Advanced Therapy Treatment Centres

LONDON ADVANCED THERAPIES

Accelerating delivery of cellular therapy trials

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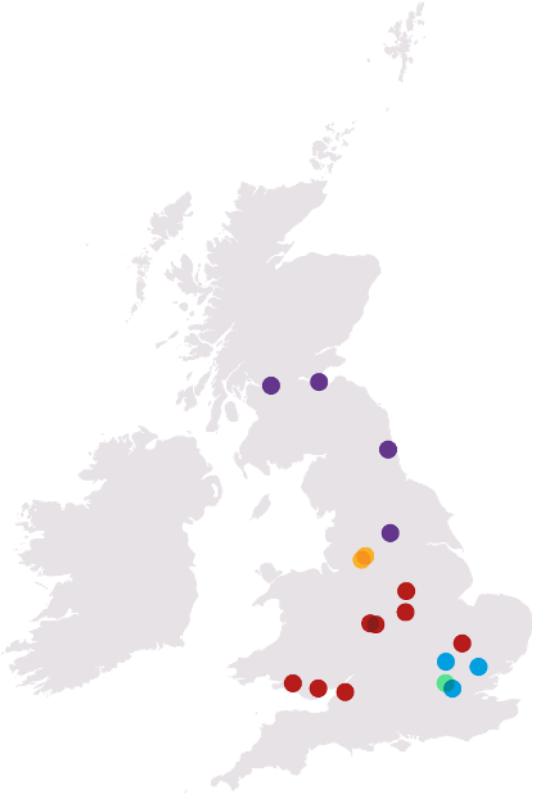


Funded by

INDUSTRIAL STRATEGY

UK Research and Innovation

Coordinated by

CATAPULT Cell and Gene Therapy

Rapid assessment of novel therapies: a global challenge

- A tsunami of novel drug, cellular and biological therapies promises to transform clinical outcomes in cancer and chronic disease
- The exponential increase in novel therapeutics coupled with genomic stratification mandates investment in new models which accelerates trial
- Registration standard trials, are currently delivered by CROs whilst IITs are the preserve of academic cooperative groups
- The global CRO sector is failing- inefficient, limited KOL involvement, minimal science- extremely expensive
- Delivery of high quality trials with embedded genomics and discovery science by academic groups is increasingly recognised as a route to FDA/EMEA registration
- The UK has unique advantages in blood cancer-presents a major opportunity to develop globally academic trials networks which compete with CROs

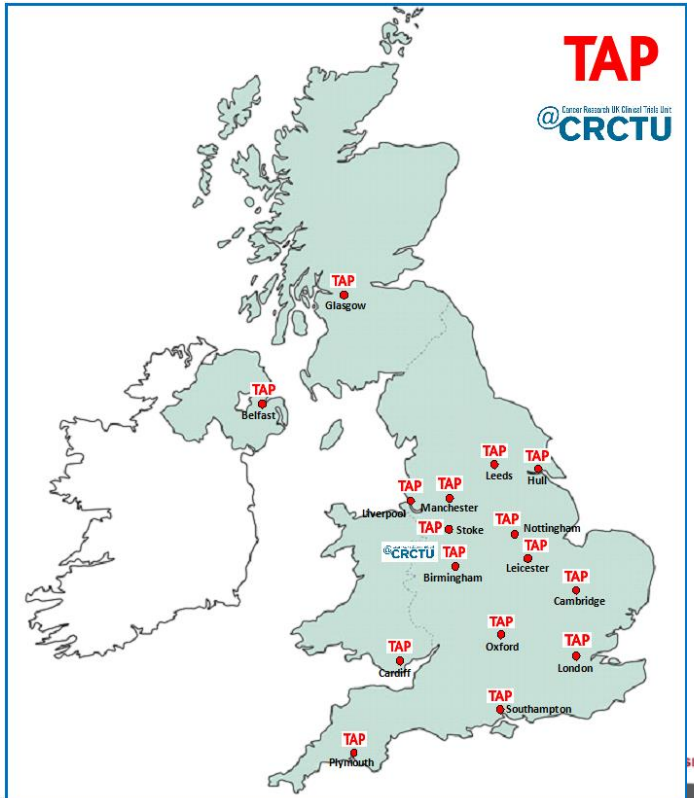
Structure of TAP

Funded Network of Centres

Hospital	City
Belfast City Hospital	Belfast
Queen Elizabeth Hospital Birmingham	Birmingham
University Hospital of Wales	Cardiff
Beatson West of Scotland Cancer Centre	Glasgow
St. James's University Hospital	Leeds
Leicester Royal Infirmary	Leicester
St. Bartholomew's Hospital	London – Barts
King's College Hospital	London – Kings
University College Hospital	London - UCLH
The Christie NHS Foundation Trust	Manchester
Nottingham City Hospital	Nottingham
Churchill Hospital	Oxford
Southampton General Hospital	Southampton

