# Gene Therapy Survey Highlights: Knowledge Gaps And Educational Opportunities

**This survey was conducted by Frontline Medical Communications in collaboration with the National Organization for Rare Disorders (NORD).**

## Key Findings

- 63% of survey respondents were unaware of current FDA-approved gene therapies, including Kymriah (leukemia), Luxterna (retinal dystrophy), Yescarta (lymphoma), and Zolgensma (spinal muscular atrophy).
- Of 4 available or developing methods of gene therapy, gene replacement was most widely recognized at 77%, trailed by silencing (69%), editing (60%), and gene addition (51%).
- Respondents pointed to cost of therapy as the greatest potential barrier to gene therapy utilization. Other important considerations identified were the need for staff training, and the potential burden for patients in terms of both immediate consequences and longer term follow up requirements.
- Survey respondents ranked educational approaches to inform them about gene and cell therapies. Continuing medical education (74%) ranked as the most preferred tactic, followed by disease specific symposia at medical conferences (72%) and expert speaker programs (71%). Medical journals (printed or online) ranked fourth with 60% of respondents identifying journal articles as a valuable learning tactic.

**The promise of gene therapy** as a groundbreaking approach to individualized medicine is being realized in clinics, bringing with it a new focus on genetic diagnostics. In 2017, the US Food and Drug Administration (FDA) approved the first gene/cell therapy and 2018 alone saw 500 gene therapy trials.[1] Efforts made by both the National Institutes of Health (NIH) and FDA to foster and streamline advances in new genetic technologies make it imperative that health care providers become well versed on gene therapy, from the identification of those who may benefit, to the needs and monitoring of recipients.[1,2] A recent survey conducted by Frontline Medical Communications (FMC) in collaboration with the National Organization for Rare Disorders (NORD) helps to identify gaps in knowledge about gene therapy and to determine provider preferences for education about this rapidly developing field.

## RESULTS

### Profile of Respondents

In an effort to gain the perspective of a wide variety of treatment prescribers, the survey captured information about the practice setting type and specialty of each respondent. Recruited participants were print or e-readers of relevant FMC publications in specialty areas including pulmonology, cardiology, endocrinology/gastroenterology, hepatology, family medicine, pediatrics, internal medicine, neurology, infectious disease, hematology/oncology, obstetrics/gynecology, rheumatology, and dermatology.

A total of 1,472 participants completed questionnaires, of which 87% were physicians (MD or DO), 10% were nurse practitioners (NPs) and 3% physician assistants (PAs). Respondents averaged 19 years in practice. Family practice providers constituted the largest group of respondents at 13%, while most other specialties contributed 7% to 9% of the total and rheumatology

## METHODOLOGY

An online survey was fielded between November 14, 2019 and January 23, 2020. The survey included 26 queries comprised of single-answer, multi-answer, and rating scale formats, with open-answer options when more detailed responses to the answer "other" was desired. In order to assess knowledge gaps, some questions could be answered with all available choices. Any option NOT chosen represented an area where a gap in knowledge exists. Participation was incentivized by awarding gift cards to 50 random respondents from the first 100 of each specialist type following a complete submission.

FMC sent the survey to approximately 92,000 health care providers (MDs, DOs, NPs and PAs) across 14 specialties throughout the United States. Of the 1,716 total responses received, a representative 1,472 responses were usable. Participants completed the survey through a provided electronic link. Follow-up emails were sent periodically to non-responders until the close of the survey. With a 95% confidence level, the margin of error for the total sample (1,472) was 3%. Within individual physician specialties, the margin of error ranged from 9% to 16%, due to variations in physician specialty sample sizes. At the lower end, family medicine, neurology/child neurology, ob/gyn, and pediatric physicians had a 9% margin of error, while at the higher end, infectious disease physicians had a 16% margin of error. The NP/PA sample had a margin of error of 7%.

NORD provided incentive for survey respondents.

and infectious disease added 4% and 2%, respectively. Another 2% responded with "Other."* Most respondent practice settings included group office single specialty (26%) or academic/university (22%), while multi-specialty group office, hospital-based, and solo office practitioners comprised a combined 42% of remaining responders.

