Executive summary

The number of advanced therapy medicinal product (ATMP) clinical trials in the UK continues to increase year on year with 127 ongoing trials observed in December 2019, with a majority employing viral vector mediated gene transfer. This represents approximately 12% of all ongoing global trials, demonstrating the appeal of the UK for the clinical development of ATMPs.

A doubling of the number of Phase III trials from 2018 is observed. In addition, the data suggest that trials are progressing through set up and reaching active recruitment more quickly than previously observed, perhaps reflecting a degree of familiarity with ATMPs within the highly developed ecosystem. The majority of these are viral vector mediated gene therapies.

The ongoing development of the Advanced Therapy Treatment Centre Network, funded by the UK government Industrial Strategy Challenge Fund, continues to support the local infrastructure. This network has been successful in building systems within the NHS to ensure that products progress effectively through clinical development and can be commercialised in the UK.

Introduction to the database

The UK Clinical Trials Database covers ATMP clinical trial activities that the Cell and Gene Therapy Catapult (CGT Catapult) believes to be ongoing in the UK as of December 2019. It supersedes the 2018 database, and both are available on our website.

Please note, a new automated methodology to identify trials has been employed for the 2019 review. This has uncovered trials missed by the manual searches used previously. As a result the increase observed in trial numbers between 2018 and 2019 is a combination of new trials and previously unidentified trials, but the numbers for new trials demonstrate sustained year on year growth seen since the survey started in 2013.

The database has been compiled and verified by the CGT Catapult team, and includes:

- academic and commercial trials,
- ongoing trials in the UK, regardless of the nationality of the Sponsor,
- all advanced therapy medicinal product trials.

The database is updated annually and provides, what we believe to be, a comprehensive and accurate review of the UK ATMP clinical trial landscape as of December 2019. The input of the cell and gene therapy community is important however to help us maintain its relevance, and we welcome updates, additions and corrections, which can be sent to us at clinicaldatabase@ct.catapult.org.uk

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The purpose of the Cell and Gene Therapy Catapult UK Clinical Trials Database

As a centre of translational excellence in the UK, the Cell and Gene Therapy Catapult collaborates on and progresses a portfolio of therapeutic projects and related enabling technologies with the UK and international community. The UK Clinical Trials Database forms an important part of the mechanism by which the Cell and Gene Therapy Catapult measures progress in the field and identifies trends. Importantly, the database should provide a platform for use by academics, researchers and commercial organisations operating in the advanced therapy space to understand the extent of advanced therapy activities in the UK.
Commentary on key findings 2019

The UK’s portfolio of advanced therapy medicinal product clinical trials continues to grow

The 2019 clinical trials database shows the continued year on year increase with 127 advanced therapy medicinal product clinical trials ongoing in the UK compared to 85 trials reported in 2018. This has been part of an ongoing trend of sector growth since 2013 (Figure 1).

Note, a new automated methodology to identify trials has been employed for the 2019 review. This has uncovered trials missed by the manual searches used previously. As a result the ~45% increase observed in trials between 2018 and 2019 is a combination of new trials and previously unidentified trials, but the numbers for new trials started in the last year are similar for previous years since the data collection started in 2013. We also see an increase in the number of trials reaching completion.

Figure 1. Number of ongoing, new and completed ATMP clinical trials in the UK from 2013-2019

- Ongoing Trials
- New Trials
- Closed Trials
- Suspended
- Withdrawn
Majority of UK advanced therapy medicinal product trials are in recruitment phase

As per previous years, the majority of UK ATMP clinical trials are in the recruitment phase, however in 2019 the number of trials recruiting is considerably larger than previous years as shown in the graph below (Figure 2).

Since we began tracking trial status in 2014, trials have gradually moved further along the project life cycle resulting in fewer trials in planning and more in recruitment, follow-up, and close-out.

As shown, trials previously in planning and set-up have moved into the recruitment phase, however this does not account for the large increase that is shown. This suggests advanced therapy trials in the UK are quickly moving through planning and regulatory approvals reaching the recruitment phase at a faster rate than previously. Two trials have been withdrawn.

Figure 2. Distribution of UK ATMP clinical trials according to trial status from 2014-2019

*Data for 2013 not collected*
**Oncology indications remain the largest sector**

The division of therapeutic indications amongst the trials remains largely unchanged. Oncology, which includes haematological malignancies and solid tumours, remains the dominant therapeutic area increasing its share from 29% in 2018 to 39%. Ophthalmology (13%) and Haematology (12%) are the second and third largest therapeutic areas this year, as shown below in Figure 3.