Affiliated centres:

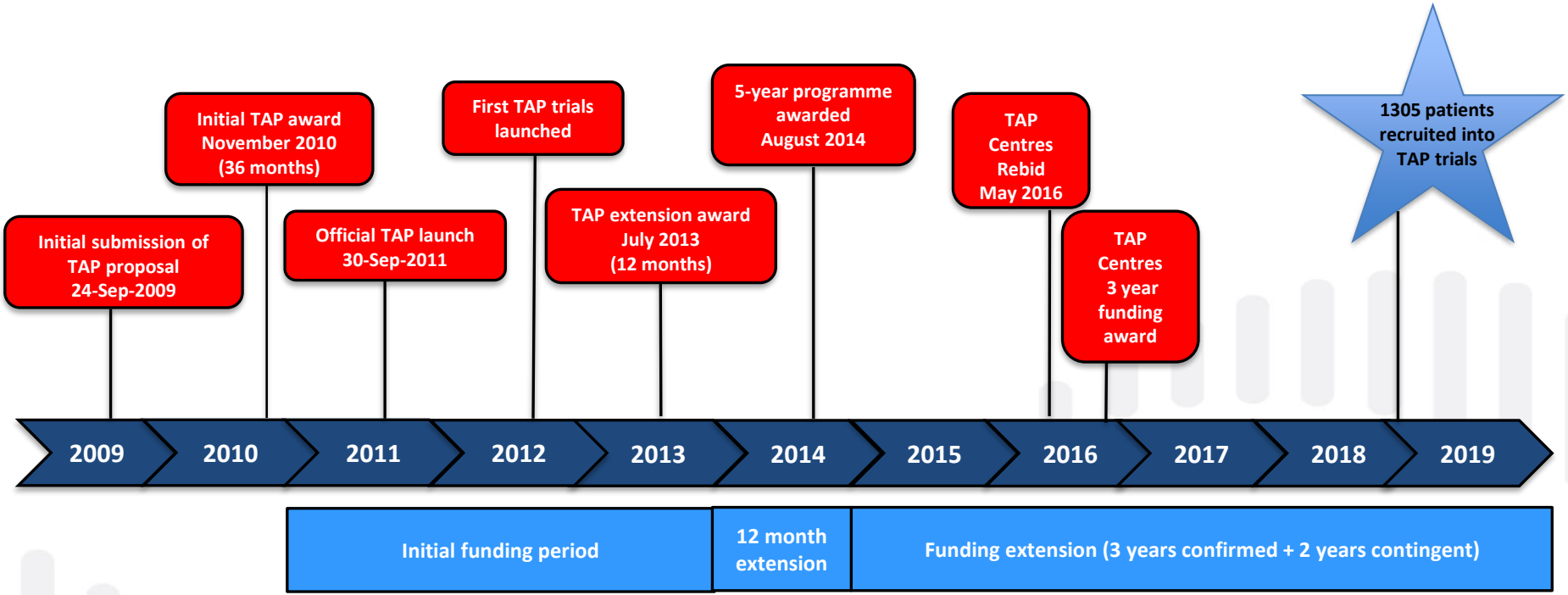
Hospital	City
Addenbrookes Hospital	Cambridge
Imperial College NHS Trust	London - Hammersmith
Royal Marsden Hospital London	London - Royal Marsden
Castle Hill Hospital	Hull
Derriford Hospital	Plymouth
Royal Stoke University Hospital	Stoke (UHNM)
Royal Liverpool University Hospital	Liverpool



Central Coordination Hub

- CRCTU (Cancer Research UK Clinical Trials Unit), University of Birmingham
  - NCRN accredited
  - NIHR registered
- Coordinated network of trial centres
- Large enough catchment areas to allow rapid recruitment

