The Landscape of Clinical Trials Research in Inherited Ophthalmic Disease

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Inherited retinal degenerations are the most common inherited eye diseases

- Affect over 4M people worldwide, leading to blindness and high societal cost
- Despite a diversity of therapeutic approaches, many clinical trials have been abruptly halted
- This raises key questions, e.g. what is a meaningful impact on patients' daily life?
- Identifying reliable outcome measures for all actors, including patients, is urgent
- Rare disease clinical trials need specifically designed studies and global regulatory pathways

Innovative therapeutic approaches

in addition to gene replacement therapy, clinical trials using a wide and diverse range of innovative therapeutic approaches such as:

optogenetics,

antisense oligonucleotides,

gene editing have multiplied,

giving hope to patients and their caregivers.

However, initial enthusiasm has recently faded, as a number of clinical trials were abruptly halted as a result of missed primary endpoints and/or because of investors withdrawal.

Objective:

To describe the current status of clinical trials of genetic eye diseases with identified molecular targets for future areas of research.

Method:

Data analysis of the clinical trials database on clinicaltrials.gov with keywords for eight common, genetically tractable inherited eye diseases and their common molecular targets was performed during the period from 20/3/2021 to 31/12/2023.

Results

288 trials involving our keywords have been identified:

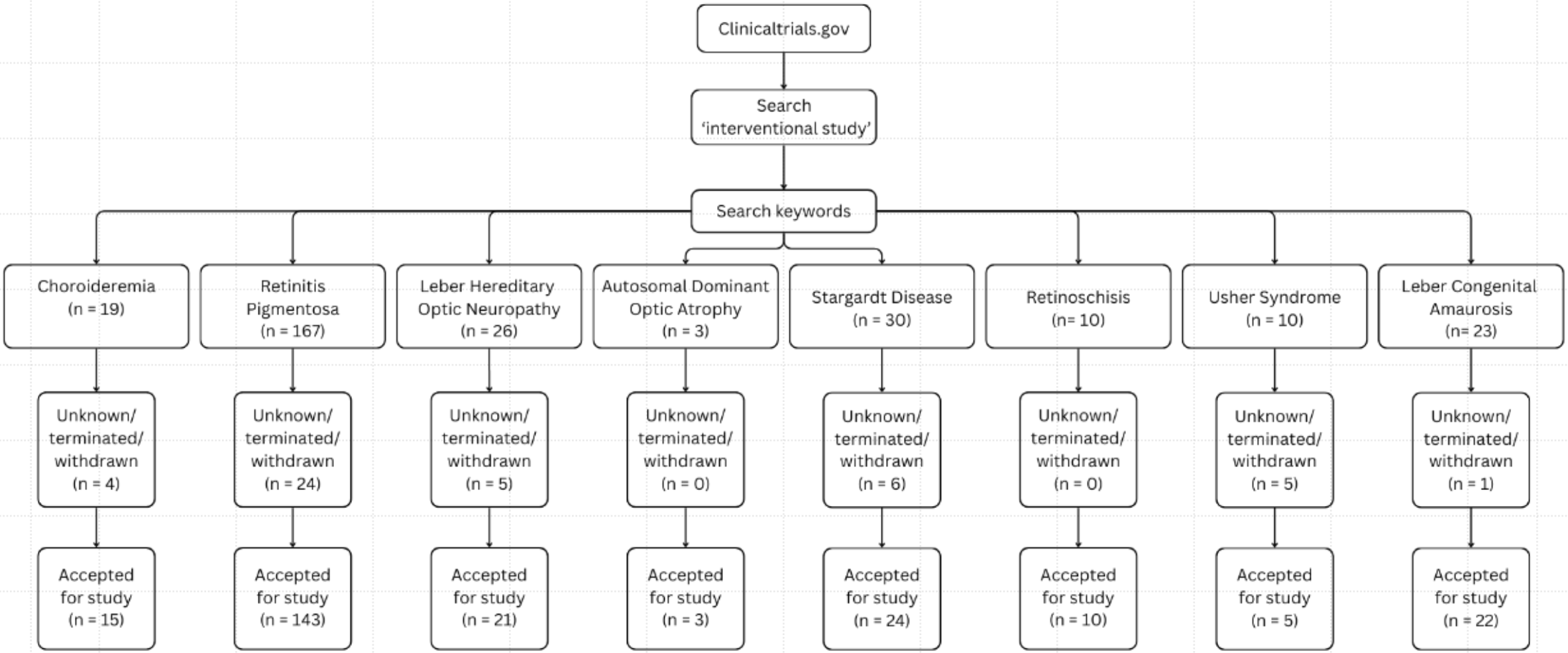
- We excluding:
  - 25 (8.7%) trials which were unknown (verification expired with no update)
  - 14 (4.9%) trials which were terminated early and
  - 6(2.1%) trials which were withdrawn

