Advanced Therapy Treatment Centres

iMATCH
ADVANCED THERAPY TREATMENT CENTRE

# Innovate Manchester Advanced Therapies Centre Hub (iMATCH)

## A Coordinated Strategy to Scale-Up Advanced Therapies for Patients in Manchester

Funded by
UK Research and Innovation

Coordinated by
CATAPULT
Cell and Gene Therapy

# Contents





# Foreword

## It is hard to believe that four years have passed since we held our iMATCH kick-off meeting in March 2018.

A lot has changed in the world since then, but remarkably the iMATCH collaboration has gone from strength to strength, fulfilling the wide ranging objectives it set out with: improving access to Advanced Therapy Medicinal Product (ATMP). This included integrating sample collection, developing sample traceability and tracking systems through digital solutions, developing an innovative data capture system to address the complexity of ATMP therapies, scale-up in the clinical setting and enhancing safe delivery through education, communication and dissemination.

Importantly, the infrastructure created through the collaboration has enabled us to develop new projects as we have gone on, flexing to the rapidly changing landscape. This includes the establishment of new working relationships, for example in COSMIC-19, and detailed Health Economic analysis. The addition of our 'Runway' projects has meant we have had the opportunity to explore new avenues. One example of this is the optimisation of patient referral pathways for ATMP trials; a project that evolved from one of our iMATCH ATMP MSc student projects.

It is testament to the strong relationships that have grown out of iMATCH that several new projects and funding streams are now building on the original work packages, enabling the collaboration to continue to contribute to this exciting and rapidly developing field going forward.

**Professor Fiona Thistlethwaite**
Medical Oncology Consultant ECMT,
Honorary Professor at The University of Manchester,
iMATCH Director,
Christie NIHR CRF Director

# Overall vision

To transform the conduct of Advanced Therapy Medicinal Product (ATMP) clinical studies to make them as routine to deliver as non-ATMP clinical studies

## Overall aims

Using exemplar products to:

- **Create easily run and ready to use systems and solutions that can be rolled out more widely to the NHS.**
- **Drive Institutional readiness and patient access to ATMPs.**
- **Share learning across UK hospitals to accelerate adoption of ATMPs.**

iMATCH consortium

# Scale up of Sample Acquisition, Processing and Storage

## Collection and Storage of Cellular Components

### Summary

We aim to generate across ovarian, renal and melanoma, and then expand into other cancer sites. This will combat the urgent need to develop protocols for the processing of surgical samples, allowing advanced therapeutics to be integrated into routine clinical care.

A rolling programme of education, pathway mapping, and tissue collection will be applied to each cancer site in turn. The focus will be on cancer teams within Manchester University NHS Foundation Trust (MFT – where most surgical oncology takes place), but also developing links and protocols with the smaller surgical sites including Salford Royal NHS Foundation Trust and The Christie NHS Foundation Trust where relevant. For each cancer site, the aim will be to obtain surgical biopsies and then apply our existing protocols to demonstrate feasibility and efficacy of T cell extraction and expansion. From here, we can develop a robust SOP for future tissue collection, thus ensuring a sustainable ongoing tissue collection pipeline.

In addition to this, we aim to use existing ethics approvals and collaborations to collect tumour samples from a range of solid tumour indications to drive pre-clinical development of gene engineered TIL (Tumour Infiltrating Lymphocytes – developed by Instil Bio). Enabling us to further understand the characteristics and functions of tumour infiltrating T cells in a wide range of solid tumour indications.

Standardised tissue collection protocols and SOPs will be developed. Tumour materials will be used to generate laboratory pre-clinical data to explore how useful current methodology that has been developed for melanoma and ovarian tumours will be when applying to a wider array of cancer indications. The phenotype, proportion of tumour reactive cells, characteristics of tumour response, TCR (T cell Receptor) repertoire and behaviour of TCR clones of TIL from different tumour indications will be assessed. Small scale process development runs will be conducted to assess the feasibility of TIL manufacturing process in multiple solid tumour indication. GMP scale runs will verify the suitability of manufacturing process to inform the design of Instil Bio's product pipeline.

### Objectives

- Collected tumour materials in multiple indications to support Tumour Infiltrating Lymphocyte research and manufacturing.
- Established scientific collaborations on solid cancer T cell immune profiling with MFT gynaecology lab (Prof Richard Edmondson) and Department of pathology.

### Case Studies

Developing a standardised pipeline for tumour sample collection across Greater Manchester
**bit.ly/3hJEFsN**

> *The ability to work with coordinated and patient focused leaders in the field will enable the UK to stay at the forefront of product development in new therapies. As proof of this, the tumour material collected within this phase of the project has been used to support Instil Bio's process development for our TIL based therapies in multiple solid cancer indications, with the collection pathways developed also informing Clinical trial design for Instil Bio.*
>
> **Instil Bio (UK)**



## Scalability of Automated TIL Processing

### Summary

The main aim is to link other aspects of the project in order to enable the resection of tissue to be processed in an automated device to improve cost effectiveness of Tumour Infiltrating Lymphocyte (TIL) processing and storage.