TAP Timeline



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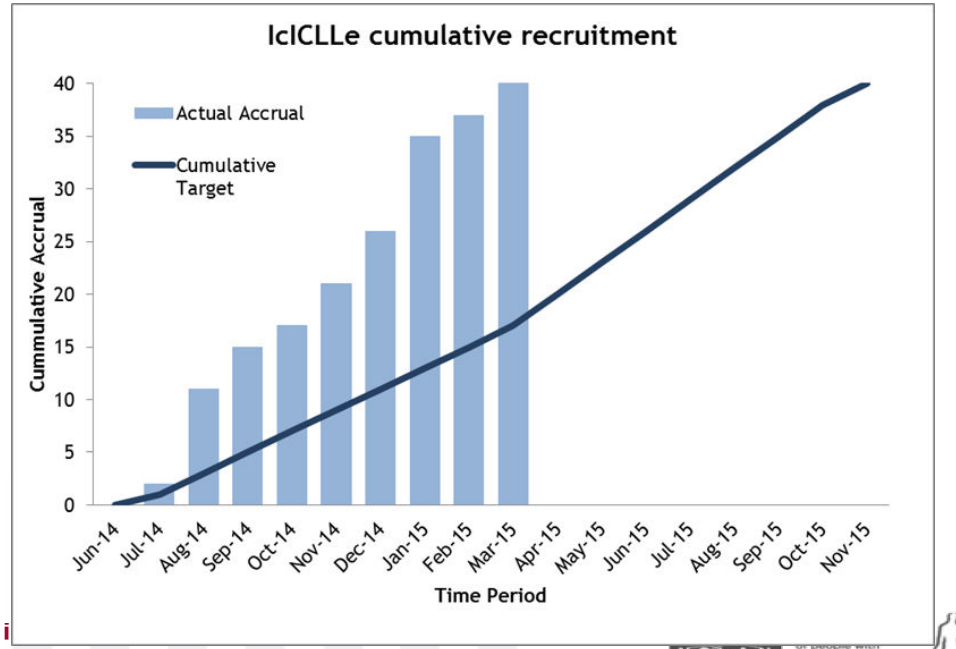
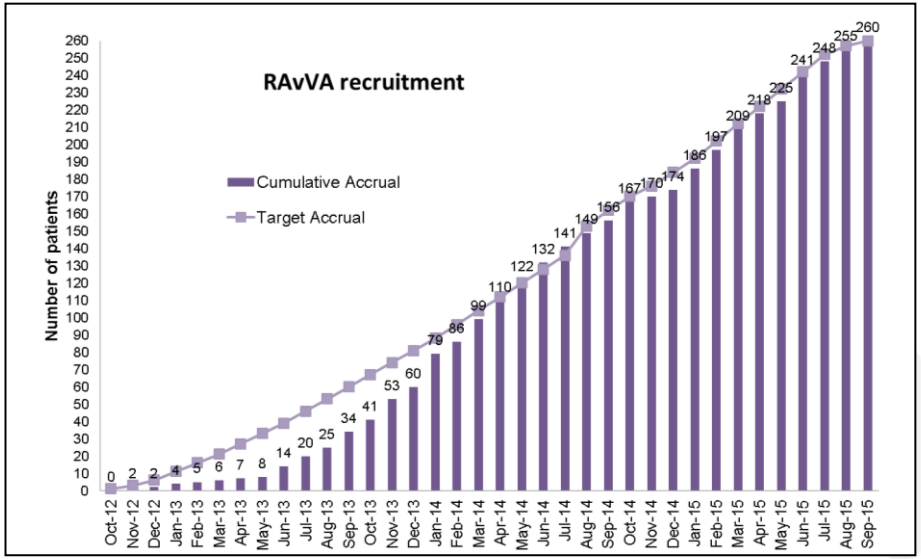
Accelerated Recruitment





