

The Cell and Gene Therapy Catapult UK clinical trials database

The UK clinical trials database covers cell and gene therapy clinical trial activities that the Cell and Gene Therapy Catapult (CGT Catapult) believes to be ongoing in the UK as of June 2016. It supersedes the database of May 2015, and both are available on our website.

A new addition for the 2016 database is inclusion of clinical trials involving *in vivo* gene therapy, either using viral or non-viral gene transfer strategies.

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 trials involving cells as therapeutic agents*; and
- all trials involving *in vivo* and *ex vivo* gene therapy.

*Excluding trials of haematopoietic stem cell transplantation regimens.

Significant changes versus the previous version of the database are discussed in more detail below.

The database is updated annually, and provides what we believe to be the most comprehensive and accurate review of the UK cell and gene therapy clinical trial landscape as of June 2016. The data presented here were collected between end of March 2016 and end of June 2016. The input of the cell and gene therapy community is important to help us maintain its relevance, and we welcome your updates, additions and corrections, which you can send to us at: clinicaldatabase@ct.catapult.org.uk

The purpose of the CGT Catapult UK clinical trials database

As a centre of translational excellence in the UK, the CGT 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 CGT Catapult identifies potential programmes for investment or partnership, and provides a highly relevant measure

of progress in the field. Importantly, the database should provide a platform for use by academics, researchers and commercial organisations operating in the cell and gene therapy space to understand the extent of cell and gene therapy activities in the UK and to identify potential partners/collaborators.

It is complemented by a UK preclinical research database, also available on our website, which covers cell and gene therapy projects that have been reported to us to be three or less years from the clinic (characterised by their technology readiness level) and enables us to track trends, make predictions about clinical pipeline development and plan strategically.

Commentary on key findings

1) The UK's portfolio of cell and gene therapy clinical trials is progressing

The 2016 clinical trials database sees the inclusion of *in vivo* gene therapies in addition to the previous inclusion of cell therapy trials including ex vivo gene therapy. Overall, this shows there are 57 active (by which we mean ongoing and new) trials in cell and gene therapy in the UK and of these, 51 are cell therapy clinical trials. The majority of trials are in the recruitment phase, according to the information in the CGT Catapult database for which approval and verification was available.

We believe 12 of the 51 active cell therapy trials in the 2016 database to be new to the database, two of which progressed from the preclinical database. Eight studies from the 2015 database have been completed and three have been suspended.

In 2015, we reported 51 cell therapy clinical trials active in the UK and this has been part of a trend of growing numbers of clinical trials in the sector (**Figure 1**). This year, there has been a new trend with an increase in the number of trials completed within the past year, showing progression of the portfolio without a net increase in the overall number of ongoing trials compared to the previous years.