To do this, Clinical Site Stakeholder interviews with The Christie NHS Foundation Trust and Manchester University NHS Foundation Trust will be conducted in order to understand what the requirements will be for both device integration within each hospital, and tumour tissue collection for human use as part of an Advanced Therapy Medicinal Product (ATMP).

It is also necessary to understand the impact that Advanced Therapy Medicinal Product manufacturing will have on the manufacturer. This includes elements such as: regulatory and associated licences, facilities and staff, and risk assessment regarding quality and safety for Advanced Therapy Medicinal Product manufacture with regards to starting material, processing, storage and issue.

### Objectives

- Enabled resection of tissue to be processed in an automated device to improve cost effectiveness of TIL processing and storage.
- Integrated feasibility into Clinical site(s) for the automated device into the clinical procedures for tumour collection Tumour Infiltrating Lymphocyte harvest.
- Conducted a Medical Device compliance review for automated devices.

### Case Studies

Clinical Feasibility and Treatment Outcomes With Unselected Autologous Tumor Infiltrating Lymphocyte Therapy in Patients With Advanced Cutaneous Melanoma. Scan the QR code to view the presentation.

> *Instil Bio have received multiple samples of tumour materials as part of the iMATCH ATTC program. These were processed using the early concept of the Instil Bio automated procedures for processing starting material, enabling manufacture of patient therapies that is dislocated from the patient's geographical location or just in time manufacturing. These learnings provided opportunities to understand the challenges facing the industry within clinical sites enabling Instil Bio to implement a suitably controlled strategy in Phase II clinical trials across multiple geographies including the UK.*
>
> **Instil Bio (UK)**

# e-Track and Trace (ATMP Supply Chain)


**Summary**

Advanced Therapy Medicinal Production is a complex multi-step process that requires integration of many interventions from the donor or patient starting material, Advanced Therapy Medicinal Product (ATMP) manufacture and back to patient 'needle-to-needle' chain of custody.

Key factors of this integration include connecting clinical and ATMP manufacturing teams with partners such as: supply chain companies, couriers, device manufacture, or suppliers and systems. This will ensure a robust audit trail for factors such as temperature integrity, labelling and data capture both external to and within the ATMP manufacturer. Importantly, the systems developed will be transferable across different ATMPs and disease types and be compliant with UK legislation such as The Human Medicines Regulations 2012.

In order to develop these systems, the aim is to scope out an optimal eTraceability solution and map regulatory requirements to make sure this is compliant. This will include testing and validating the eTraceability solution using InStil Bio exemplars and selecting and defining a User Requirement Specification (URS) for the eTraceability Solution in order to review and assess the market.


## Objectives

- Developed a collaborative solution with key players in the delivery chain, manufacturers, and clinical sites to assess an electronic platform which now stakeholder requirements can be collated, tracked, and documented to minimise the duplication of labour and records, providing transparency for oversite by the relevant stakeholders, regulators and ultimately investors.
- The software as a minimum has enabled scheduling procedures and integrated the data associated with starting material procurement, courier chain, critical devices, and where it is designed for data transfer and can be uploaded (such as Cytiva freezers, thawers and shipping containers & apheresis devices).
- We used iMATCH partners current practice initially to develop clinical advice that would assess an optimal electronic platform by which stakeholder requirements can be collated, tracked, and documented to minimise the duplication of labour and reduce the risk of error between records. Ultimately providing transparency for oversite by the relevant clinical stakeholders, ATMP manufactures, regulators and payers.

> *As part of the iMATCH project, Instil Bio scoped out an end-to-end eTraceability strategy which clearly aligned the 'Chain of Custody & Identify' from patient consent & surgery (where we collect the patients' cells) through to final cell therapy drug receipt at the clinical site. These learnings were then used to guide the final electronic solution which was designed, qualified, and implemented for use in the Instil Bio Delta-1 ITIL-168 clinical Phase II trial with material being harvested within US hospitals and used for TIL therapy manufacturing in Instil Bio's Manchester GMP site.*
>
> **Instil Bio (UK)**



# Intra Manufacture e-Traceability


**Summary**

We aim to test in the 1st instance the University of Manchester's Advanced Therapy Medicinal Product (ATMP) exemplar adoption of a LIMS (Laboratory Information Management System) system to connect the research laboratory to the patient (bench-to-bedside) and the ability to manage samples in a secure and fully auditable system, critical to the development of Advanced Therapies

Further work will look to evaluate cell freezing preservation technology and associated software from Cytiva with several ATMP cell types


## Objectives

- Understood the potential for and integration of an eTraceability infrastructure to enable other iMATCH partners to learn and potentially adopt the system.
- Compared freezing/thawing with VIA Freeze and conventional methods.
- Compared VIA freeze for viability, expansion, and differentiation at varying timepoints.

