Gene Therapy in Hemophilia: An Assessment of Hematologists’ Knowledge Gaps and Attitudes

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BACKGROUND

Currently available treatments for hemophilia A and B require frequent intravenous infusions. Gene therapy, by contrast, offers the hope of a functional cure through exogenous expression of the factor VIII or factor IX genes. To identify and address practice gaps among healthcare providers who manage patients with hemophilia, a collaboration between the National Hemophilia Foundation (NHF), European Haemophilia Consortium (EHC), World Federation of Hemophilia (WFH), and Medscape Education was established. The objective of the current study is to assess clinicians’ needs with regard to understanding the science and mechanism for gene therapy, the different technologies being proposed, identifying candidates for gene therapy, disease areas for which gene therapy is being explored, and the latest data on the potential role of gene therapy in hemophilia A and B.

METHODS

A continuing medical education (CME)-certified clinical practice assessment comprised 25 multiple choice questions that measured knowledge, attitudes, and perspectives about gene therapy as it was developed. The instrument was made available online to physicians without monetary compensation or charge. A total of 1894 healthcare providers, including 1129 physicians, have participated as of November 26, 2018. This CME-certified activity was supported by an independent educational grant from BioMarin. Other areas in which the clinical practice assessment identified gaps in knowledge include: (data not shown)

RESULTS

INVOLVEMENT IN PATIENT CARE

Approximately one-quarter of hematologists/oncologists cared for 20 or more patients with hemophilia within their practice.

Approximately how many patients with hemophilia do you manage in a year?

[21%] 20+ 12% 8+ 25% 4+</p>

OVERALL UNDERSTANDING GENE THERAPY

The majority of hematologists/oncologists had access to gene therapy in their practice.

How confident are you about your understanding of gene therapy for hemophilia? (Please select the % that you believe)

[54%] I have limited knowledge of gene therapy 21% I have moderate knowledge 12% I have good knowledge 5% I have in-depth knowledge

Ongoing education in gene therapy is

[54%] essential for continued success 21% helpful for continued success 12% not necessary for continued success 5% I’m not sure

36% of hematologists/oncologists could not identify the vector construct that is currently the basis for the majority of gene therapy trials in hemophilia.

Which of the following is the most popular approach to gene therapy?

[63%] Adenovirus vector 16.9% Retrovirus vector 12.2% Adenovirus vector

42% of hematologists/oncologists were unsure with respect to the causes of or treatment for − transient ALT elevations that have been observed in patients with hemophilia.

Which of the following best describes hematologic gene therapy to date?

[45%] Direct delivery of expression vectors to target tissues 22% Integration of genetic material into the genome 12.2% Gene editing in vivo

32% of hematologists/oncologists were unsure about the potential impact of gene therapy on the likelihood of − or treatment for − transient ALT elevations that have been observed in patients with hemophilia.

Which statement is true regarding ALT elevations in hemophilia AAV gene therapy?

[27%] Only affect germline cells 23.8% 18%

34.4% 19.4% 32.5% 9.1%

30% of hematologists/oncologists identified germline transmission as the most significant barrier to the adoption of gene therapy.

Which of the following do you perceive to be the biggest barrier to the implementation of gene therapy?

[27.2%] Cost, accessibility, and the availability of long-term safety data 25%

[17%] The unknowns 16.9%

13% 6.1% 10.2% 3.9% 42.5%

APPROPRIATE USES FOR GENE THERAPY

Nearly half of hematologists/oncologists felt that the greatest potential benefit that gene therapy could offer is improvement in patients’ quality of life.

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Which of the following do you feel is the most important potential benefit associated with the promise of gene therapy?

[43.9%] Reduced risk for reduced risk for breakthrough bleeds 10.3% 15.2% 6.1% 31.7%}

Which of the following do you feel is the most important potential benefit associated with the promise of gene therapy?

[10.8%] Reduced risk for breakthrough bleeds 15.2% 6.1% 31.7% 39% 6.1%

PERSPECTIVES ON/ATTITUDES TOWARD GENE THERAPY

Approximately 70% of hematologists/oncologists felt that patients with severe hemophilia or those who have frequent breakthrough bleeds would be the most appropriate candidates for gene therapy.

Which of your patients with hemophilia do you perceive to be the most appropriate candidates for gene therapy?

[54.3%] Patients with severe hemophilia or those who have frequent breakthrough bleeds 22.1% patients with severe hemophilia 18.8%

Approximately 70% of hematologists/oncologists felt that patients with severe hemophilia or those who have frequent breakthrough bleeds would be the most appropriate candidates for gene therapy.

Which of the following do you feel is the most important potential benefit associated with the promise of gene therapy?

[13.4%] Reduced risk for breakthrough bleeds 25.7%

[11% 12.6% 24.7% 8.4% 16.9%]

CONCLUSION

This educational research identified clear deficits in the knowledge about gene therapy among healthcare providers who currently care for patients with hemophilia.

The great majority of healthcare providers indicated a lack of confidence in their understanding of gene therapy for hemophilia A.

These findings will be used to inform the development of educational programs and to prepare providers for anticipated changes to the hemophilia treatment landscape.

ACKNOWLEDGMENTS

The CME activity was supported by an independent educational grant from BioMarin. Other areas in which the clinical practice assessment identified gaps in knowledge include: (data not shown)

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■ The characteristics of different end-stage products

■ The latest data on clinical trials for hemophilia A and B

■ The patient populations in which gene therapy will most likely be evaluated

■ The duration of effect seen with gene therapy to date

■ A known reduction in the clinical significance of transient ALT elevations

REFERENCES


DEVELOPED IN COLLABORATION WITH

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MISCONCEPTIONS ABOUT GENE THERAPY


Which statement is true regarding ALT elevations in hemophilia AAV gene therapy?

[27.2%] Only affect germline cells 25% 18% 16.9% 21.5% 12.8%

Which statement is true regarding ALT elevations in hemophilia AAV gene therapy?

[4.5%] They are typically associated with a high annual risk of − or treatment for − transient ALT elevations that have been observed in patients with hemophilia.

Which statement is true regarding ALT elevations in hemophilia AAV gene therapy?

[23.6%] 11% 12.6% 24.7% 8.4% 16.9%

Which statement is true regarding ALT elevations in hemophilia AAV gene therapy?

[23.6%] 11% 12.6% 24.7% 8.4% 16.9%