TAP Publications

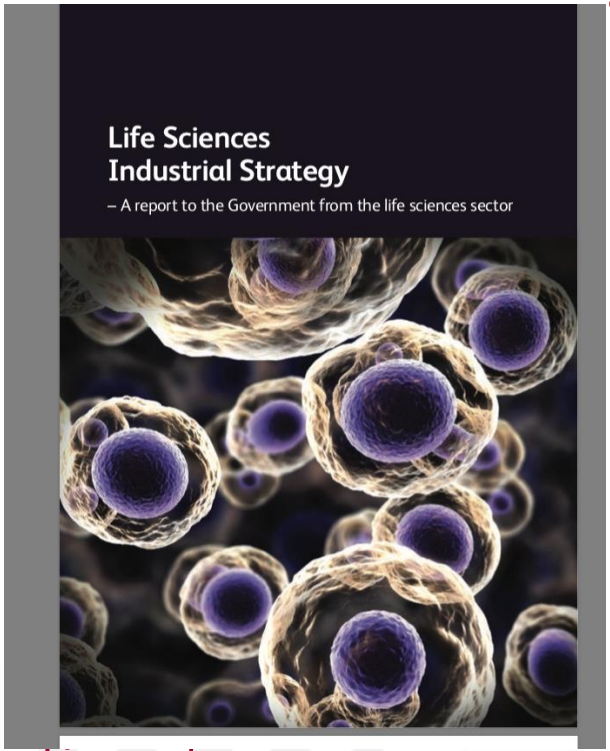
- Craddock C, Jackson A, Loke J et al (2020) Augmented reduced intensity regimen does not improve postallogeenic transplant outcomes in Acute Myeloid Leukaemia **Journal of Clinical Oncology. 2020** epub online
- O'Sullivan J, Hamblin A, Yap C (2019) The poor outcome in high molecular risk hydroxycarbamide-resistant/intolerant ET is not ameliorated by ruxolitinib **Blood 2019** 134: 2107-2111
- Hillmen, P; Rawstron, A; Brock, K. (2019) Ibrutinib plus venetoclax in Relapsed/Refractory CLL: The CLARITY Study. **Journal of Clinical Oncology. 2019** 37:2722-2729
- Craddock, C; Slade, D; De Santo, C; (2019) "Combination lenalidomide and azacitidine: a novel salvage therapy in pati who relapse after allogeneic stem cell transplantation for acute myeloid leukemia". **Journal of Clinical Oncology. 2019; 3 (7), 580-588.**
- Harrison, CN; Mead, AJ; Panchal (2017). "Ruxolitinib versus Best Available Therapy for ET intolerant or resistant to Hydroxycarbamide in a Randomized trial". ***Blood.*** **2017;130(17):1889-1897**
- Craddock, C; Houlton, AE; Quek, LS. (2017). "Outcome of Azacitidine Therapy in Acute Myeloid Leukemia is not Improve by Concurrent Vorinostat Therapy but is Predicted by a Diagnostic Molecular Signature". ***Clin Cancer Res.*** **2017; 23(21):6430-6440**
- Brock, K; Billingham, L; Copland, M; Siddique, S; Sirovica, M; Yap, C. (2017). "Implementing the EffTox dose-finding design in the Matchpoint trial". ***BMC Medical Research Methodology.*** **20 July 2017**. **17(1), 112-27.**
- Yap, C; Billingham, LJ; Cheung, YK; Craddock, C; O'Quigley J. (2017). "Dose Transition Pathways: The missing link between complex dose-finding designs and simple decision-making". ***Clin Cancer Res*****. 2017;23(24):7440-7447**

Selected as one of the top ten most outstanding manuscripts published in Blood in 2017

TAP Highlights

- TAP has transformed the number of patients entering early phase haemato-oncology trials in the UK- over 1,300 patients recruited over a 5 year pilot.
- Facilitated patient access to > £250 million novel agents.
- Created a resource for the UK Haem-Onc community permitting exploration
- of novel trial concepts (60 expressions of interest in 5 years).
- Trial set up times have substantially reduced, verifying that TAP is delivering acceleration compared to the published average of 2.5 years.
- TAP enables sample collection from prospective, well characterised clinical cohorts, underpinning delivery and publication of transformational science.
- TAP has served as a magnet for inward investment by the global pharmaceutical sector

The TAP programme highlighted in UK Life Sciences Industrial Strategy



UK Haemato-oncology Trials Acceleration Programme
Birmingham Health Partners and Bloodwise

The haemato-oncology Trials Acceleration Programme (TAP) represents a novel national trials infrastructure which was established by the charity Bloodwise in 2012 in response to the dramatic increase in the number of potential new drugs for the treatment of blood cancer.

Based on a 'hub and spoke' model, a central trials acceleration hub hosted by Birmingham Health Partners facilitates trial set up and delivery within a national network of 13 major leukaemia centres, each with dedicated research nurse funding and collectively covering a catchment region of 20 million. This integrated delivery structure has significantly reduced trial set up time from 30 to 9 months at the same time as accelerating patient recruitment. By recruiting 260 patients ahead of schedule and collecting more than 2000 samples for next generation sequencing it has also identified a novel molecular signature of clinical outcome. In total the TAP has facilitated recruitment of 950 patients across a portfolio of 19 early phase trials and resulted in industry partners bringing around £150 million of potentially life-saving new treatments to patients across the UK.

The TAP model is now being applied in other diseases including arthritis and stem cell transplantation. By accelerating the set up and delivery of complex clinical trials of novel agents with integrated genomics, this novel infrastructure has the potential to further establish the UK as a globally unique environment for the rapid delivery of practice informing studies, in turn driving inward investment by the global pharmaceutical sector.

The UK Government should improve the UK's clinical trial capabilities so that the UK can best compete globally in our support for industry and academic studies at all phases.

Strategic goal: To support a 50% increase in the number of clinical trials over the next 5 years and a growing proportion of change of practice and trials with novel methodology over the next 5 years.