> *There is an urgent need for well validated pipelines for expansion and utilisation of pluripotent stem cell derivatives for cell therapy. iMATCH has allowed us to explore the use of associated technology for LIMS (Laboratory Information Management System) pipeline sample management.*
>
> **Professor Sue Kimber,**
> **Professor of Stem Cells and Development,**
> **The University of Manchester**

## Manufacture of ATMPs in Later Phase Trials

### Summary

We have been developing haematopoietic stem cell gene therapy for neurological lysosomal storage diseases for several years with Advanced Therapy Medicinal Product (ATMP) based trials planned for Mucopolysaccharidosis IIIA (MPSIIIA), MPSIIIB and MPSII.

Whilst we have already made vector for MPSIIIA and performed much of the required safety data for this trial, a significant bottleneck remains in the clinical scale up of the ATMP for future trials and the generation of appropriate release criteria prior to phase I/II clinical trials.

We will therefore develop a GMP (Good Manufacturing Practice) process for ATMP production with clinimacs CD34 cell separation and GMP transduction of CD34 cells and establish a clinical process for future ATMP trials.

(Work conducted at UoM and NHSBT Barnsley Facility)

### Objectives

- Established scale up at GMP for autologous hCD34+ cell transduction with appropriate release criteria.
- Established working protocols for scale-up of GMP Advanced Therapy Medicinal Product (ATMP) manufacture of CD34+ cells for clinical trial.
- Defined appropriate release criteria for ATMP products at GLP (Good Laboratory Practice).
- Developed and incorporated transduction enhancers (lentiboost and protamine sulphate), as used in the recent MPSIIIA clinical trial, into our clinical stem cell transduction protocol.
- A range of GMP MPSII lentiviral vector MOIs (multiplicity of infection) were evaluated with the TEs at small scales to determine which is the most effective. Optimum transduction conditions were taken forward and a full 'at scale' transduction run in GMP-like conditions was conducted in the Bigger research lab with the same reagents and consumables (as used at GMP), all the necessary samples for QC analysis were collected throughout and the Batch Manufacturing Record and associated documentation was updated in preparation for transfer to a cleanroom facility.

*Leveraging our successful collaboration with NHS BT in Barnsley, iMATCH enabled us to develop a new GMP manufacturing capability for haematopoietic stem cell gene therapy (HSC GT) using transduction enhancers to improve lentiviral transduction of HSCs. This is available to be used for downstream clinical trials, such as our upcoming HSC gene therapy trial in Hunter disease funded by Avrobio, planned for delivery at Manchester University Hospitals Foundation Trust, as well as other candidate products currently under development and other trials requiring this kind of manufacturing.*

**Professor Brian Bigger,**
**Professor of Cell and Gene Therapy,**
**Stem Cell & Neurotherapies,**
**The University of Manchester**



# Management of Clinical Data

## Robust Systems for Clinical Data Collection

### Summary

The overall aim is to establish a robust system for the clinical data collection of complex Advanced Therapy Medicinal Product (ATMP) trials. From here, best practice can be developed to ensure cost-effective data collection and visualisation solution is there for later phase ATMP databases.

An Innovation Hub is aimed to be built so that a compliant platform for collaborators within the iMATCH consortium can share data and content with each other in a single 'end-to-end' solution that is compliant with Good Clinical Practice (GCP) and all relevant regulations.

### Objectives

- Established robust systems for clinical data collection for complex Advanced Therapy Medicinal Product (ATMP) trials by developing a scalable, cost-effective data collection and visualisation solution.
- Explored complex requirements to determine best practice for later phase ATMP databases, and built a library of data collection and data analysis standards that are applicable across different types of ATMP studies.
- Scoped, built, and delivered an Open Innovation Hub which provided a compliant platform for collaborators within the iMATCH consortium to share data and content with each other in a single 'end-to-end' solution that is compliant with Good Clinical Practice (GCP) and all relevant regulations.

### Case Studies

Enabling data science to support cell therapy clinical trials
**bit.ly/3uVhOme**

*We are delighted that these interactions and collaborations led to Aptus being entrusted to manage the clinical data for both COSMIC-19 and EMBRaCE-GM studies.*

*We have also benefitted from the co-development of an eTMF (electronic Trial Master File) and several pieces of data aggregation infrastructure in partnership with Datatrial. These are in use in several other projects and are a key component of both COSMIC and EMBRaCE. We're supporting the collation and processing of data from various sources, to aid with the development of the AI model.*

*These studies are at the forefront of digital advancements and to have been able to facilitate the data management demonstrates Aptus' passion for developing with technology whilst maintaining clinical integrity.*

**Aptus Clinical**

# Early Warning Systems (Toxicity Management)


## Summary

An ELISA, for analysis of a panel of 12 cytokines associated with cytokine storms in plasma and/or serum, will be developed and validated as an exploratory endpoint. Factors such as cross-reactivity and assay plexs will be taken into account to cover the 12 cytokines and an initial assessment performed to confirm the feasibility of these assays. Following this, a Standard Operating Procedure (SOP) will be drafted, and a validation plan generated.