In total there were 243 (84.4%) trials included

Out of the 243 trials:

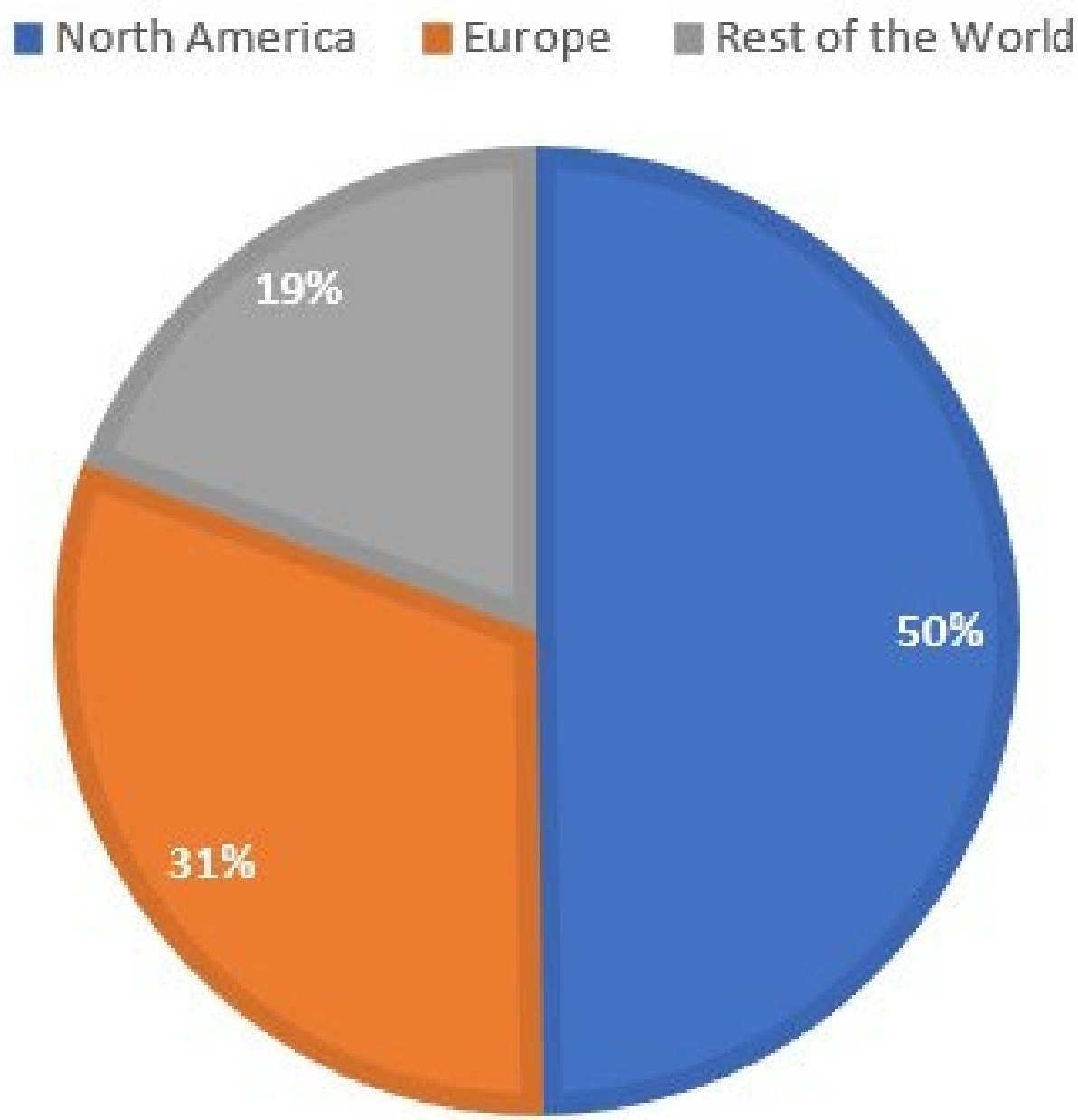
- 120 trials were completed
- 76 trials were active and still opened to recruitment and
- 44 trials were active without any more recruitment on the way