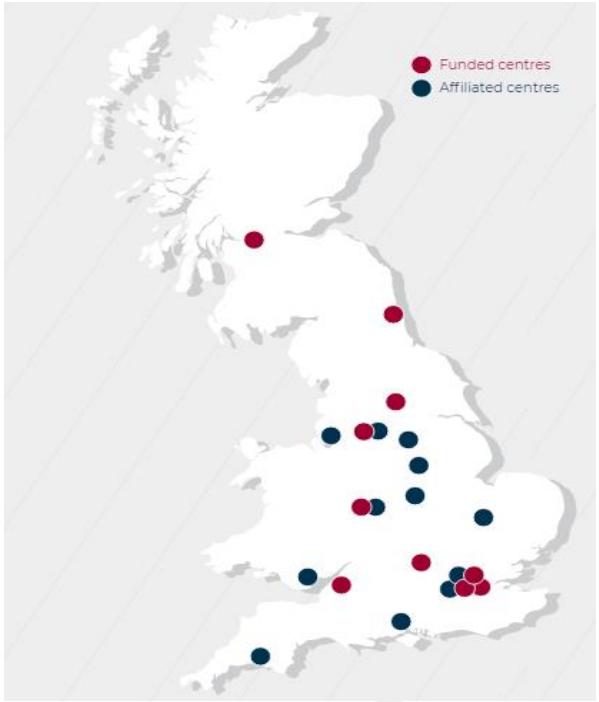
Clinical Studies in Stem Cell Transplantation: a Major Unmet Need in 2021

- Stem cell transplantation is an increasingly important curative treatment modality for children and adults.
- Despite the almost universal availability of stem cell donors many patients die of transplant toxicity or recurrent disease.
- >50% of patients die post transplant as a result of regimen related toxicity or relapse.
- <5% of patients enter prospective transplant trials.
- Basic scientific advances have underpinned the development of new therapies but their adoption into routine transplant practice is very slow

IMPACT Overview

- £3.4 million funding secured from Anthony Nolan, NHSBT and Leuka for four year pilot of IMPACT (Platform for Accelerated Trials) with aim of delivering 9-12 stem cell transplant RCTs
- IMPACT Oversight Committee meets 6 monthly-representatives of funders, BSBMT, NIHR
- Trials Hub based at Birmingham CRCTU- to work with major UK BMT centres in order to facilitate trial set up and delivery
- All UK transplant centres who fulfil basic criteria for delivery of clinical trials invited to join network
- IMPACT embedded within NCRI and NIHR governance structures