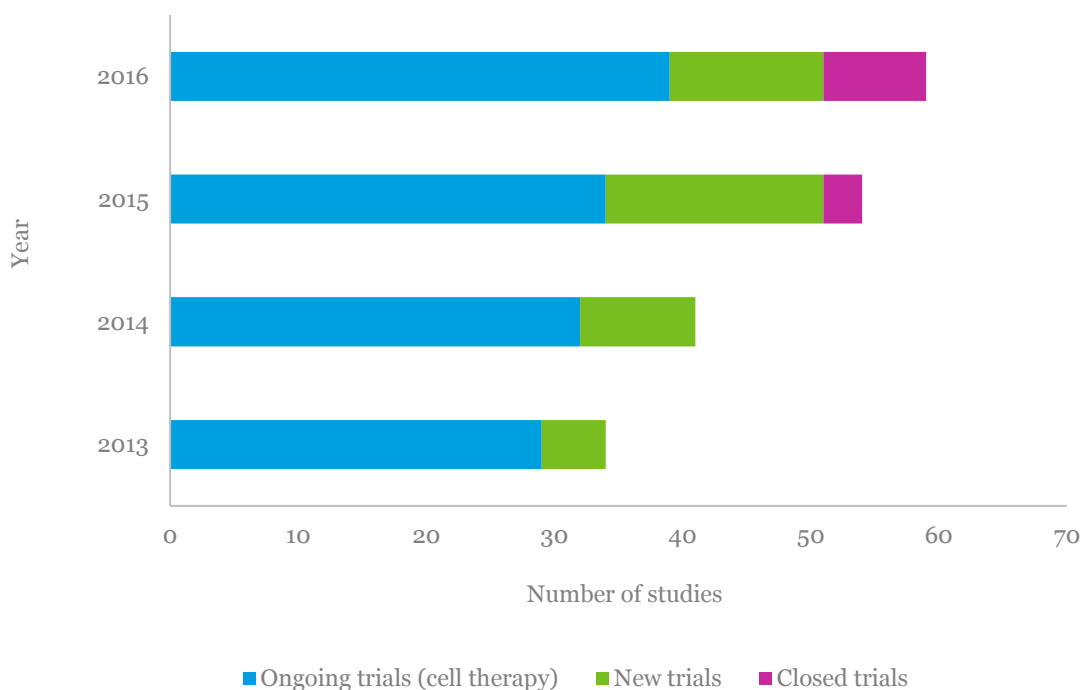


Figure 1. Number of ongoing, new and completed cell therapy clinical trials in the UK from 2013-2016

2) The *in vivo* gene therapy landscape

For the first time, the 2016 database also includes clinical trials of *in vivo* gene therapy which have been reported to us as currently ongoing in the UK. A total of six trials have been identified, of which five are commercially-sponsored. Five trials are in the recruiting phase and only one in follow-up. In terms of vector type, the majority of trials use an AAV vector (four) and only one a lentiviral-based vector. The database also includes one trial of antisense therapy using a single stranded antisense oligonucleotide designed to reduce the production of the huntingtin (HTT) protein, which is the genetic cause of Huntington's disease (HD). The *in vivo* gene therapy landscape is changing and growing and we welcome additional information from developers to add to the completeness of our databases.

3) Majority of UK cell and gene therapy trials in recruitment phase

The majority of UK cell and gene therapy clinical trials are in the recruitment stage, as shown in the graph below (**Figure 2**). In 2016, the data show that there are more trials currently recruiting having progressed from set-up in 2015 and also an increase in the number of completed trials. This shows the progression of the portfolio, meaning that an increased number of subjects have been treated with cellular-based therapies in the UK.

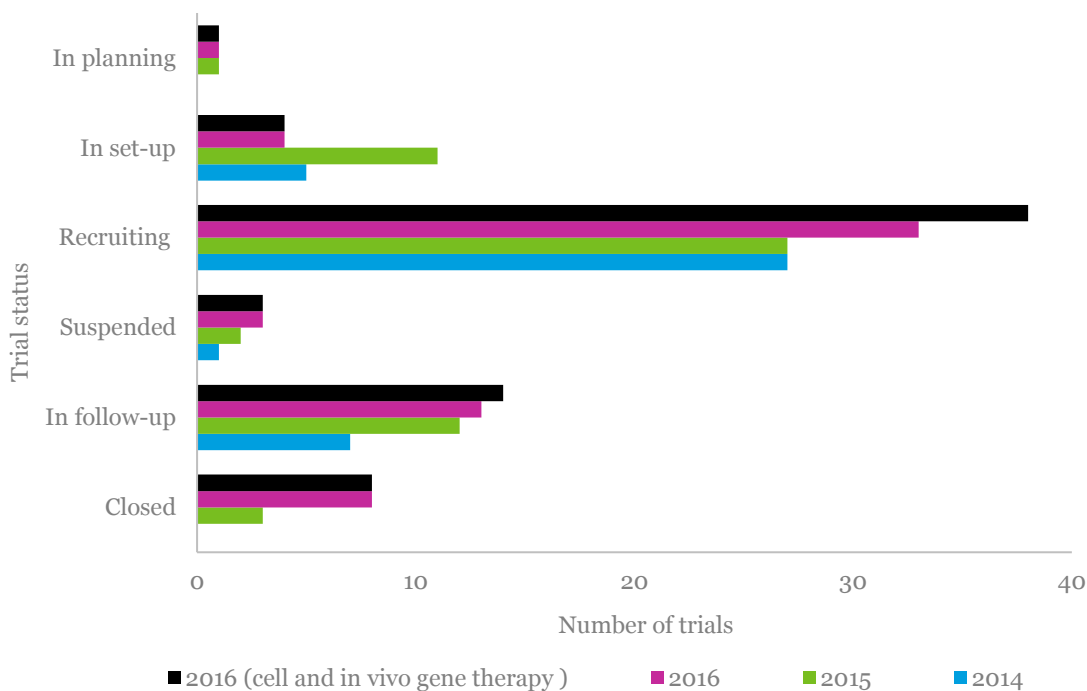


Figure 2. Distribution of UK clinical trials according to trial status from 2014-2016. (Data for 2013 not available)

4) Oncology indications remain the largest sector

Oncology, which includes haematological malignancies and solid tumours, remains the dominant therapeutic area (21%) as reported in previous years. Neurology is the second main therapeutic sector (16%; nine trials of which two use *in vivo* gene therapy), followed by trial activity involving ophthalmology (six trials; three of which use *in vivo* gene therapy), cardiovascular and gastroenterology disorders (**Figure 3**).