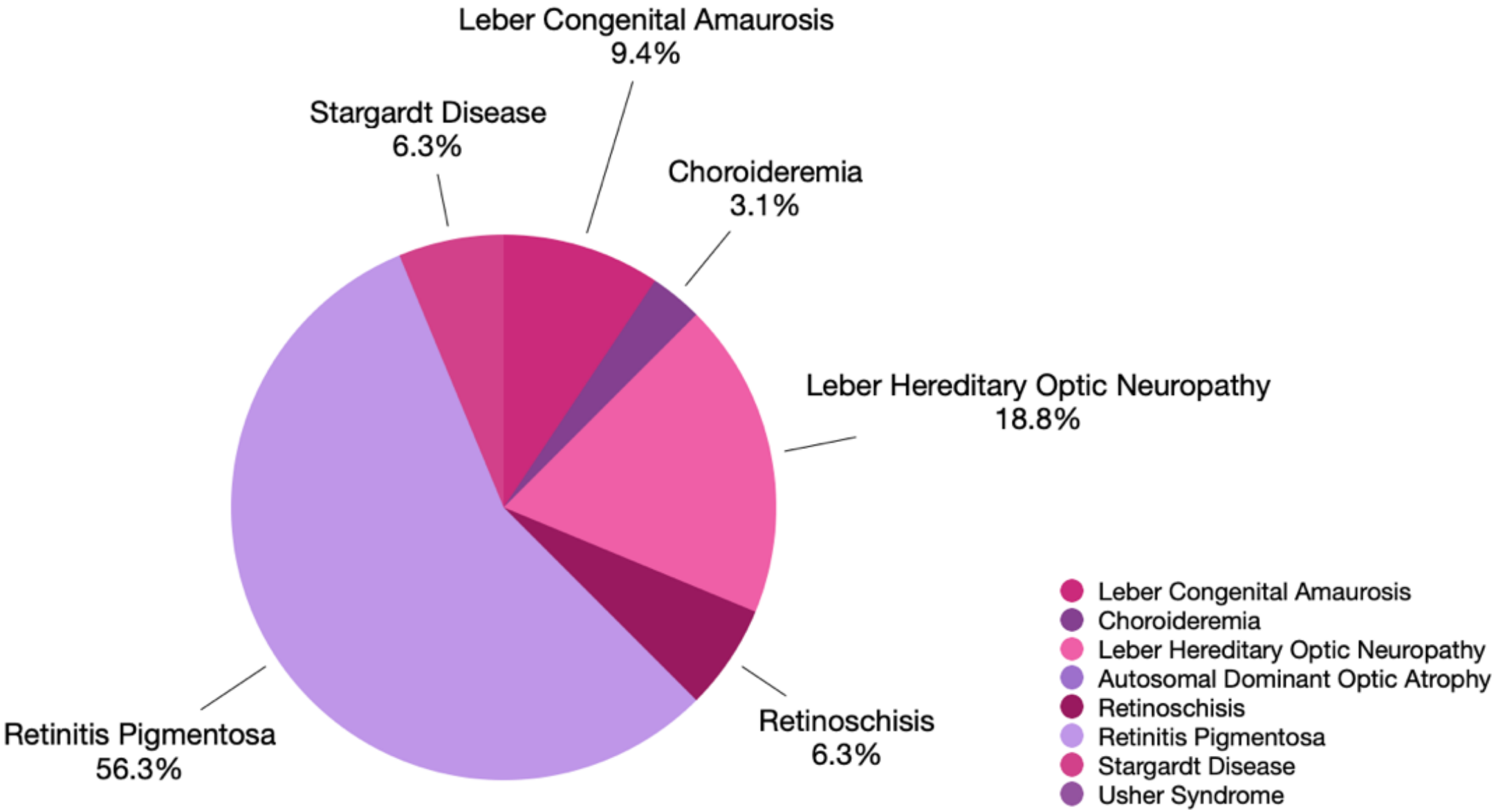
There were only 32 (13.2%) trials with posted results

