics committees, central coordination of costing and contracting and harmonisation of risk assessment review committees'.

The DMD Hub has initiated discussions around harmonising and sharing resources / template documents relevant for GMSC risk assessment reviews.

In the first instance, the two neuromuscular centres of excellence agreed to share GMSC risk assessment reports with the DMD Hub to review and identify if there were any specific points of interest between the reviews. The Principal Investigators (PIs) for the trial are currently seeking approval from the GMSCs and Sponsor for the DMD Hub to share the reports with less experienced trial sites, to support and facilitate their GMSC's review.

With limited spaces available for patients and competitive recruitment at sites, the PIs are keen for sites in the UK to open in quick succession. By sharing the risk assessment report from the lead site it is expected that site set up will be accelerated and facilitate a harmonized approach.

The DMD Hub feels well placed to help facilitate a central discussion between the chairs of appropriate GMSC with a view to reaching consensus on any points of discussion. (This suggestion was included in the DMD Hub 'lessons learnt' document available as part of the DMD Hub Toolkit).

Feedback from industry on the proposal to share resources, streamline reviews and facilitate a joint meeting between the GMSCs has been positively accepted and the DMD Hub aims to add resource / processes approved and developed to its central coordination activities.

With increasing numbers of DMD gene therapy trials in the UK, the DMD Hub intends to work with the NA-ATTC to align efforts on the development of a national template for gene therapy risk assessments. The information required by the sites from industry, to complete the GMSC risk assessment, should be consistent and therefore a standardised list of questions to be discussed during the GMSC reviews could be developed.

Outputs

Working with Patients – Understanding & Informing
Within the NA-ATTC, it is understood that collaboration is vital for success and that patients are key collaborators. The Alliance has undertaken a range of activities to ensure a patient-centred approach to promote successful, accessible and effective trial delivery to patients.

Patient Advocacy within the NA-ATTC
We have ensured patient and public involvement remains at the core of the NA-ATTC Clinical Advisory Group with patient advocates part of the core membership.

Patient and Carer perspectives of CAR-T Treatment at NA-ATTC centre
An evaluation of patient and carer experience of the CAR-T treatment pathway at the Northern Centre for Cancer Care (Newcastle) has been conducted. This specifically aimed at understanding the acceptability of the current service and seeking feedback on areas of need in order to deliver truly patient-centred care.

The CAR-T-Cell Therapy Clinical Trial Journey - A Guide for Patients and Carers
A Patient Advisory Board was organised by Autolus, which comprised of patients who had previously received CAR-T therapy and their caregivers, who had been intimately involved with the treatment journey.

Feedback provided during the workshop indicated that information for both patient and caregivers is scant and is perceived as a significant gap by both parties. Autolus, in partnership with NA-ATTC, took these comments, as well as similar feedback from site staff from UK centres experienced in CAR-T delivery, to provide a comprehensive guide to help patients and carers through their journey.

The guide provides patients and caregivers with support via education and advice throughout the whole treatment journey whilst also providing a teaching aid for clinical staff. This resource, The CAR T-Cell Therapy Clinical Trial Journey – A Guide for Patients and Carers can be accessed via **https://www.theattcnetwork.co.uk/car-t-patientguide**

Informing Patients
Healthcare professionals within NA-ATTC centres have contributed to and provided feedback on AT specific resources for patients and carers. They have also presented at a variety of educational events for patients and patient advocates.

Find out more about NA-ATTC:
Web: **https://www.theattcnetwork.co.uk/centres/northern-alliance**
Twitter: **@naattc**
Email: **nuth.NAATTC@nhs.net**

We would like to thank everyone who contributed to the 'Lessons Learned' audit and creation of this document.