**Figure 3. Distribution of UK ATMP clinical trials according to therapeutic area in 2019**

- **Oncology** 39%
- **Haematology** 12%
- **Ophthalmology** 13%
- **Cardiovascular** 7%
- **Neurological** 8%
- **Renal and Urogenital** 2%
- **Musculoskeletal** 2%
- **Metabolic and Endocrine** 1%
- **Inflammatory and immune system** 9%
- **Respiratory** 1%
- **Skin** 1%
- **Liver** 3%
- **Other** 2%
- **Bone and cartilage** 1%
- **Other** 2%
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Diverse cell types with T cells predominant

For cell-based therapies, T cells remain the dominant cell type under investigation. This is as expected since research into oncology, the largest therapeutic sector, is largely T cell focused, and is consistent with previous years. CD34+ and/or CD133+ stem cells (19%) and mesenchymal stem/stromal cells (13%) remain the second and third most investigated cell types (Figure 4).

Figure 4. Breakdown of UK ATMP clinical trials by cell type in 2019
Split between autologous and allogeneic

Autologous cell products remain more frequently used than allogeneic products, as seen in Figure 5 below.

Figure 5. Distribution of autologous and allogeneic cell therapies in the UK clinical trials database from 2013-2019
Therapies are moving into later phase trials

The majority of trials remain in phase I/II however in 2019 there was a large increase in the number of trials in phase III. One phase IV trial has been initiated (see Figure 6, below). This shift is indicative of the ATMP space maturing and Sponsors progressing through their clinical development programmes and approaching long-term safety studies. Many new umbrella trials have started grouping together long-term safety follow-up of subjects from various trials having been exposed to the same therapy. In the coming years, this will be reflected by more trials in follow-up and these trials will have longer follow-up periods than previously observed.

Figure 6. ATMP clinical trials in the UK by clinical phase from 2013-2019
Growing numbers of UK clinical trials are sponsored by a commercial organisation

The percentage of commercially-sponsored clinical trials has continued to increase year on year, accounting for approximately three quarters of clinical trials in 2019 (Figure 7).

Figure 7. Proportion of commercial and academic/non-profit ATMP clinical trial sponsors from 2013-2019

Percentage Trials

- Academic/non-profit
- Commercial sponsor
**Majority of therapies in the database are genetically modified**

In keeping with the trend seen in 2018, the database shows that 74% of the clinical trials in the UK involve genetic modification (both *in vivo* and *ex vivo*). The remaining 26% are cell-based therapies without genetic modification (Figure 8).

For genetically modified trials, the split between *in vivo* genetic modification and *ex vivo* genetic modification was 41% and 59% respectively in favour of *ex vivo*.

![Figure 8. Genetically modified therapies vs non-genetically modified therapies in the UK in 2019](image)
Gene delivery technologies

As shown in Figure 9 below, the majority of in vivo therapies used in clinical trials utilise AAV vectors (89%), essentially unchanged from last year, with 5% using lentiviral delivery and 3% using non-viral methods.

For ex vivo trials, lentiviral delivery dominates (57%) with retroviral vectors the next most used at 39%.

Figure 9. Distribution of gene delivery technologies in vivo and ex vivo
**Genome editing technologies**

The trials identified in 2018 using genome editing technologies continue in 2019. These trials represent the three main approaches to genome editing with CRISPR and TALEN being used for *ex vivo* modification of haematopoietic stem cells (HSCs) and T cells respectively and a zinc finger nuclease approach being used for *in vivo* insertion of factor IX (FIX) to treat Haemophilia B (the latter now in follow-up). An increase in activity in the genome editing space, previously identified in our pre-clinical landscape review, is still expected to result in an increased presence in the clinical trials database.
Conclusions

The 2019 CGT Catapult database of UK ATMP clinical trial activity reveals an industry that continues to grow and mature, with a significant increase in the number of trials recruiting in the UK. The majority of commercially sponsored trials are backed by non-UK based companies demonstrating the appeal of the UK ecosystem for these types of trials due to the regulatory environment and scientific and clinical expertise available.

The 2019 data continues to demonstrate the year on year increase in clinical trials in the UK with 127 trials indicated, which is approximately 12% of all global ATMP trials. The proportion of commercially sponsored trials continues to increase, with these now accounting for approximately 77% of all trials. Gene modified product (ex vivo and in vivo) trials account for approximately 74% of all ongoing trials in the UK.

As well as providing CGT Catapult with important information on industry progress, we hope this database serves the advanced therapy community as a resource for planning future clinical programmes. For example, knowledge of which UK hospitals have experience in advanced therapies for specific therapeutic areas, or in the use of a certain cell type, as well as which sponsors are supporting the advanced therapy area can be important information in clinical trial planning and the search for potential funding.