LONG-ACTING GENE THERAPIES: CURRENT DEVELOPMENT ACTIVITIES AND CHALLENGES FOR THE SHI-SYSTEM IN GERMANY

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Objectives

Highly innovative gene therapies open up new treatment options for critically ill patients, but could put different burdens on health insurance companies. To assess the potential impact on the German health system, this study quantifies the number of gene therapies in late stages of clinical development. It also provides an overview of the resulting challenges for the statutory health insurance (SHI) system and links the development pipeline with specific challenges for the existing reimbursement system.

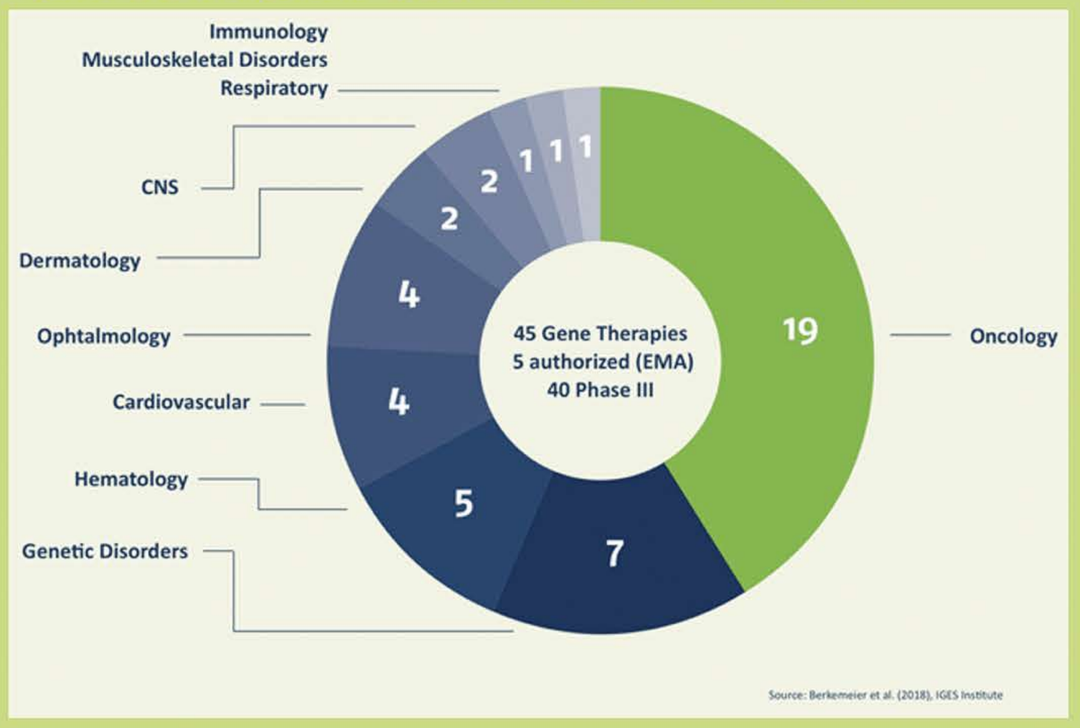
Methods

Long-acting gene therapies were identified through their clinical trials (from phase III, ongoing/planned/completed) in various clinical trial registries via a systematic search. For all long-acting gene therapies (EMA GTMP definition), all diseases in ongoing clinical development from phase II were identified. For all resulting indications, the potential SHI population in Germany was quantified through epidemiologic estimates (incidence and prevalence) for the disease. The results are used to assess the relative importance of different types of challenges for the SHI system resulting from the introduction of long-acting gene therapies. The search was conducted in May 2018, which represents the data cut-off for the study.

Results

45 long-acting gene therapies in late stages of development were identified. These are in development (phase II+) for 42 different diseases. 19 of these diseases are oncological, which represents the disease area with the most development activity (Figure 1).

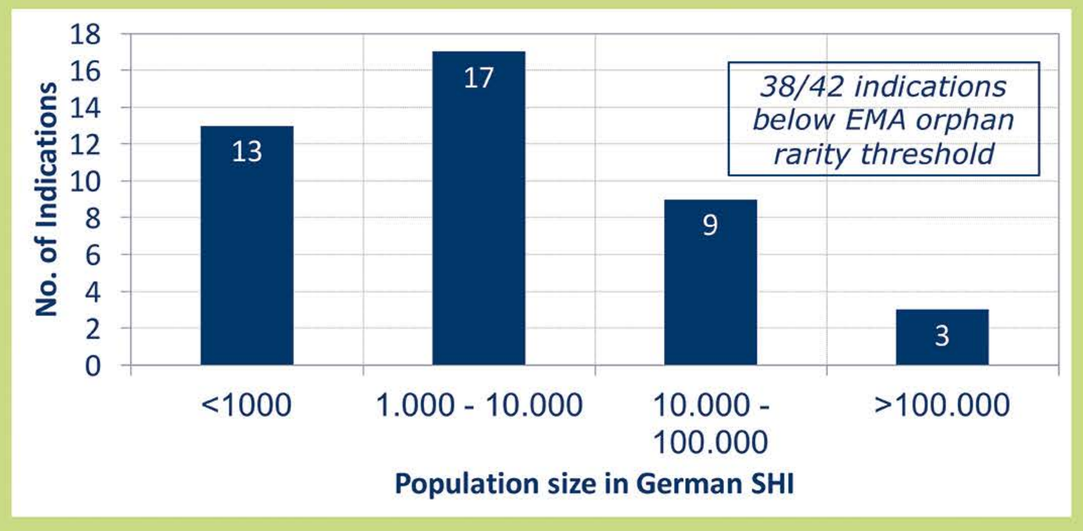
Figure 1: One-shot gene therapies (authorized by EMA or Phase III+)