In addition, plasma and/or serum samples from 20 patients who did and did not progress to cytokine storm, will be identified and analysed for cytokine levels using the exploratory ELISA assay. After the Cytokine data is uploaded to an electronic database for visualisation and development of algorithms, either all or a subset of the 12 cytokines will be selected for the final ELISA panel, prior to validation of the assay to GCP levels.

Further work explores the logistics for sample collection including patient compliance, sample collection, tracking and transport to laboratory.

These studies will use the Neoteryx Mitra in-home micro-sampling device, of which there are two versions capable of collecting either 10µl or 30µl of blood respectively. Digital ECMT will establish the processes for supply of devices to patients, shipping to the Cancer Research UK (CRUK) MI CBC laboratory and tracking of samples.

CBC will develop workflows for the process and analysis of cytokine levels from the micro-sampling device. This will include optimization of the procedure for cytokine extraction, assessment of stability on storage both before and after extraction from the device and analysis using the multiplex ELISA assay. Assessment of extraction procedures will include varying the time, temperature and components of the extraction solution. Processes will be developed and optimized using healthy normal volunteer blood samples spiked with recombinant cytokines and used to simulate the collection from a patient. Feasibility of cytokine detection in patients will be confirmed using a training set of samples collected from patients with clinical symptoms consistent with cytokine elevations eg Advanced Therapy Medicinal Product (ATMP) patients with cytokine storm symptoms and COVID19 patients. Initial demonstration of feasibility of the micro-sampler for analysis of cytokine levels in patients will use a pilot sample-set collected from ATMP patients undergoing cytokine storms and from COVID19 patients.).

The work described above will pave the way for implementation of the micro-samplers in the proof of concept study NOTION: iN-home Sampling Of cyTokines in ImmunOtherapy patieNts , led by digital ECMT.


## Objectives

- Established a 12 cytokine enzyme-linked immunosorbent assay (ELISA) panel, validated to GCP, for rapid identification of changes in cytokine levels associated with cytokine storms.
- Created and developed algorithm/s to identify patients developing a cytokine storm and made appropriate adaptive decisions to ensure safe delivery of ATMPs.
- Used the iMATCH ELISA panel to analyse cytokine levels in these patients
- Understood the logistics for home blood sample collection including patient compliance, sample collection, transport to lab and sample tracking.



## Case Studies

Early warning systems to flag evolving toxicities through rapid turn-around monitoring capabilities and integration into digital algorithms
**bit.ly/36koDU0**

*The funding from iMATCH enabled the CRUK MI Cancer Biomarker Centre to validate an ELISA assay which detects marked cytokine excursions in patients on advanced therapies who are experiencing a cytokine storm. The ongoing transfer of our ELISA assay to the Christie Hospital Diagnostic Laboratory will maximise access to the assay for clinicians in Manchester and beyond, including the wider ATTC network.*

*In addition to this, our digital ECMT team are integrating the growing ELISA dataset with data on clinical vital signs to develop an algorithm to act as an early warning system for patients entering a life-threatening cytokine storm.*

*The ELISA assay has also allowed us to develop workflows for recovery and analysis of cytokines from dried blood spots which can be collected in the patient's own home, the feasibility of this home-monitoring system will be tested in the NOTION study.*

**Dr Elaine Kilgour,**
**Cells and Protein Team Leader.**
**CRUK Manchester Institute**
**Cancer Biomarker Centre,**
**The University of Manchester**

*The iMATCH programme provided the digital ECMT with the impetus to develop, design and implement the NOTION study, which utilises the ELISA cytokine assay, developed by Dr. Elaine Kilgour and team, in a patient home setting using dry blood spot technology. It also has enabled us to apply and implement our CRS algorithm in the broader context of immunotherapy toxicity, including those caused by immune checkpoint inhibitors.*

**Donal Landers,**
**Senior Director Physician,**
**Digital Experimental Cancer Medical Team**

# Wearable Technology

## Summary

The aim is to use the systems for clinical data collection that have been developed by the iMATCH team to construct a pilot study to assist with the COVID-19 pandemic. This means that the feasibility protocol will be worked up in the CAR-T setting but pivoted in light of the pandemic.

This pilot study (COSMIC-19) will assess whether artificial intelligence combined with continuous vital signs monitoring from wearable sensors can predict clinically relevant outcomes in patients with suspected or confirmed Covid-19 infection on general medical wards.