### Current Experience and Awareness

Despite an impressive rate of contact with patients who have rare genetic diseases, responses indicated that knowledge about gene therapy is limited. A solid majority of respondents indicated having patients diagnosed with a rare genetic disorder within the year prior to taking the survey (weighted mean of 5.37 patients per participant). Only 21% had none, while most (54%) had between 1 and 5 patients. Neurology/child neurology carried the greatest per-respondent rare genetic diagnosis experience, having an average of approximately 11 patients, and internal medicine had lowest experience at approximately 3 patients on average. Referral patterns for genetic or biochemical testing were similar. Only 22% stated they had made no such referral, while 45% referred 1 to 5 patients (per-respondent weighted mean was 8.45 patients).

Hematology/oncology specialists referred more patients for testing at upwards of 17 patients, while dermatology was least likely to have pursued DNA/biochemical testing at less than 4 patients per year. When asked for what reasons clinicians had or would refer patients for genetic testing 85% selected family history of a potential genetic disorder while 69% selected to confirm a diagnosis. A smaller sampling (38%) considered genetic testing to assist in developing a care/treatment plan.

### Knowledge Gaps Identified

Respondents reported a low level of comfort discussing gene therapy with patients, which might be rooted in a tenuous understanding of the potential modes and benefits. Most respondents (62%) reported that they preferred to refer patients to an expert to discuss gene therapy. Only 20% discuss gene therapy options or clinical trials with their patients, with hematology/oncology specialists discussing gene therapy most often at 45% followed by neurology/child neurology at 43%. Remaining responders were either unaware of, or did not have patients that might benefit from gene therapy while just 3% actively choose not to refer or discuss gene therapy.

When asked about current FDA-approved gene therapies (Kymriah [leukemia], Luxterna [retinal dystrophy], Yescarta [lymphoma], Zolgensma [spinal muscular atrophy]), 63% were unaware of these therapies. The respondents most aware of these options were specialists in hematology/oncology (87%), neurology/child neurology (71%), rheumatology (56%), and pediatrics (42%), while dermatology showed least awareness (17%). More than three-quarters of clinicians surveyed (78%) have not had patients for whom an approved gene or cell therapy was an option. Of those who did have such patients, 61% were hematology/oncology specialists.

Lack of understanding of mutagenesis and gene therapy techniques may hinder a provider's decision to discuss gene therapies with patients. Although most respondents were able to identify various causes of gene mutations, including inheritance from a parent (93%), natural error in DNA replication (91%), and mutagenesis (84%), no respondent chose all 3 options, indicating that this is a potential topic for additional education. If faced with explaining somatic vs. germline mutations, only 24% of respondents rated themselves as comfortable or extremely comfortable. When asked about potential effects of gene mutations, 95% indicated abnormal or non-functional protein, 84% indicated lack of protein and 84% indicated improper amount of protein. No respondent selected all 3 which indicates another education need.

When asked about types of gene therapies currently available, gene replacement was most widely recognized at 77%, trailed by silencing (69%), editing (60%), and gene addition (51%). When asked to choose which method of gene delivery was typical, viral vector, non-viral vector, both, or neither, 68% correctly chose both, with viral vectors only being the most frequent incorrect answer (26%). The use of both in vivo and ex vivo administration methods, depending on therapy type, was correctly identified by 76%, but the remaining 24% designated only one or the other. Understanding the mechanisms by which gene therapy corrects faulty genes also presents an opportunity for learning as no one selected all correct possibilities: producing new or modified proteins (79%), reducing disease-causing proteins (69%), and increasing disease-fighting proteins (59%). Most either were not aware (11%) or unsure (41%) that somatic gene modifications were not passed to offspring. Of the 48% that were aware, 75% were hematology/oncology physicians. Few were aware that viral vector therapies could generate serotype-specific antibodies precluding prior clinical trial participants from receiving further gene therapy for the same disease; 65% responded no or unsure, while 35% indicated awareness, with hematology/oncology specialists most likely to be informed. As gene therapy technologies progress, educational content directed at practitioners can help clarify misconceptions about mutagenesis as well as delivery methods for gene therapy.