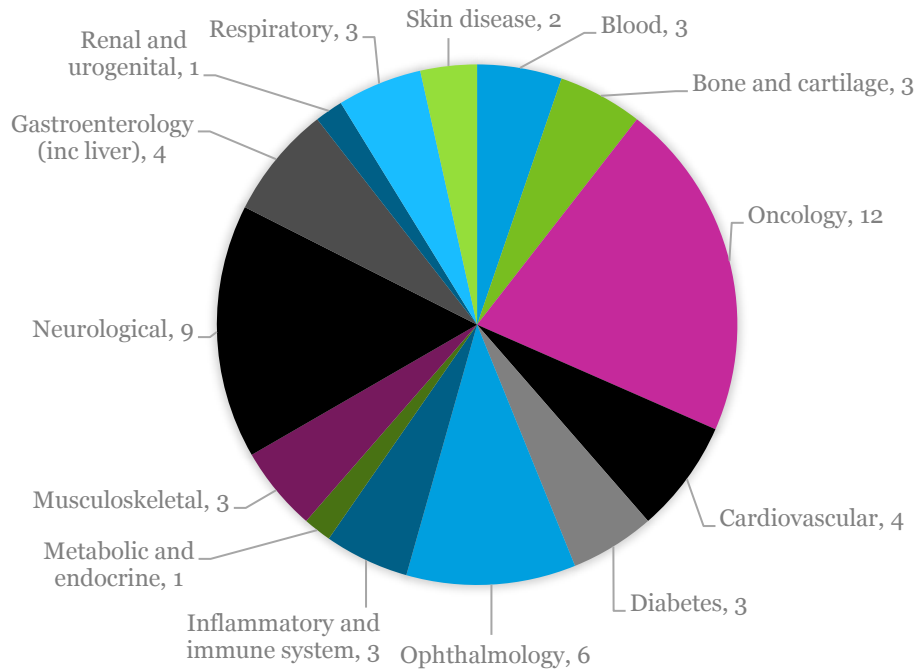


Figure 3. Distribution of UK cell and gene therapy clinical trials according to therapeutic area in 2016

† Therapeutic areas new to the clinical trials database

*Includes haematology

5) Diverse cell types with bone marrow-derived and T cells predominant

For cell based therapies, the diversity of cell types in development is still reflected in this year database. T cells (12 trials, 23%) and bone marrow-derived cells (21 trials, 41%) continue to be the predominant cell types used in the clinic (**Figure 4**), followed by neural cells (five trials, 10%). Two new cell types have emerged in this year database; blood cells (erythrocytes) and epithelial cells (epidermal).