Outputs from this work will then be fed directly back into iMATCH and applied and modified for CAR-T patients both in the hospital (in-patient) and ambulatory setting as part of the EMBRaCE – GM study.

We have collaborated with Zenzium Ltd for their AI capabilities on both projects (an additional interaction outside of the iMATCH Consortium).

## Objectives

- COSMIC-19: Collected 'continuous vital signs' data using wearable sensors from patients with suspected or confirmed COVID-19 infection on general medical wards. Used this data to develop AI models to predict clinically relevant outcomes for ward-based patients such as: significant deterioration on the ward, admission to critical care, and clinical improvement (no ongoing requirement for oxygen therapy for 6 or more hours).
- Created a report on the quality and utility of the collected continuous vital signs data used in for the analysis in objective 1.
- Examined the collected data for evidence of circadian disruption in the vital signs of the enrolled patients.
- Leveraged existing patient wearable outputs, data collection and AI modelling infrastructure from COSMIC 19 to use in the case of CAR-T patients.
- EMBRaCE-GM – As part of an umbrella protocol, we assessed the practicality and feasibility of the Isansys platform to continuously monitor vital signs in patients on CAR-T hospital wards. This included patient symptoms and ePRO self-reporting in patients post CAR-T infusion that require monitoring whist remaining within 1hr of the site (ambulatory care/home setting).

## Case Studies

Development of novel wearables and AI capabilities to support the monitoring of COVID-19 patients
**bit.ly/3hX5Q3J**

See pages 22 for news & awards

*COSMIC-19 is a trial that exemplifies the profound impact that iMATCH and the ATTC network has had. At extremely short notice we were able to divert a workstream that we had planned in the CAR-T setting into the COVID setting. The established relationships within iMATCH meant that we were able to proceed from concept idea to recruitment of our first patient into COSMIC-19 in 4 months. We worked effectively as a team to recruit on target and even extend our recruitment to incorporate blood-born biomarkers. This is a key example of clinical, academic and pharma partners working together to deliver a project rapidly, co-operatively and at pace. Crucial to this success was the pre-existing infrastructure of iMATCH and the ATTC network. We have built on our experience in COSMIC-19 to develop the EMBRACE GM platform which now has cohorts open and recruiting in the ATMP setting.*

**Professor Fiona Thistlethwaite,
Chief Investigator for COSMIC 19**

*Cancer places a huge burden on the lives of people everywhere. The EMBRaCE study uses cutting-edge technology that can monitor people during their treatment, with devices that they can wear all the time. We therefore hope that this will provide new insights into how people cope with cancer treatment and what we can do to improve their recovery.*

**Dr Anthony Wilson,
Chief Investigator for EMBRaCE**

*Through the relationships generated by iMATCH, I have gained two years NIHR funding to work at the interface of industry, academia and the NHS, placed at Zenzium Limited and Aptus Clinical. This has in turn afforded me the time to lead blood analysis components of COSMIC19 and EMBRACE. I have also led the Supervision of Master Student Alex Dalton, who presented some interim analysis of COSMIC19 at a National Anaesthesia Conference with his abstract published in the British Journal of Anaesthesia.*

**Dr Gareth Kitchen.
Senior Clinical Lecturer, The University of Manchester. Honorary Consultant Anaesthetist.**

*We passionately believe patient wearable technologies will play an important role in improving clinical outcomes for patients and become a key part of clinical trials in the future. We are immensely proud of our contribution and support to the COSMIC-19 and EMBRaCE-GM studies, in collaboration with our AI partner, Zenzium.*

*The collaboration of expertise and technology demonstrated within these studies has also been ground-breaking and we have been delighted to offer our services and to hopefully make a difference to patients and their quality of life in the future.*

**Aptus Clinical**

*We firmly believe the future of healthcare will be driven by continuous rather than episodic measurements to improve patient outcomes on an individual basis. We are excited to be part of these ground-breaking collaborations with some of the best entities in the field, which gives us the opportunity to bring our technology, knowledge and expertise in wearable devices enabled by AI to potentially make a real difference in the lives of patients.*

**Anthony D. Bashall,
Managing Director of Zenzium**

# Scaling up in the Clinical Setting

## Pharmacy

### Summary

We aim to create and implement pharmacy SOPs which will formalise associated process for review, set-up, screening and support of new ATiMPs (Advanced Therapy Investigational Medicinal Products) in the Trust with a joint agreed process involving the Pathology Department.

After this we aim to create and implement study specific ATIMP Request Forms for use on the new electronic prescribing software.

### Objectives

- Improved Institutional Readiness across sites delivering Advanced Therapy Medicinal Products (ATMP)s as Standard of Care and in the Clinical Trial Setting.
- Streamlined and standardised approach to ATIMPs to maximise up-scale of deliver.
- Enhanced knowledge across Manchester and fed into wider ATTC platforms.
- Identified and collaborated to expand institutional readiness in order to deliver GMO clinical trials
- Streamlined GMO delivery in the Community using the Cytiva mobile unit model.
- Generated modules to provide bite size learning to pharmacists based in the community.