*"Other" specialty areas comprised of genetics, weight management, ER/urgent care, restorative medicine, nephrology, chemical pathology, urology, sports medicine, gerontology, anesthesiology, psychiatry, pain management, radiology, orthopedics, physiatry, neurosurgery, palliative medicine, occupational medicine, and stem cell transplant.

### Perceptions of Gene Therapy Benefits and Drawbacks

It is important to understand providers' perceptions of the benefits and limitations of gene therapies in order to develop effective educational strategies. Most respondents chose "improved quality of life/positive effect on indirect and intangible costs (eg, ability to work)" (77%) and "reduction/elimination of costly, painful, or invasive life-long treatments" (70%) as potential gene therapy benefits. "Targets cause of disease" and "transformative nature of therapy fulfills unmet needs" received 69% and 63% acknowledgement respectively, while less than 50% felt "economic value/overall reduction in health care costs" and "high efficacy/efficiency, usually via single administration" applied.

Respondents identified the top 4 barriers to gene therapy as "out-of-pocket cost of treatment" (69%), "lack of access or coverage by patient's insurance" (67%), "limited knowledge among health care professionals" (54%), and "therapies are specific to a limited number of conditions" (52%). When asked what they had observed as misconceptions among their colleagues, 73% indicated lack of insurance coverage while the next most common misconceptions were related to safety and impact on childbearing. These findings suggest that a clearly rationalized cost/reimbursement method may be an important component to advancing utilization of gene therapy, even if it offers a potential cure.

### Opportunities for Education and Information Sourcing

Decisions about how to disseminate new information to providers about gene therapy should be based on provider preferences. Past usage patterns of education resources were evaluated by questioning what sources respondents had accessed to learn more about approved gene, cell, and tissue therapies or those in clinical trials. Medical literature (eg, PubMed) was cited most frequently (49%), followed by clinical trial websites (38%), and the NIH National Human Genome Research Institute (38%). NORD's website was cited by 30% of respondents (physicians accessed more often than NPs/PAs). Print or digital journal articles were utilized by 50%, while 40% reported reading print or digital medical news articles regarding new product approval. Only 26% learned about gene therapy topics from attending a session at a local, regional or national meeting. Surprisingly, 32% had not sought any type of specific training on gene therapy.

Current trends in reimbursement models and cost structuring represent a strong area of educational interest. A majority of respondents (73%) identified cost to patients/payment and reimbursement terms as the primary considerations before offering gene therapy as a treatment option. Another important factor reported was a clearer understanding of how to prepare a patient for the gene therapy process and after-care. More than 50% of respondents reported that staff training, patient counselling requirements (loss of productivity, caregiver burden, non-medical costs) and utilization expectations (patient registries, long-term follow-up) were important considerations. When asked to rank methods for delivering new information on a 1-5 scale (1=not at all valuable, 5=extremely valuable), CME/CE opportunities (live or online) received the top rank at a weighted mean of 4, with 74% of respondents giving it a 4 or 5 rating. Lowest ranked were non-CME interactive quizzes designed to assess knowledge (weighted mean of 3.08; only 38% gave this option a 4/5 rating). This indicates that offering a professional benefit can help motivate continued learning about gene therapy.

## CONCLUSIONS

Despite relatively common exposure to patients with rare genetic diseases, fewer than one-quarter of respondents feel comfortable explaining gene mutations to patients and caregivers. As the identification of rare genetic disorders continues to expand and new targeted gene therapies are developed, it is important that efforts be directed at helping physicians and other clinicians feel more secure in their genetics knowledge base. Health care providers in specialties that have currently available gene therapies (hematology/oncology, neurology/child neurology) appear to have a greater grasp of genetic diagnosis and gene/cell therapies. This survey indicates that efforts should be undertaken to improve awareness about the mechanisms of gene therapy, routes of administration, known safety and efficacy, as well as the recognition of patients who could benefit from gene therapy. Clarifying clinical trial availability and discussion of future approaches to minimize cost and maximize reimbursement are important topics for provider engagement. Offering CME/CE regardless of presentation style (live, online, print) and inclusion of gene therapy discussions at medical conferences and events appear to be a valuable motivators for providers and worth pursuing in the interest of assuring the best care for rare genetic disease patients.

**REFERENCES**

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