Accelerating Clinical Trials (ACT): What We Achieved in leukaemia

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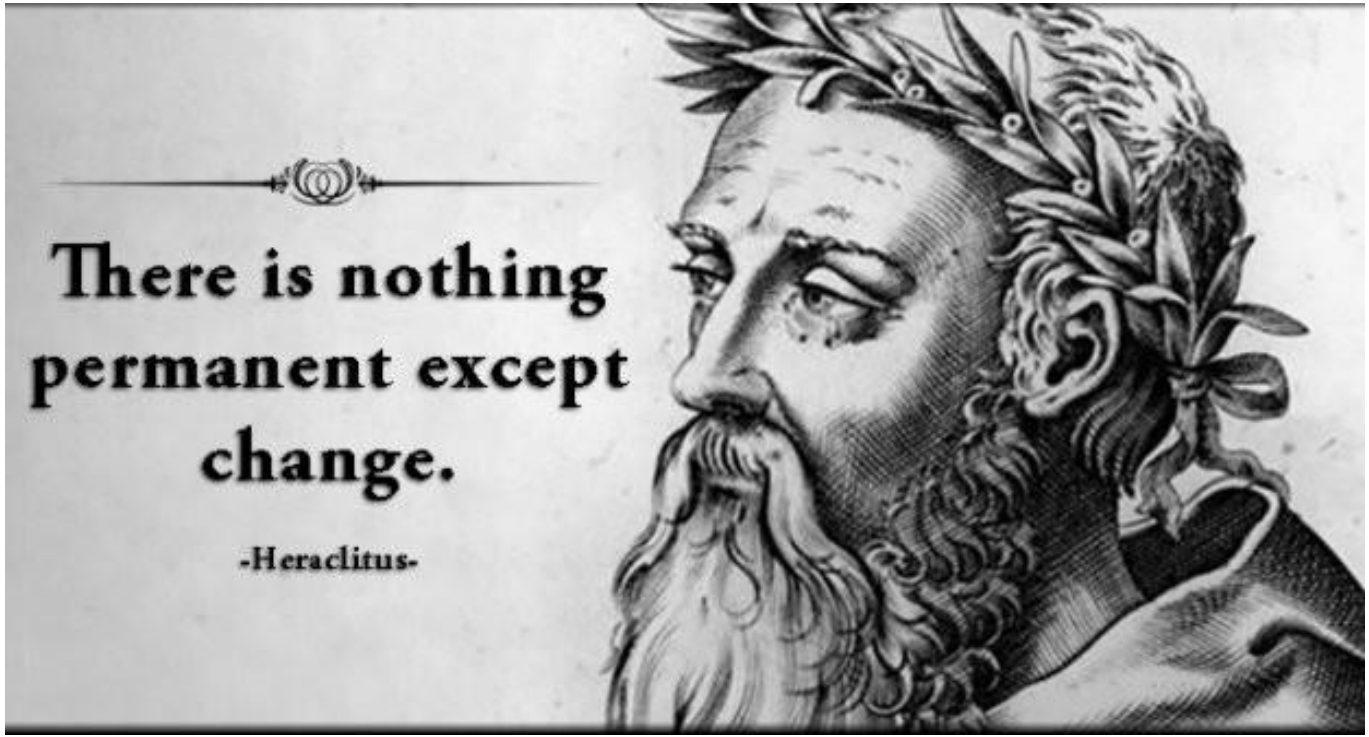


The Opportunity for Academic Cooperative Groups

- The exponential increase in novel therapeutics and devices has transformed the trials landscape and consequently commercial clinical trials are of ever increasing importance
- There has been a dramatic fall off in UK clinical commercial trial delivery and we are failing to compete internationally
- The global CRO model is failing patients, clinicians and pharma but remains the default trial delivery model for registration studies
- Academic cooperative groups possess key strategic assets but have historically struggled to deliver trials of the quality required by FDA and EMA
- HOVON, LYSARC, European Myeloma Network and the US BMT CTN are innovative academic research organisations (AROs) capable of delivering registration enabling trials
- The COVID-19 pandemic underlined the transformative impact of changes in trials capacity and the regulatory landscape eg the RECOVERY trial

