Forecasting Gene Therapy:

New Treatments, New Modeling Challenges

Problem Statement

The field of gene therapy is evolving rapidly and presents new challenges for those forecasting both disease cases and annual sales. Gene therapies are expected to be, in many cases, curative and will be launched at unprecedented prices, two nuances which require novel methods to predict both the future epidemiological and market landscapes.

Background

To date, there have been few gene therapies approved in the United States. In the oncology space, there's Kymriah, launched in August 2017 for the treatment of acute lymphoblastic leukemia, and Yescarta, launched in October 2017 for large B-cell lymphoma; these work by modifying patients' T cells to attack cancer cells.[1]

In the orphan space, there's Luxturna, launched in November 2018 for the treatment of biallelic RPE65 gene mutation-associated retinal dystrophy, which works by delivering a normal copy of the gene directly into the patients' cells.[2] This paper will focus on gene therapies for genetic diseases and conditions that may be administered at birth.

Methods

Estimating Prevalence

The clear first step in forecasting the uptake of a potential gene therapy is to determine the total prevalent cases of the disease in the countries of interest.

Prevalence is most effectively estimated through a systematic review of peer-reviewed epidemiological literature and subsequent meta-analysis of point estimates. Such point estimates can be applied to populations to generate prevalent cases. Claims databases or registries may also be used to identify patients, although these may underestimate prevalent cases given their intrinsic selection bias.

Changing birth rates and extended survival, sometimes due to novel medical treatments, require analyzing population demographics. With some diseases where life expectancy is only moderately reduced by the condition, this may require analyzing historical data dating back several decades to fully account for the prevalent cases.

Patient Survival

Understanding the survival curve is integral for an accurate analysis of gene therapy uptake, particularly for diseases that are typically reported in terms of birth prevalence, which is common for genetic conditions. This facilitates conversion from birth prevalence to overall prevalence, which is needed to understand total number of patients in a country. Drugs that are launched prior to the release of gene therapy often improve survival and should be incorporated into an updated survival curve at the time of its launch. Typically, two survival curves are needed at this point in the analysis to account for those who receive the life-extending therapy (Figure 1).

Age-specific analysis is becoming increasingly important as payers begin to restrict high-cost drugs to only age groups included in clinical trials.