IMPACT
THE UK'S STEM CELL TRANSPLANT CLINICAL TRIALS PARTNERSHIP

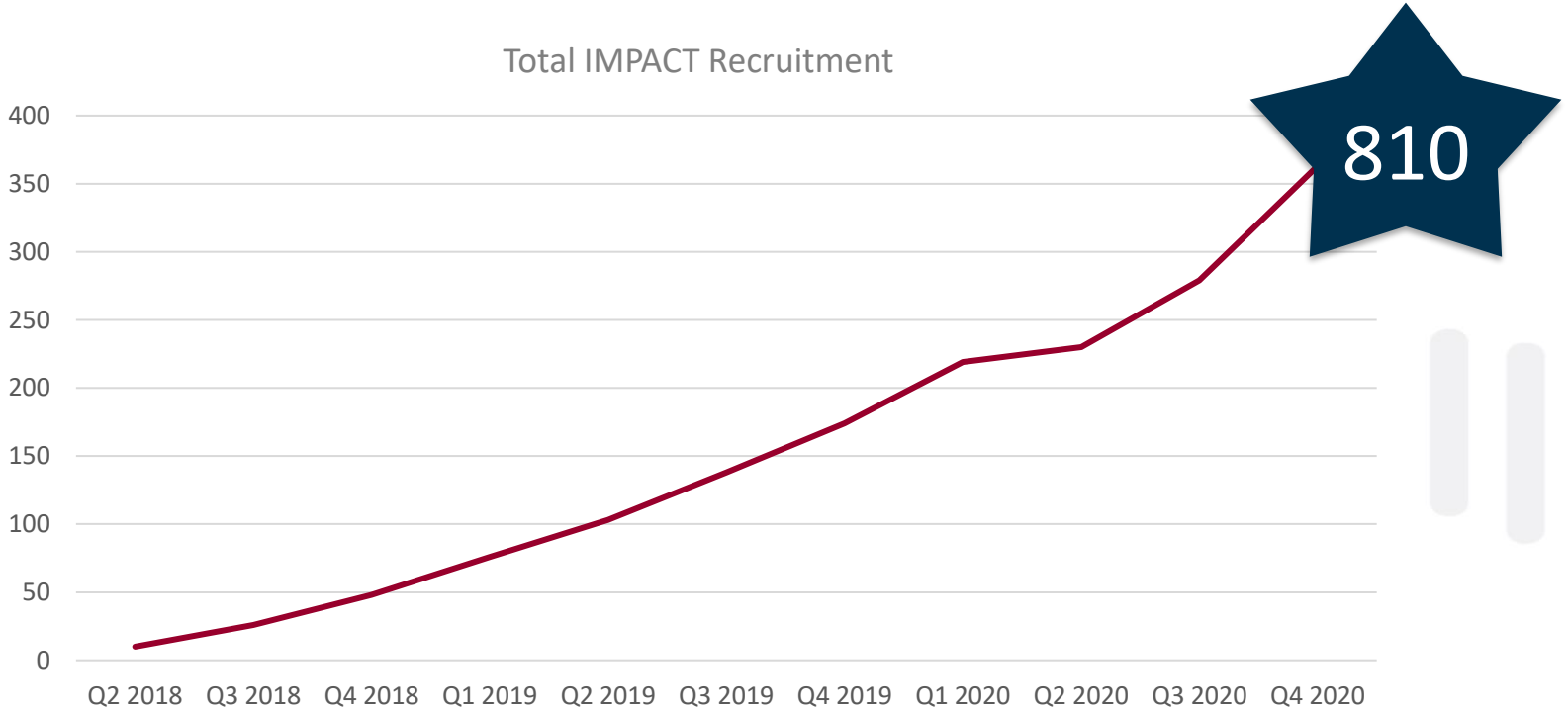


- ✓ Central Hub at the CRCTU: responsible for trial design, setup, management and publication
- ✓ 11 funded transplant centres able to recruit to IMPACT studies
- ✓ 11 affiliated transplant centres able to recruit to IMPACT studies

Achievements since establishment of IMPACT

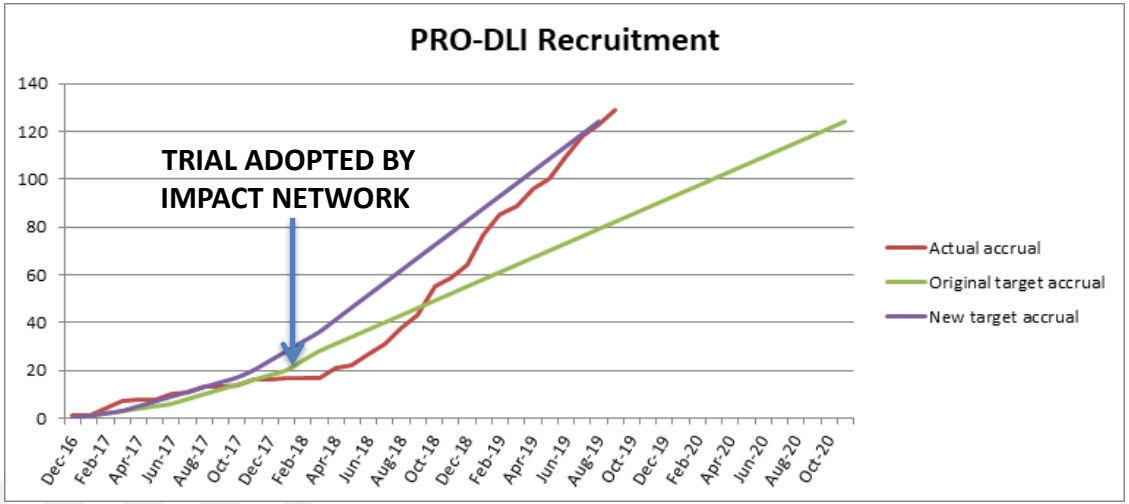
- IMPACT launched by Sir John Bell November 2017
- 22 IMPACT centres appointed – 9 funded IMPACT research nurses in post
- Five trials already opened:
  - **Pro-DLI – The first randomised trial of donor lymphocyte infusion after allogeneic SCT – FULLY RECRUITED April 2020**
  - ALL- RIC – The largest randomised trial of conditioning regimen in ALL
  - AMADEUS – The first randomised trial of maintenance azacitidine post-transplant
  - COSI – The first randomised trial of (a) pre-transplant MRD reduction (b) thiotepa based regimen
  - COVID19_BMT – Non-interventional study of COVID19 infection response in allo-SCT patients