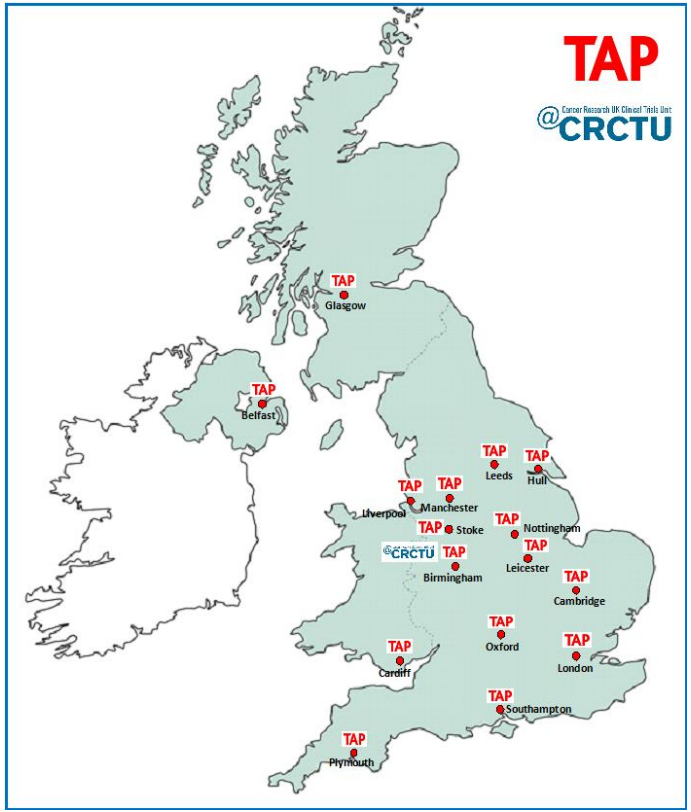
Structure of TAP

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

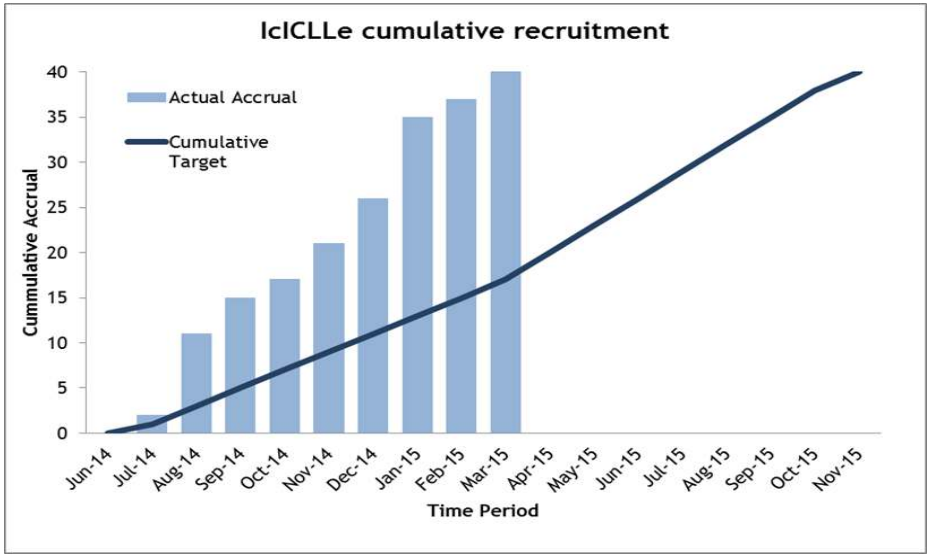
TAP Portfolio

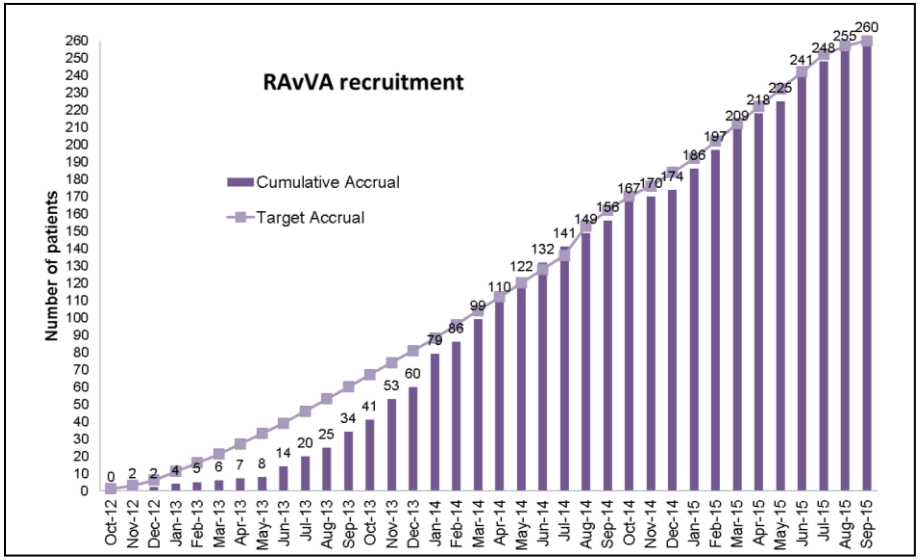
- **24 trials closed to recruitment**
- **3 trials open to recruitment**

Trial	Chief Investigator	Disease Area	Phase	Status
RavVA	Charles Craddock	Acute Myeloid Leukaemia (relapsed)	Phase II	Closed to recruitment
MAJIC	Claire Harrison	Myeloproliferative Neoplasms (ET and PV)	Phase II	Closed to recruitment
BREVITY	John Radford	Classical Hodgkin Lymphoma (naïve)	Phase II	Closed to recruitment
CyCLLe	Stephen Devereux	Chronic Lymphocytic Leukaemia (early-stage adverse risk)	Phase II	Closed to recruitment
IcICLLe	Peter Hillmen	Chronic Lymphocytic Leukaemia (naïve, relapsed/refractory)	Phase II	Closed to recruitment
Viola	Charles Craddock	Acute Myeloid Leukaemia (relapsed HSCT)	Phase I	Closed to recruitment
TORCH	Graham Collins	Diffuse Large B-Cell Lymphoma (relapsed/refractory)	Phase II	Closed to recruitment
CLARITY	Peter Hillmen	Chronic Lymphocytic Leukaemia (relapsed/refractory)	Phase II	Closed to recruitment