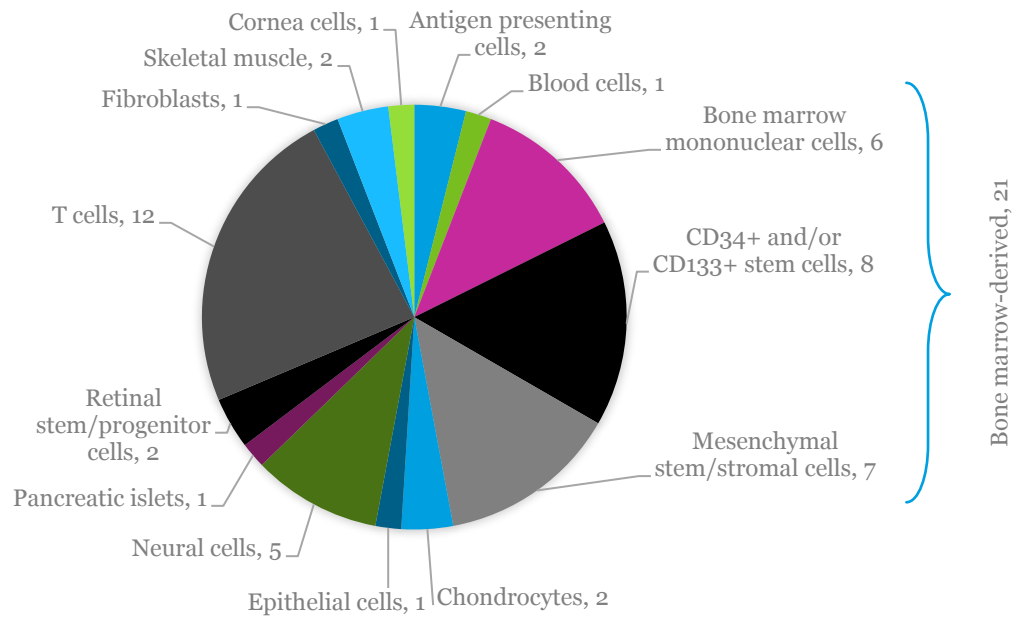


Figure 4. Breakdown of UK cell therapy clinical trials by cell type in 2016

6) Split between autologous and allogeneic 2:1 in 2016

Autologous cells products are more frequently used than allogeneic products (2:1 ratio), and this has remained relatively constant as a ratio over the past three years (Figure 5).

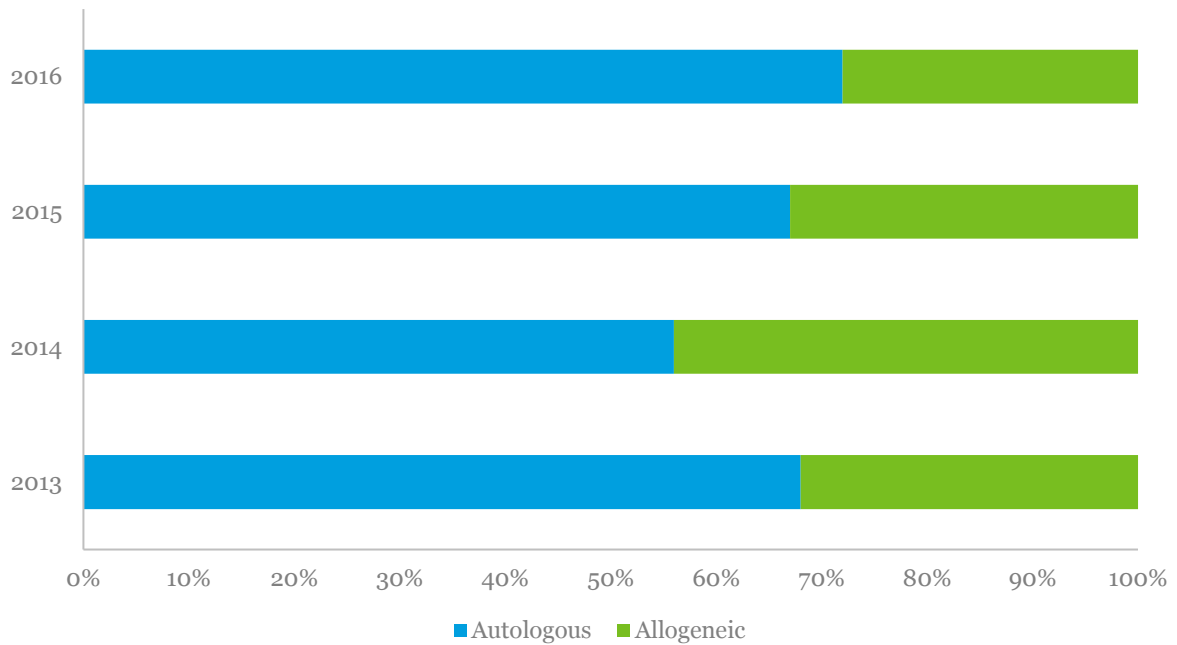


Figure 5. Distribution of autologous and allogeneic cell therapies in the UK clinical trials database from 2013-2016

7) The majority of therapies are in early phase trials

There has been a steady increase in the number of trials in phase I, phase I/II and phase II as new entities enter development and therapies previously at phase I progress to phase II (**Figure 7**). However, whilst there has been an increase in the number of phase III trials in 2016, the UK portfolio of activity remains at an early phase with still relatively few therapies in phase II/III or phase III.