> *My role as part of the work package focused on the final objective; creating some bite sized e-learning modules. This was aimed towards informing and supporting community and GP practice based Pharmacists who may come into contact with patients and/or their carers for advice. Although we were unable to achieve this due to various challenges, we have produced a survey that has been distributed out to our contacts in community pharmacy and GP practice's, with a view to get feedback and their views, that will hopefully aid in informing the need and requirements for any future e-learning modules. Through Bahareh's contacts, we were also able to get a short letter published detailing this, in the "Pharmaceutical Journal", with the survey attached.*
>
> **Nimesh Bhenswala,**
> **Deputy Lead Pharmacist for Clinical Trials,**
> **The Christie NHS Foundation Trust**



## Capacity Building

### Summary

The aim is to scale up in a clinical setting to ensure that patients can access Advanced Therapy Medicinal Products (ATMPs) and the treatments can run smoothly.

An example of this is increasing the capacity for cell storage. This includes purchasing and installing a new apheresis machine, developing clinical governance processes, and restructuring teams

Additionally, we will increase space and capacity by structuring a larger facility with the provision of increased storage capacity for ATMPs. Developing shared policies and procedures for receipt, storage and issue of frozen ATMPs will establish best practice within the clinical setting and enable ATMP storage space to be used flexibly with other partners in the consortium to maximise the potential capacity. We will also examine new technologies for short term storage of cells and delivery to patients.

### Objectives

- Developed robust processes for clinical governance of Advanced Therapy Medicinal Product (ATMP) between Pathology Department and Pharmacy.
- Expanded on-site cell storage facilities specifically designed for ATMPs.
- Scale up of apheresis capacity to increase patient access to Advanced Therapy Medicinal Products.
- Developed shared apheresis SOPs for patients of all ages across sites.
- Created joint robust governance structure and quality control measures for apheresis in ATMP trials.
- Enhanced capacity for apheresis of patients in ATMPs trials.

### Case Studies

Increasing capacity to deliver advanced therapy trials
**bit.ly/3oOuHKT**

> *Christie Pathology Partnership (CPP) were able to increase their storage capacity for ATMPS by refurbishing an existing space on site so that a larger and better equipped storage area could be developed. This came into use in May 2020 and has made receipt and storage of frozen products much more efficient. In addition to this, a joint governance document was drawn up between the Christie Pharmacy and the CPP stem cell Lab for the receipt, storage and joint issue of ATMPs and ATIMPs.*
>
> *From the extension of the iMATCH program we were able to obtain more racks and cassettes in different sizes and some more equipment, including two new dry shippers with logging devices which are required by the sponsors/manufactures for the transport of AT(i)MPs.*
>
> *As a result of all of this, Capacity for storage of ATMP's and ATIMP's has been increased over 400% and the spare capacity means we can offer storage to partners if needed.*
>
> **Diane Sweeney,**
> **Stem Cell Laboratory Manager**
> **and HTA Designated Individual,**
> **The Christie Pathology Partnership**

# Clinical Trial Acceleration

## Summary

From a global perspective it is recognised that there is a regulatory and ethical framework to support the development of Advanced Therapy Medicinal Products (ATMPs) here in the UK, with good access to patients and a great reputation for high quality trial conduct.

However, despite this, the UK is not considered a good place to conduct ATMP research because of long and overly bureaucratic approvals, set-up, and contracting processes associated with dealing with bodies such as the NHS, HTA and more.

## Objectives

- Improved Institutional Readiness across sites delivering Advanced Therapy Medicinal Products (ATMPs).
- Streamlined and standardised approach to ATiMPs to maximise up-scale of delivery.
- Enhanced knowledge across Manchester and fed into wider ATTC platforms.
- Scoped and engaged with relevant pathway boards to develop referral for advanced cell therapies.

> *Set-up time for clinical trials is a crucial metric for pharmaceutical companies. Through our Clinical Trials Acceleration Team we have worked effectively to increase the speed and efficiency that ATMP trials across iMATCH and the wider network can be opened. This work package is helping the UK to strengthen its reputation in this area, enhancing the attractiveness of the UK for pharma to run their innovative ATMP trials here.*
>
> **Professor Fiona Thistlethwaite, iMATCH Director**



# Safe Patient Management

## Summary

We aim to build upon our existing programme board to co-ordinate the operational patient pathway.

This would mean the involvement of appropriate service support departments to streamline activities, developing nurse led studies, share and construct join SOPs to allow for joint working, and scoping and defining patient pathways whilst ensuring best practice across both sites.