IcICLLe Extension	Peter Hillmen	Chronic Lymphocytic Leukaemia (naïve, relapsed/refractory)	Phase II	Closed to recruitment
CALiBRe	Peter Hillmen	Chronic Lymphocytic Leukaemia (naïve, relapsed/refractory)	Phase II	Closed to recruitment
MATCHPOINT	Mhairi Copland	Chronic Myeloid Leukaemia (blast phase)	Phase I/II	Closed to recruitment
ELASTIC	Alexander Sternberg	Myelodysplastic Syndromes (high-risk)	Phase Ib	Closed to recruitment
ROMAZA	Charles Craddock	Acute Myeloid Leukaemia (relapsed/refractory)	Phase I	Closed to recruitment
Bubble	Kwee Yong	Myeloma (relapsed/refractory, t(4;14) or t(14;16))	Phase Ib	Closed to recruitment
RomiCar	Graham Collins	Peripheral T-Cell Lymphoma (relapsed)	Phase I/II	Open to recruitment
TIER	Christopher Fox	Primary Central Nervous System Lymphoma (relapsed)	Phase I/II	Open to recruitment
PHAZAR	Mark Drummond	Myeloproliferative Neoplasms (accelerated phase, blast phase)	Phase Ib	Open to recruitment
TAMARIN	Claire Harrison	Myeloproliferative Neoplasms	Phase II	Open to recruitment
AVAIL-T	Simon Wagner	Peripheral T-Cell Lymphoma (relapsed/refractory)	Phase IIa	Open to recruitment
STELLAR	Anna Schuh	Richter's syndrome (naïve)	Phase II	In-set-up