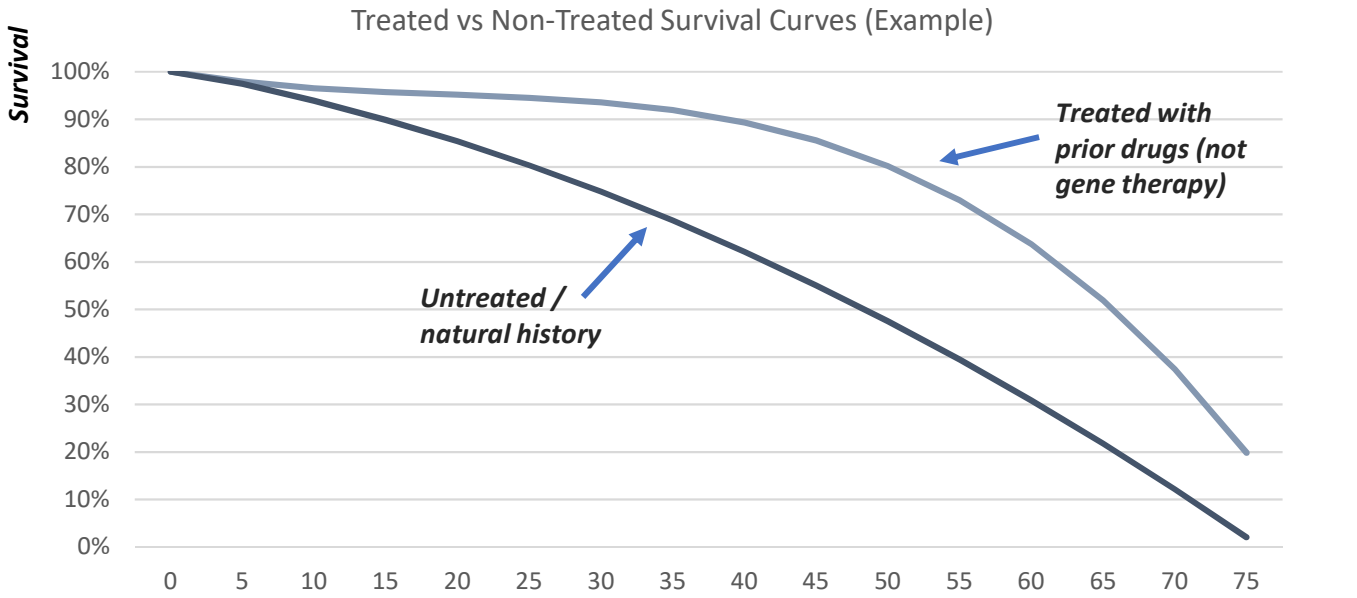

Figure 1.

Newborn Screening

When a curative or life-extending therapy is released, there will likely be a push for the disease to be included in standard newborn screening panels, e.g. cystic fibrosis. Once this takes effect, the uptake forecast shifts from focusing on the prevalent population to the incident population, as prevalent patients will either have been treated or denied for treatment. In this case, the majority of revenue will be within the first few years of launch, then decrease and stabilize as new patients are treated at birth, and the older patients are either cured or removed from the drug-treatable population.

Care must be taken to model the integrated relationship between screening/diagnosis, death rate, and cure rate to ensure accurate forecasting.

Gene Therapy Uptake

After generating the necessary survival curves and the prevalent population, the uptake of gene therapy itself needs to be carefully considered and will be impacted by several crucial components: physician willingness to prescribe the drug; payer willingness to reimburse the drug; and existing therapies.

1) Physician willingness to prescribe the drug:
   - In some instances, a gene therapy will only be considered beneficial if a patient is very young and in the early stages of a disease. Receiving gene therapy after the patient's disease has fully progressed likely will not reverse any damage or physical decline and physicians may thus not see a clear benefit to their patients.

2) Payer willingness to reimburse for the drug:
   - Given that they are single dose and potentially curative, gene therapies are much more expensive than typical drugs; Luxturna, for example, costs

approximately $850,000, or $425,000 per eye.[3] Because of this, payers may act to restrict access to only certain subsets of the patient population (e.g., those who will benefit the most) to keep costs under control
- Severity of restrictions will vary widely by country and within the US. Patient access criteria will also differ across Commercial/Medicare/Medicaid coverage in the US, and by country in the EU

3) Existing therapies:
   - If a patient has shown improvement on an existing therapy, physicians, patients, and/or caregivers may be hesitant to switch treatments.
   - Analyzing uptake of existing therapies can also be used to predict the speed of gene therapy uptake. This aspect of the analysis incorporates lag time of physician and patient awareness, as well as payer negotiations and approval processes.

Considerations for Cancer Gene Therapies

Since cancer therapies are not necessarily curative and are often administered later in life, forecasting uptake for these drugs will require different considerations. Cancer incidence data is widely available in many countries, but gene therapy treatments are often indicated for only refractory cancers. Therefore, a patient flow through prior lines of therapy is necessary to estimate the percentage of patients who are not responding to standard treatment. Data on disease stage at diagnosis as well as stage-specific survival curves are needed to calculate the total prevalent population with the disease, which can be sourced from literature, datasets, and some publicly available cancer registries.

Conclusion

Forecasting gene therapy uptake requires advanced epidemiological tools and methods, as well as expertise in commercial dynamics. The landscape for gene therapies is changing rapidly as more high-cost treatments are coming to market, and payers are navigating appropriate approaches to restriction and value-based arrangements. A nuanced approach including a combination of literature reviews, patient registries, and other datasets, as well as primary research is fundamental to an accurate forecast.

References

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