IMPACT Recruitment



Pro-DLI

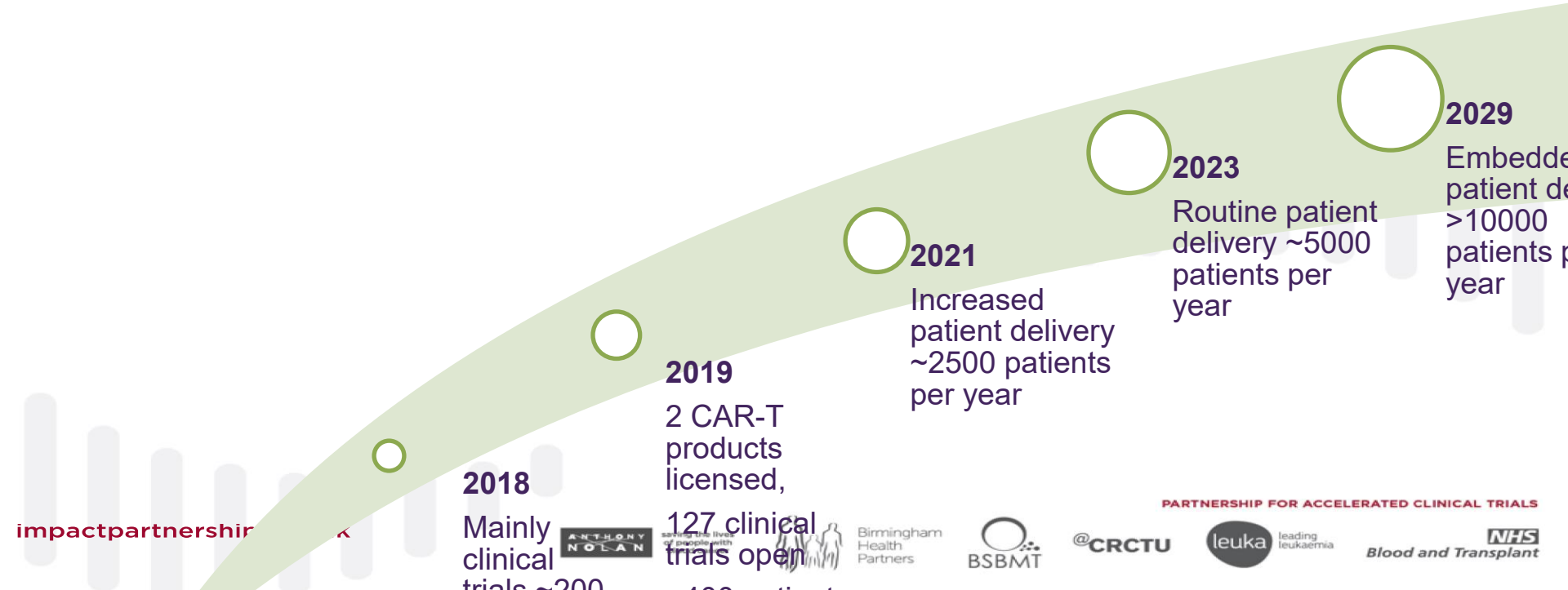
- Bloodwise funded - first randomised trial of donor lymphocyte infusion after allo-SCT
- Slow recruitment until trial adopted by IMPACT in February 2018
- Recruitment target of 148 patients achieved in April 2020
- Excellent recruitment demonstrates importance of a networked approach to trial delivery



Accelerated trials networks - what can we conclude?

- The TAP model permits highly effective, efficient trial models which deliver rapid recruitment, matched genomics and data and overcome current rate-limiting steps
- By leveraging a 10-20 multiple of free drug TAPs represent an important route for patients to access novel agents minimising geographical inequities of access
- The integrated hub and network model leverage the UK's unique trials assets as never before- notably size of catchment region and academic engagement
- TAPs are a disruptive and scaleable technology, superior to CROs, and permit rapid delivery of regulatory standard trials now attracting interest from global pharma
- Despite this TAP and IMPACT's dependence on philanthropic funding mandates mandating the exploration of novel funding models

The adoption challenge: Increasing patient demand



PARTNERSHIP FOR ACCELERATED CLINICAL TRIALS

The ATICs currently run 53% of ATMP trials in the UK,
this is representative of almost 7% of global ATMP trials.