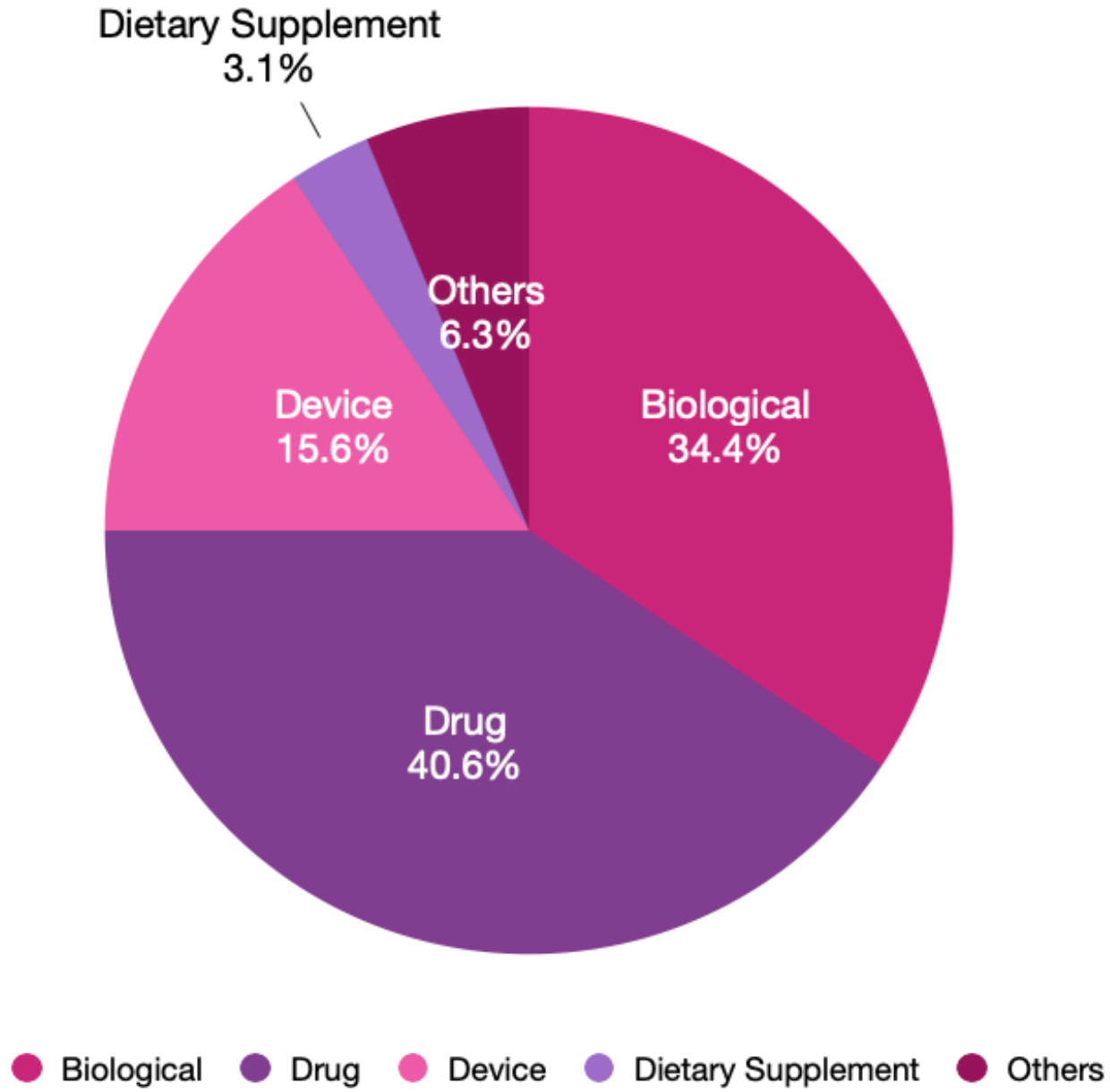

Clinicaltrials.gov
Search 'interventional study'
Search keywords
Choroideremia (n = 19)
Retinitis Pigmentosa (n = 167)
Leber Hereditary Optic Neuropathy (n = 26)
Autosomal Dominant Optic Atrophy (n = 3)
Stargardt Disease (n = 30)
Retinoschisis (n= 10)
Usher Syndrome (n = 10)
Leber Congenital Amaurosis (n= 23)
Unknown/ terminated/ withdrawn (n = 4)
Unknown/ terminated/ withdrawn (n = 24)
Unknown/ terminated/ withdrawn (n = 5)
Unknown/ terminated/ withdrawn (n = 0)
Unknown/ terminated/ withdrawn (n = 6)
Unknown/ terminated/ withdrawn (n = 0)
Unknown/ terminated/ withdrawn (n = 5)
Unknown/ terminated/ withdrawn (n = 1)
Accepted for study (n = 15)
Accepted for study (n = 143)
Accepted for study (n = 21)
Accepted for study (n = 3)
Accepted for study (n = 24)
Accepted for study (n = 10)
Accepted for study (n = 5)
Accepted for study (n = 22)

TRIALS STATUS OF VALID TRIALS

LOCATION OF TRIALS




Leber Congenital Amaurosis
9.4%
Stargardt Disease
6.3%
Choroideremia
3.1%
Leber Hereditary Optic Neuropathy
18.8%
Retinitis Pigmentosa
56.3%
Retinoschisis
6.3%
Leber Congenital Amaurosis
Choroideremia
Leber Hereditary Optic Neuropathy
Autosomal Dominant Optic Atrophy
Retinoschisis
Retinitis Pigmentosa
Stargardt Disease
Usher Syndrome


Dietary Supplement
3.1%
Others
6.3%
Device
15.6%
Biological
34.4%
Drug
40.6%
Biological
Drug
Device
Dietary Supplement
Others

Findings highlighted several issues

(1) the small populations involved with suboptimal numbers often further hampered by the lack of uniform access to genetic testing

(2) the difficult selection of appropriate controls, further hindered by phenotypical variability, even within one sibship

(3) the relatively long duration of trials in slowly progressive retinal conditions

(4) balancing between limiting the burden of repetitive testing to avoid poor performance and patient drop-out, and obtaining sufficiently reliable data from individuals with limited, inherently variable visual function

Conclusions

A low percentage of results were posted for completed trials

However, current and future clinical trials in the genetic eye diseases with molecular targets identified, have a promising future

The results of these trials will enhance allow a better understanding of the potential to develop treatments for these conditions