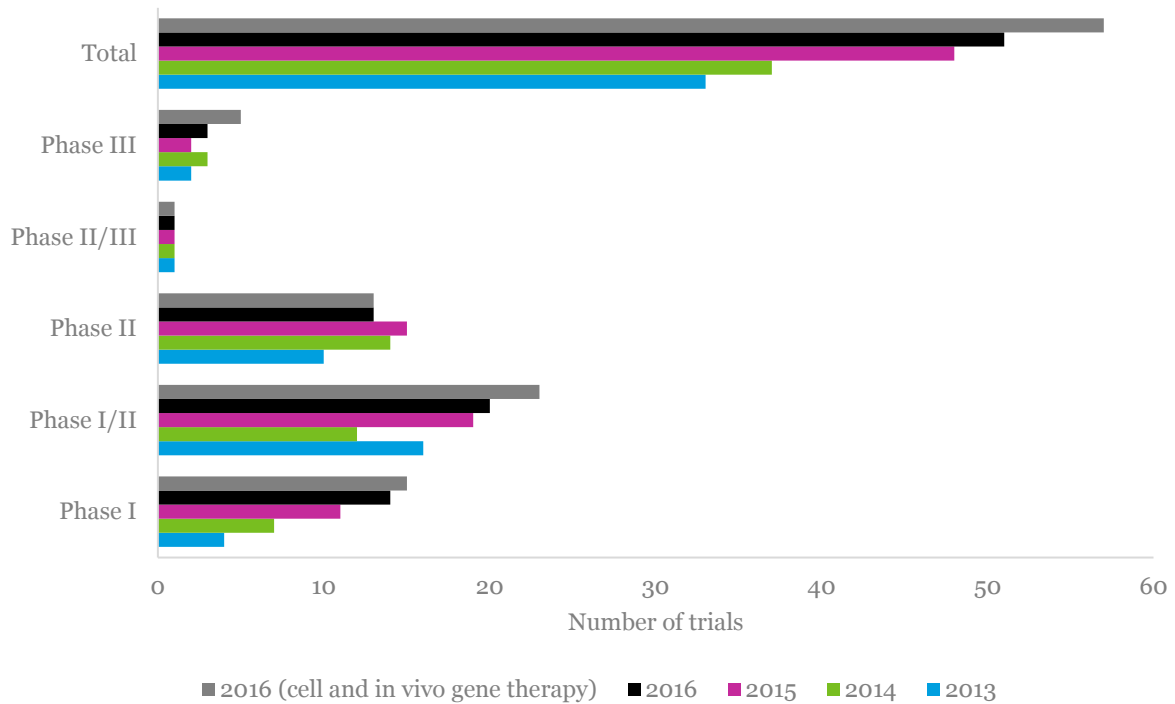


Figure 7. Cell therapy clinical trials in the UK by clinical phase from 2013-2016 (2016 figures also show the total for cell and gene therapies combined)

8) Growing numbers of UK clinical trials are sponsored by a commercial organisation

The number of commercially-sponsored clinical trials has increased in 2016 (Figure 8), likely reflecting the growing confidence in the cell and gene therapy industry attracting private companies and indeed a significant increase in UK spinouts over the past 12 – 18 months. Trials sponsored by academic and research institutions remain the majority (60%).