TAP

Accelerated Recruitment





TAP Highlights

- TAP has transformed the recruitment to complex haemato-oncology trials- over 1,200 patients recruited in comparison with 7 prior to establishment of TAP
- 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
- **Increased interest from global pharmaceutical partners in provision of registration enabling trial data**

TAP

Clinical Studies in Stem Cell Transplantation: a Major Unmet Need in 2025

- Stem cell transplantation is a key curative treatment modality in children and adults with hematological diseases
- >50% of patients die post-transplant as a result of procedural toxicity or relapse
- <5% of patients enter prospective transplant trials
- Registry studies whilst of substantial value in advancing the field are compromised by potential selection bias and often contradictory
- Capacity, speed and sustainability remain challenges in transplant trial delivery
- CAR-T therapy has similar transformative promise and trials requirements

PARTNERSHIP FOR ACCELERATED CLINICAL TRIALS

ANTHONY NOLAN saving the lives of people with blood cancer

Birmingham Health Partners

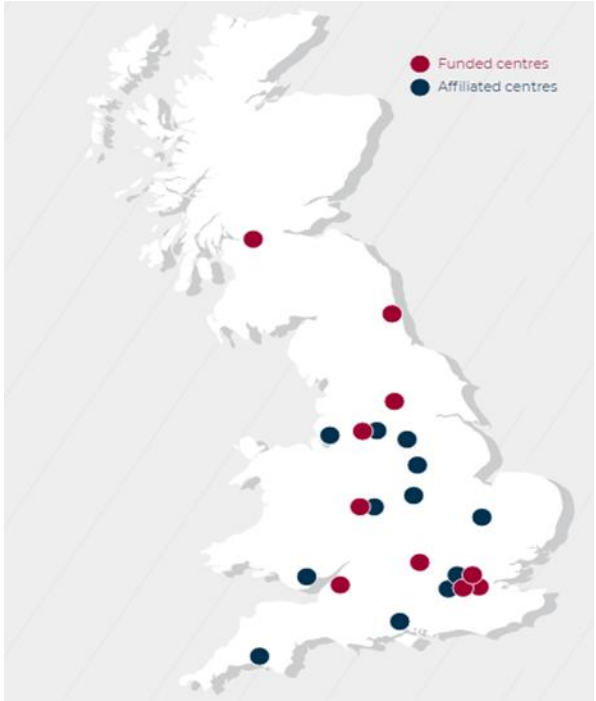
BSBMT

@CRCTU

leuka leading leukaemia

