EVOLUTION OF INTERVENTIONAL TRIALS FOR GENE THERAPIES

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BACKGROUND

- ClinicalTrials.gov (CT) is a web-based resource that provides patients, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions. [1]
- Provided free of charge downloadable snapshots of CT database contains the full information available on the CT website.
- However, due to the relational structure opens up a great potential for exploration of the whole database content beyond the limitations imposed by the CT's web-based search interface.
- Rapidly evolving area of gene therapies provides opportunity to treat medical conditions, for which the available interventions are ineffective, or no intervention exist.
- CT database mining was used to follow the maturing and trends of gene therapy development.

OBJECTIVE

The aim of this analysis was to describe the trends regarding methodological design, status and target indication among studies aiming to assess gene therapies (GTs) for various designations.

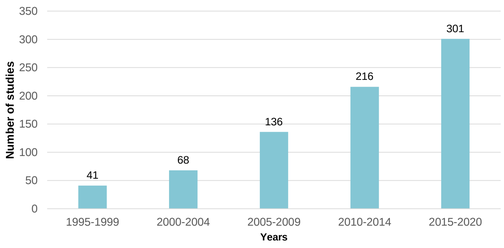
METHODS

- CT database snapshot (as at June 1, 2019) was downloaded through the link provided on the Clinical Trials Transformation Initiative webpage. [2]
- Uncompressed 44 flat pipe-delimited files (total size >5.7GB) were used to populate relational database, comprising information about 307,196 clinical studies from 209 countries.
- The largest file was related to reported events (>1.5GB) and the outcome measurements (~1.2GB).
- The database mining was performed using Creativ-Ceutical in-house search engine written in R language. [3]
- CT database was searched for trials with at least one occurrence of keyword phrases: "gene therapy", "gene transfer" or "AAV" (adeno-associated vectors).
- The search was carried out for records in the database tables containing information about: trial keywords, title, summary, description, interventions, design, outcomes and participant flow.
- Identified data related to title, study description, study design, presumed and actual study timeframes, inclusion/exclusion criteria, enrolment, health condition, intervention applied, the outcomes and the results reported were transferred to Excel tables for further analysis.
- A descriptive analysis was conducted to describe the trends regarding: the rates of emerging clinical trials, contribution of advanced studies, contribution of ongoing studies, distribution of treatment indications.

RESULTS

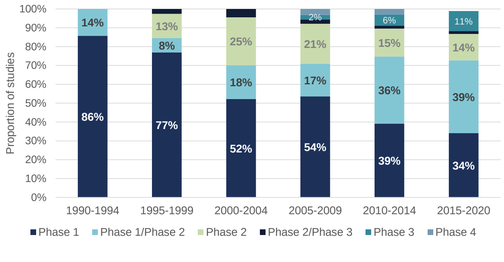
- The number of emerging interventional trials for GTs grow exponentially with 301 studies registered between 2015 and 2019. (Figure 1)

Figure 1. The number of emerging interventional trials for GTs between 1995-2019



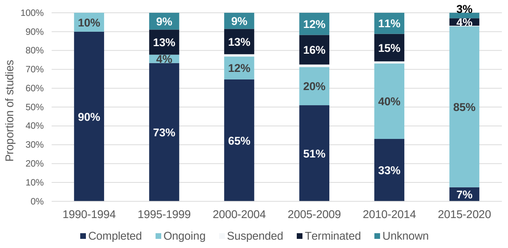
- Between 1990 and 2019 the contribution of respective study phases to overall number of emerging records decreased for phase 1 studies (from 86% to 34%), increased for phase 1/2 (from 14% to 39%) and phase 3 (from 3% to 11%) studies, and remained stable for phase 2 (~14%) and 2/3 trials (2%). (Figure 2)

Figure 2. The distribution of phases among 1990 and 2019



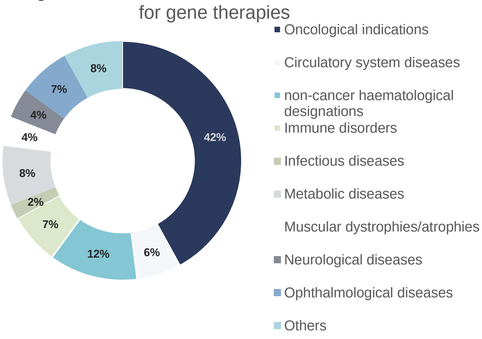
- The proportion of ongoing trials has been growing from 10% to 86% between 1990-2019. At the same time period the contribution of completed studies has been dereasing from 90% to 7%. The overall proportions of ongoing, completed and terminated studies registered between 1990 and 2019 were 48%, 32% and 11%, respectively. The proportions of completed and terminated studies since 2015 were 7% and 4%, respectively (Figure 3)

Figure 3. The distribution of study status between 1990 and 2019



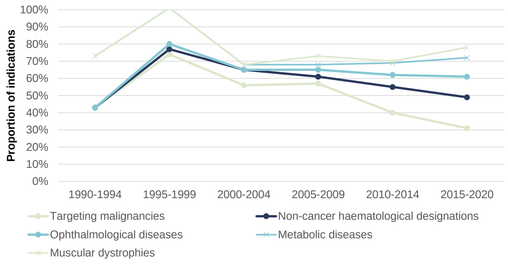
- Overall, studies targeted primarily oncological indications (42%) (Figure 4), followed by non-cancer haematological designations (12%). (Figure 4)

Figure 4. The overall distribution of indications for gene therapies



- The proportion of targeting malignancies decreased over time (-2% annually), while growing contribution of non-cancer haematological designations (0.7% annually), metabolic and ophthalmological diseases (both 0.5% annually), and muscular dystrophies (0.3% annually) were observed. (Figure 5)

Figure 5. The proportion of different indication in interventional trials for GTs



CONCLUSIONS

- Only few gene therapies have received market authorisation so far, and their availability is limited due to high costs, safety concerns and uncertain efficacy. Despite these limitations over the past 2 decades:
  - The number of trials assessing gene therapies has been growing exponentially
  - The contribution of advanced clinicla trials (at least phase 1/2) has grown from 14% to 66%
  - The proportion of ongoing studies has reached 85%
- The raising number of advanced clinical trials give hope that new therapies will be made available to treat patients in the coming years.

REFERENCES
1. https://clinicaltrials.gov/ct2/about-site/background
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3. R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

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