## Objectives

- Coordinated safe patient management in the inpatient setting and on follow up.
- Identified mechanisms for streamlining co- ordination of patients receiving Advanced Therapy Medicinal Products.
- Conducted a qualitative study looking at materials given to CAR-T patients.
- Developed SOPS to ensure consistency across sites
- Coordinated activities for safe patient management and to ensure quality and governance management standards across sites.

## Case Studies

Successful patient recruitment to a TCR T-cell therapy trial: bringing together multiple outputs from iMATCH to scale-up future ATMP clinical trial activity
**bit.ly/3sJAHWk**

> *The patient pathway for ATMPs is complex and requires substantial training and co-ordination. Through this wide-ranging workpackage we have established and enhanced our clinical infrastructure such that we are now able to treat many more patients with ATMPs than previously. The work has encompassed training, enhanced clinical facilities, patient education and quality and governance infrastructure build. As we see increasing indications being approved for ATMPS it strongly positions Manchester and the ATTC network as a whole to deliver these within a modern NHS.*
>
> **Professor Fiona Thistlethwaite, iMATCH Director**

# Education and Training

## Summary

To help increase the scope and expand the use of ATMPs, an education programme will be developed to increase knowledge and best practices about the implementation of ATMPs.

In order to achieve this, national and international workshops and conferences will be attended to ensure that education materials are current and relevant for sharing of best practice. From here a core team of staff will be used to develop educational materials that could be used across all disciplines.

## Objectives

- Developed the current internal Education Programmes into a broad education programme in Advanced Therapies applicable to all individuals involved in the delivery of ATMPs across the City.
- Established a modular MSc in Advanced Therapies.
- Following interest generated in line with the MSc in ATMPs rolled out at the University of Manchester, we have offered the 2 ATMP specific modules as standalone short courses for CPD. These were the 'Introduction to ATMPs' and the 'ATMP Clinical Trial Design Module'.
- Developed training videos to enable best practice to be shared.

## Case Studies

Ensuring safe delivery of Advanced Therapies through education
**bit.ly/3511Pry**

*The iMATCH education work package has had a significant and lasting impact both because of its broad reach across professional disciplines, but also because of the wide range and levels of materials produced, from basic teaching sessions all the way up to the provision of masters level materials and courses. As well as the teaching materials, we have been able to produce an exemplar framework for embedding education and training into governance structures which NHS organisations moving into advanced therapy delivery can replicate. Delivering these tangible outputs has required a huge team effort from across the consortium, resulting in so many collaborations and projects that will absolutely have a positive and lasting legacy.*

**Michelle Davies,**
**Advanced Nurse Practitioner,**
**The Christie NIHR Clinical Research Facility**

*The aim of the video was to provide and introduction to the key concepts surrounding Cytokine Release Syndrome, in conjunction with immunotherapies, and how nurses should approach the treatment of it.*

*The development of the script and video itself was through the partnership and team work of experts in the field, providing a prime example of the successes of collaborative work in healthcare.*

*This video is to be used in conjunction with practical training and the implementation of individual Trust policies.*

**Maria Farrell,**
**Senior Practice Facilitator,**
**Advance Immune and Cell Therapies**



# Health Economics

## Summary

The aim is to generate economic evidence of the value of using strategies to reduce the impact of capacity constraints on the delivery of exemplars of ATMPs.

This will build on the proposed decision-analytic model-based cost-effectiveness analysis that aims to understand the effect of bottlenecks in the delivery system (also called 'capacity constraints') on the relative costs and health (quality-adjusted life-year) consequences of using TIL compared with current management strategies for people with malignant melanoma. This plan of work will develop indicative estimates of the cost-effectiveness of strategies to reduce the impact of key capacity constraints in the delivery of ATMPs. Relevant strategies will be identified over the duration of the iMATCH project, such as techniques to optimise sample storage and apheresis. A decision-analytic model will, using dynamic modelling approaches, estimate the cost and health consequences associated with reducing the identified capacity constraints. Costs will be measured from the perspective of the NHS and health outcomes will be measured using quality-adjusted life years. This approach will ensure that the findings have direct relevance to national decision-making criteria used to inform the allocation of resources for health care.

## Objectives

- Created a systematic review of capacity constraints in cost-effectiveness analysis of ATMPs.
- Compared the cost and benefits of TIL versus current practice for advanced melanoma in the NHS.
- Compared the costs and benefits of different strategies to improve the implementation of TIL.

*Insights from health economics are essential to deliver advanced therapies at scale. We integrated health economics within iMATCH to consider the benefits and costs of different ways to overcome key constraints on getting these treatments to patients. As we look forward, a value-based approach to implementing advanced therapies is vital to help health care systems achieve maximum patient benefit from their limited resources.*

**Dr Sean Gavan,**
**Research Fellow in Health Economics,**
**The University of Manchester**

# Patient Reported Outcome Measures (PROMs)


**Summary**

We are contributing to the overall evaluation of the use and role of PROMs within ATMP trials.