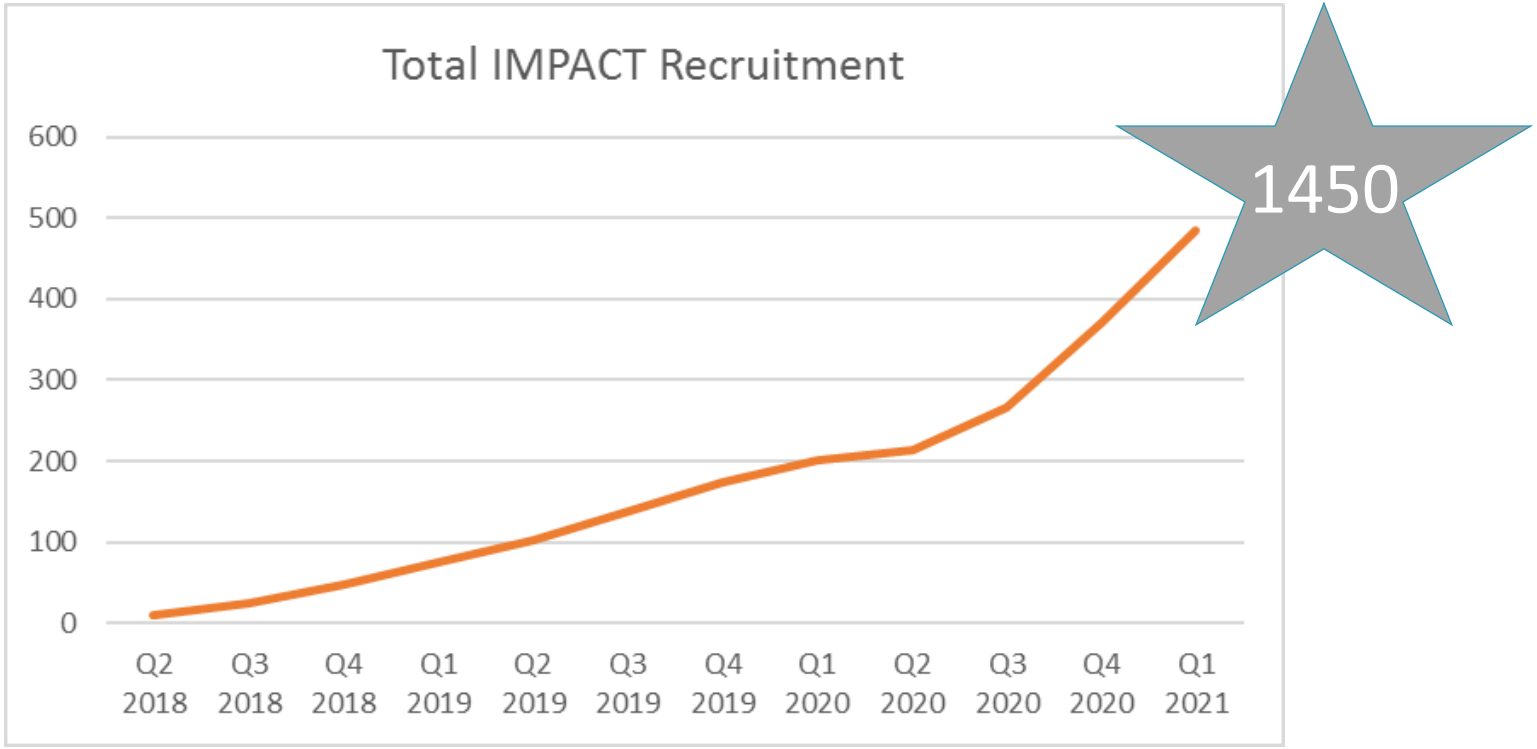
NHS Blood and Transplant

IMPACT Structure: a Trials Delivery HUB with an Integrated National Research Nurse Network



- ✓ Central Hub: responsible for trial design, setup, management and publication
- ✓ 11 funded transplant centres able to recruit to IMPACT studies
- ✓ Conditions of funding:
  - Prioritisation of feasability return
  - PIS offered to all eligible patients
  - Prompt CRF completion

IMPACT Recruitment



Lessons from the IMPACT pilot 2018-2022

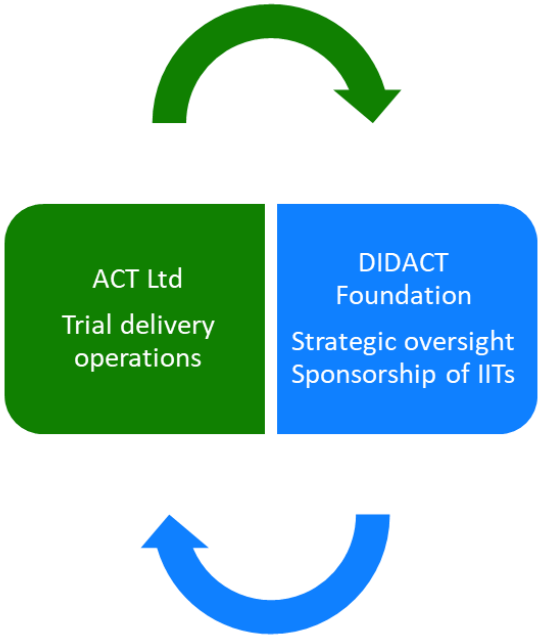
- The IMPACT pilot has demonstrated the effectiveness of a transplant trials acceleration network –with funded research nurses
- A pump-priming investment of £3.4 million has resulted in more than 1400 patients being recruited to practice changing prospective transplant trials
- Prospective, sequential well curated sample collection is supporting transformative basic science initiatives
- Access to innovative therapies in stem cell transplantation has been levelled up across the UK
- Importance of registration standard data increasingly identified by global pharma as of pivotal importance
- Achievements of European ARO model increasingly apparent-HOVON, European Myeloma Network, LYSARC