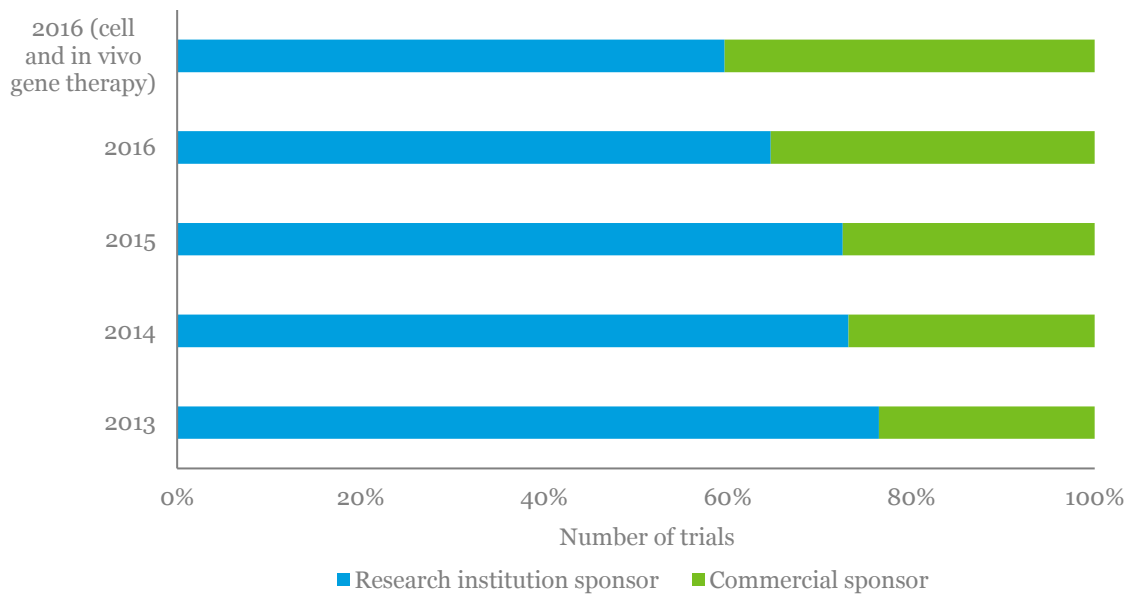


Figure 8. Proportion of commercial and research institution trial sponsors from 2013-2016

9) Majority of therapies in the database are non-genetically modified

The 2016 database shows that 37% of trials involve cell therapies modified *ex vivo* with a vector or *in vivo* gene therapies, the majority of which use a lentiviral-based vector (**Figure 6**). The database also shows for the first time the start of a clinical trial utilising gene editing technology. The remaining 63% of cell therapies currently used in clinical trials in the UK do not involve genetic modification.

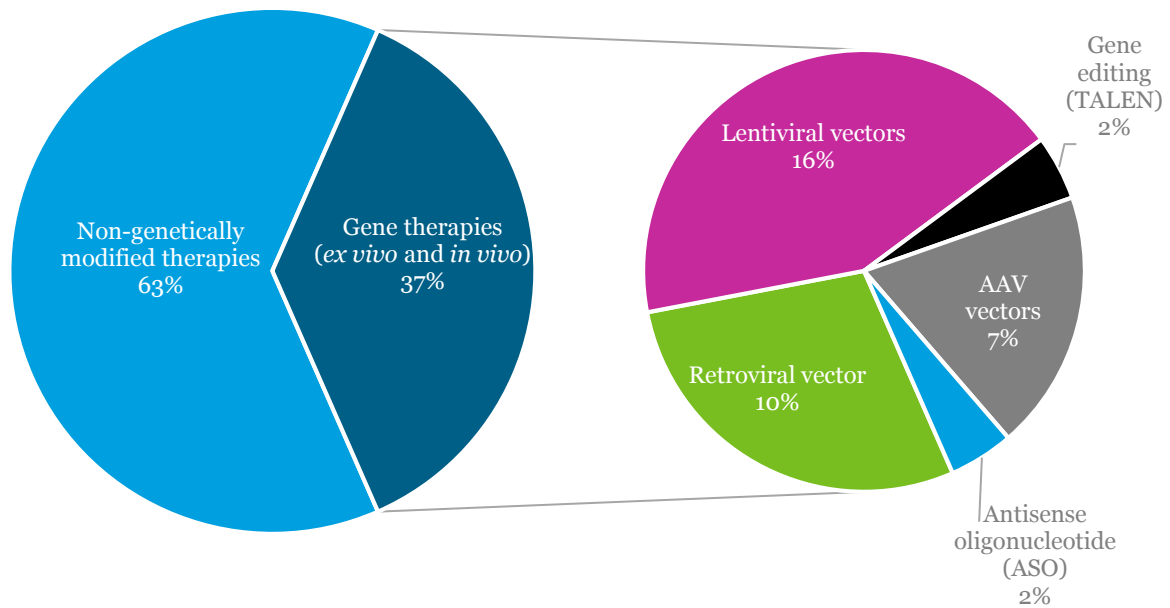


Figure 6. Genetically modified cell therapies used in UK clinical trials in 2016

10) Database utility for developers

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

Conclusions

The CGT Catapult's database of UK clinical trial activity reveals an industry that is growing and maturing in the UK with increasing numbers of companies involved in development of therapies and increasing numbers of clinical trials in recruitment or reaching completion. For the first time, the 2016 database also includes *in vivo* gene therapy trials and whilst the number of these is relatively low, this part of the sector is attracting significant investment and we expect future years to demonstrate growth of these types of trials in our database.

We hope that cell and gene therapy researchers and organisations will find our UK clinical trials database informative and useful. As the CGT Catapult and others focus on translational activities, we expect the analyses of future years to show an industry undergoing significant growth and moving towards maturation.