In terms of epidemiological dimensioning, the 42 diseases are characterized by a high level of heterogeneity. Populations range from ultra-orphans with a handful of patients to very large populations (e.g. heart failure, osteoarthritis).

A large part of the identified diseases (17) affects between 1,000 and 10,000 insured persons in Germany (Median 2,675). The vast majority of therapies are expected to target relatively small populations. Of the 42 indications with one-shot gene therapy development activities, 38 are characterized by a rarity below 5 per 10,000, which constitutes the threshold for EMA's orphan drug designation (Figure 2).

Figure 2: Characterization of indications with gene therapy development by German SHI population size estimates



These therapies will provide new therapy options for critically ill patients but also likely require further development of the German reimbursement and SHI financing system.

Four areas of the German healthcare system were identified, in which one-shot gene therapies are likely to lead to challenges for depiction and reimbursement:

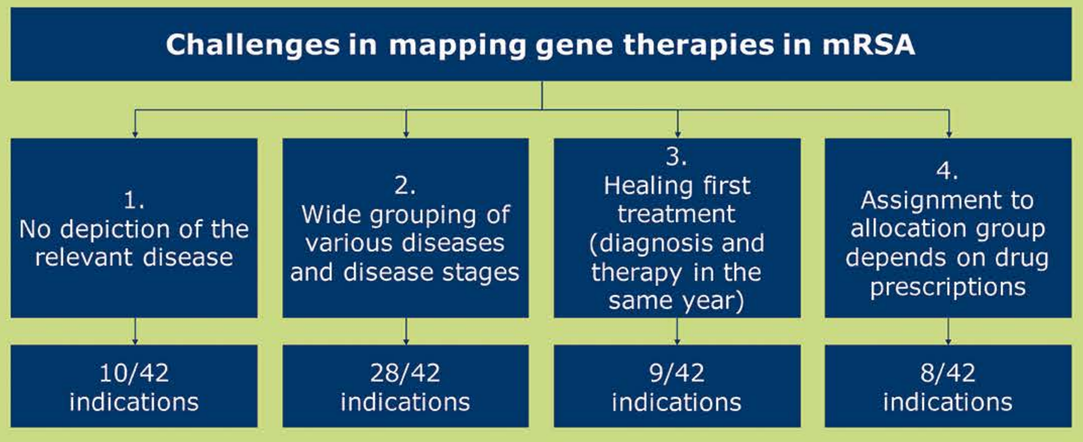
- AMNOG benefit assessment: Additional benefit based on early evidence in areas of high medical need and depiction of duration of efficacy in cost comparisons
- Timely depiction of gene therapies in the hospital financing system (DRG-system) to ensure early and sustainable patient access
- Effects of one-shot therapies on the allocation of funds to German sickness funds through the morbidity-based allocation system (morbiditätsorientierter Risikostrukturausgleich, mRSA)

The potential effects of one-shot gene therapies on the morbidity-based allocation system of funds (mRSA) were classified and quantified in more detail. For types of challenges were identified:

1. No depiction of the relevant disease
2. Grouping of a wide range of diseases and disease stages into one allocation group
3. Non-depiction of therapy costs in case of curative first line therapies
4. Loss of funds linked to continuous pharmaceutical therapy

All types of challenges result in fund allocation to sickness funds that will likely not cover the costs associated with one-shot gene therapies. Figure 3 shows the number of indications with one-shot gene therapies in development that are affected by a specific challenge.

Figure 3: For main challenges for depicting gene therapies in the allocation system of funds for German sickness funds (mRSA)



Conclusions

To the authors' knowledge, this is the first study to cover the systematic identification of gene therapy interventions in advanced stages of clinical development or in approval. By assigning diseases to long-acting gene therapies and quantifying their epidemiologic dimension, it becomes possible to obtain a picture of potential future market launch developments.

With regard to possible economic effects, the study results suggest that the introduction of long-acting gene therapies will be associated with challenges for depiction in the reimbursement framework, for which early addressing would be recommended. However, it is currently not possible to make an evidence-based quantification of future expenditures. The degree of uncertainty regarding success rates of clinical development, actual approval and exact authorized indications, utilization, and pricing is too big to justify expenditure forecasts at present.

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