ACT: a new model for delivery of new TAP and IMPACT trials

- Nov 2021: Funding obtained from Cure Leukaemia, NHSBT and Anthony Nolan to establish ACT
- Commercially effective- competitive with CRO sector
- Mutualised
- Quaker principle
- Financial surplus to be distributed to the benefit of the UK haem-onc patient community as advised by funders and academics
- Clinical prioritisation by TAP and IMPACT investigators essential for selection of academic and industry sponsored trials through matching charity DIDACT

Structure of ACT and DIDACT

- ACT will be an effective and responsive trial delivery vehicle for UK blood cancer patients
- ACT will be commercially competitive with CRO sector
- ACT will provide a comprehensive portfolio of clinical trial services



- DIDACT Foundation will be a registered charity
- Provides sponsorship for academic IITs
- ACT Trial prioritisation delivered by TAP and IMPACT Leadership Teams
- Advises on distribution of financial surpluses for the benefit of UK blood cancer patients

ACT and DIDACT: Progress to Date

- £5 million funding secured from Cure Leukaemia, NHSBT and Anthony Nolan to establish ACT and DIDACT in December 2021
- ACT operational team established (leadership from Pharma and CRO sector)
- TAP and IMPACT networks refunded in Jan 2023
- Trials secured:
  - ACT-AML-101 Randomised phase II in fit adults with high risk AML- IIT funded to deliver registration enabling data
  - -ACT-AML-102 Phase I/II in fit adults with high risk AML- IIT funded to deliver registration enabling data approved in principle
  - EVOLVE 1 (VEN/AZA/Ivo) and EVOLVE 2 (VEN/AZA/Revumenib)- multinational trials sponsored by HOVON-ACT to deliver UK patients
  - PRIOTHERA- post transplant maintenance
  - Industry sponsored CAR-T trial-ACT will deliver only European sites

ACT and DIDACT: Progress To Date

- Four additional enhanced IITs/industry sponsored trials at contracting stage and two contracts with Global Cell therapy companies signed
- DIDACT Academy –inaugural meeting 2023, meets 6 monthly-has established formal mentoring process for junior consultants and trainees
- ACT cited as model of innovative trial delivery by O'Shaughnessy Report

Department for Science, Innovation & Technology

Department of Health & Social Care

Office for Life Sciences

Independent report

Commercial clinical trials in the UK: the Lord O'Shaughnessy review - final report

Updated 26 May 2023

Part 3: transforming how the UK does clinical trials

Case study: Accelerating Clinical Trials – a new blood cancer trial delivery vehicle

Blood cancers remain one of the most common malignancies and there is justified excitement that the recent development by the global biopharmaceutical sector of a wave of potentially transformative new drug and cellular therapies could transform clinical outcomes. To take advantage of this opportunity, Accelerating Clinical Trials (ACT) Ltd (a company limited by guarantee) was established in December 2021 to accelerate the delivery of high-quality trials for blood cancers by addressing barriers to trial delivery, including: insufficient trial capacity to match the sudden expansion in the number of potential new therapies; outdated delivery models; and challenges to patient recruitment including the need to utilise genomic stratification.

Commercial clinical trials in the UK: the Lord O'Shaughnessy review - final report - GOV.UK (www.gov.uk)

Progress to date
Business Development

Summary

- The TAP and IMPACT trial delivery networks are transformational vehicles for accelerated delivery of haemato-oncology and transplant trials
- ACT is acting as magnet to global pharma attracting trials of new drug and cell therapies
- Models such as LYSARC, the European Myeloma Network and ACT are financially sustainable models delivering registration informing clinical trials
- ACT funds the TAP and IMPACT networks and in future will create capacity for IIT delivery
- The ARO model is scaleable and can create a new UK industrial sector
- Failure to develop a commercially competitive ARO model would represent an existential threat to the UK Life Sciences sector, the NHS and its patients