2017	2018	2019	2020
39% of trials (23 / 59)	36% of trials (31 / 85)	50% of trials (64 / 1[illegible]8)	
2% of trials	3% of trials	6% of trials	

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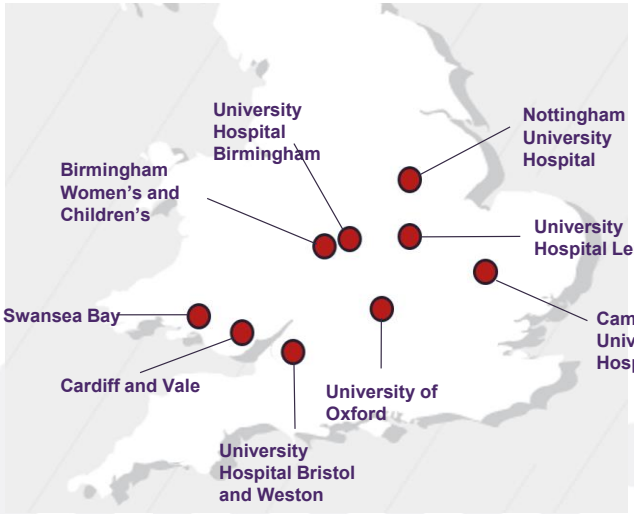
PARTNERSHIP FOR ACCELERATED CLINICAL TRIALS

TAP-CT
Trials Acceleration Programme in Cellular Therapy

We work with both commercial and academic sponsors to facilitate accelerated set up and opening of exciting cell and gene therapy trials across a network of clinical sites spanning a large geographical area.

- Large Patient Population
- Dedicated Nursing Resource
- Rapid Feasibility
- Access to Key Opinion Leaders
- Cost effective



The network has a diverse clinical remit with expertise in:

Cardiology, Covid-19, Diabetes, Gastrointestinal, Haematology, Immunology, Liver, Metabolic and Endocrine, Neurological, Oncology, Renal and Urogenital and Respiratory

CAR-T | MSC | T-Cell | DC Vaccine | CMV Vaccine | Stem Cells | and more...

PARTNERSHIP FOR ACCELERATED CLINICAL TRIALS

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For more information please contact: tapct@contacts.bham.ac.uk

TAP-CT Delivery

- **<u>Accelerating high-quality, academically strong clinical trials in cell and gene therapy through rapid feasibility and opening of trials across a national network of clinical sites</u>**

- Support high-quality, academically strong trials
- Access to large and diverse patient population
- Provides access to engaged clinical sites and key opinion leaders
- Single point of contact for feasibility and set up of cellular therapy trials across a network of clinical sites
- Streamlined process for successful site study registration and approval to open
- Feasibility completed within 2 weeks of TAP-CT adoption
- Repository for trial feasibility checklists/site facilities matrices (including regulatory) and educational resources in ATMP trials
- Cost effective

The Future of IMPACT & TAP

- Despite their success IMPACT and TAP are highly vulnerable in the future
- At the same time there is widespread recognition that the current model for blood cancer trial delivery-focussed around individual trials units is sub-optimal
- There is no model for succession planning and no real ownership
- The success of TAP and IMPACT in attracting income generating academically validated trials which contribute income provides a future model for engagement with global pharma
- Other European countries have developed mutualised trial delivery vehicles owned by the haemato-oncology community- LYSARC, HOVON

TAP and IMPACT- achievements to date

- The advent of a wave of new drug, transplant and cellular therapies are transforming outcomes of patients with blood cancer
- It is therefore of overwhelming importance that we accelerate access to new treatments for blood cancer patients through pivotal clinical trials
- The TAP and IMPACT models were established to:
  - Increase trial capacity at UK haem-onc and transplant centres by funding dedicated research nurses covering a population of 20 million
  - Accelerate clinical trial set up and empower UK investigators to lead pivotal trials
  - Facilitate world class translational research
  - Deliver trials approved by the TAP and IMPACT clinical networks
- To date TAP and IMPACT have recruited >2,000 patients to trials and informed clinical practice in the UK and worldwide and created access to innovative therapies worth >£200 million - many of which have been subsequently approved by NICE

The future of TAP and IMPACT is bleak unless we develop a new funding model

- The COVID-19 pandemic has dramatically reduced philanthropic income and resulted in reduced funding for clinical trials and research nurses
- TAP is exclusively funded by Cure Leukaemia which lost £1.5M during the COVID-19 pandemic
- The IMPACT pilot was a 4-year project with no provision for long term support
- To maintain the momentum of both networks innovative, sustainable funding mechanisms must be developed

Future considerations

- Commercial trials represent an increasingly important route for providing patients with rapid access to novel treatments such as CAR-T cell therapies and novel targeted therapies

- Expanding the trials portfolio of TAP and IMPACT to include both academic IITs and industry-sponsored trials is important to maximise patient benefit – providing that the principle of clinical prioritisation by the networks is preserved

- A number of European and US academic networks have pioneered financially sustainable trial delivery models eg LYSARC, HOVON, CIBMTR