Our aim is to provide a quantitative approach within the oncology setting in line with the evaluation of the use of PROs (Patient Reported Outcomes) in ATMP Development and Optimising Patient and Public Involvement (PPI) in the Co-Design of ATMP Research and Regulation.


## Objectives

- Provide a quantitative approach within the oncology setting in line with the evaluation of the use of PROs in ATMP Development and Optimising Patient and Public Involvement (PPI) in the Co-Design of ATMP Research and Regulation.
- Utility and measurement issues of each PRO instrument and its applicability in the context of advanced therapies for cancer treatment will be evaluated. This will feed into a high-level stakeholder event which will focus on the key requirements of PROs in the licencing of ATMPs. This will in turn aid the development and understandings required to drive regulatory decision making, provide industry facing resource and the creation of a specific ATMP PROM tool/tool for use in future clinical trials.

> *Patient Reported Outcome Measures (PROMS) are hugely important because they provide an opportunity for patients to report their own lived experience of a treatment or disease. For complex and expensive treatments such as advanced therapies, the patient narrative is even more critical because pre-registration clinical trials are often small and early phase. Regulators and commissioners can use information from PROMS to inform and influence decision making. iMATCH has supported the exciting work which will lead to specific guidance in the use of PROMS for advanced therapy patients where there is currently a gap.*
>
> **Michelle Davies,**
> **Advanced Nurse Practitioner,**
> **The Christie NIHR Clinical Research Facility**



# Plans for 2022/23

**ATiMP Clinical Trial Acceleration Coordination**

**ATMP Patient Referrals Pathway Analysis**

**Ambulatory Delivery of ATMPs**

**Calculating the Carbon Footprint of ATMPs**

**Apheresis Service Horizon Scanning**

# News and Awards

## Wearable Technology

**PRESS RELEASES**

Read about the official press release of COSMIC 19; the innovative clinical trial that uses Artificial Intelligence. The iMATCH consortium redirected funds towards this project, collaborating with Aptus Clinical and Zenzium.
**bit.ly/36wGU0t**

Have a look at the official press-release for EMBRaCE. The trial from the same collaborators of COSMIC 19 that is focused on wearables in the CAR-T setting. The technologies can assess a range of vital signs, including electrocardiogram (ECG), heartrate, temperature, physical activity levels and sleep, to continuously monitor a cancer patients vital signs.
**bit.ly/3rSDH3k**

**COSMIC 19 ACHIEVEMENTS**

An abstract that focuses on COSMIC 19 was published in the British Journal of Anaesthesia (BJA), with a master's student mentored by the collaborators of COSMIC 19 also being awarded the chance to present at the yearly BJA national conference. Read more about it here **bit.ly/3v0lx1T**

COSMIC 19 was shortlisted for the NIHR CRN Greater Manchester's Evening of Excellence 2021 in the category of 'Innovation Influencers.' The award recognised the achievements made in the delivery of COVID-19 and non-COVID research during March 2020–August 2021 and was organised to celebrate the staff behind the health and care research that has taken place in Greater Manchester during the pandemic.
**bit.ly/3JvlWx8**

## Scaling up in the Clinical Setting

**RESEARCH VAN**

A research van, which is only the second of its kind in the UK, has been designed to bring research conveniently to local communities in Greater Manchester, East Cheshire and East Lancashire. This project spun out of the initial concept of a mobile Advanced Therapy unit proposed by Cytiva within the iMATCH consortium and across the ATTC network.
**bit.ly/3v98hYM**

## Education And Training

**EDUCATION ACHIEVEMENTS**

Jess Ritchie, who is a Clinical Research Nurse in the Advance Immune and Cell Therapies (AICT) Research Team at The Christie Hospital in Manchester, received a distinction from the new MSc in ATMP at the University of Manchester. Jess was sponsored by iMATCH and was the first student to graduate from this course.
**bit.ly/3Bp1QSp**

**TRAINING**

The Midlands-Wales Advanced Therapy Treatment Centre (MW-ATTC) and Innovate Manchester Advanced Therapy Centre Hub (iMATCH) collaborated to produce a new clinical scenario video intended to support training in the management of cytokine release syndrome (CRS) following chimeric antigen receptor (CAR) T cell therapy.
**bit.ly/3sKnrAO**



# Further resources

Our website has a lot of useful resources to help you learn more about Advanced Therapy Medicinal Products (ATMP)!

One example of this is our NHS Readiness Toolkit, it provides easy access to a portfolio of resources created by the ATTC network (Midland Wales [MW-ATTC], Northern Alliance [NA-ATTC] and iMATCH). Read more about this in our case study **bit.ly/3BIJkVq**

Visit us at **www.theattcnetwork.co.uk**
or follow us on Twitter **@iMATCH_ATTC**

Innovate Manchester Advanced Therapies Centre Hub (iMATCH)

**www.theattcnetwork.co.uk/imatch**

@iMATCH_ATTC

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