CSL Behring – Global Program Call For Grants

Therapeutic Area: Coagulation

Disease State: Hemophilia B

Call for Grants Application Details:

- Your title must begin with ID Information **"GT2021"**
- Refer to Grant Submission Instructions for further information on submitting your formal grant application at CSLBehring.com/grants under Independent Medical Education.
- Additional communication on the process will be conducted exclusively through Educational.Grants@cslbehring.com or the portal grant record.

Submission Deadline:	January 14, 2022
Proposal:	US continuing medical education programs. Multi-support encouraged
Program Format:	Interactive US live/web programs seeking key expert opinion leaders (such as a moderator, dosing center, referral center healthcare professional) engaging in active panel discussion with audience involvement on resources needed and potential protocols to ensure HTCs are adequately prepared for gene therapy.
Program Cost:	up to $250,000.00

CSL Behring is interested in providing grant support to a reputable and certified Continuing Medical Education (CME) provider to provide healthcare providers (HCPs) an educational, non-promotional opportunity to learn more about the operational aspects of implementing gene therapy. Propose a model that allows for appropriate screening, delivery and monitoring gene therapy in hemophilia B patients. Examine the logistical aspects needed to ensure appropriate implementation, such as timing of implementation, defining key roles, staff education.

Needs Assessment: Identification of appropriate pathway for successful implementation of gene therapy in hemophilia treatment centers

Many unanswered questions are on the minds of stakeholders who treat hemophilia about how to successfully operationalize or develop a care model around gene therapy implementation. There will be a need for a multidisciplinary pathway for gene therapy.

Hemophilia treatment centers (HTC) offer a comprehensive, integrated care by multi-disciplinary teams to improve outcomes in patients with hemophilia (PWH).[1] The arrival of advanced therapies and particularly gene therapy requires further

thought on appropriate ways to organize hemophilia treatment centers.[2] HTC will have to determine the appropriate time to begin preparation for upcoming gene therapy products (ex. pre or post-FDA approval). Hemophilia gene therapy consists of three main work streams: Supervising (overseeing all aspects of care); infusion (storage, preparation, administration and disposal of gene therapy); and follow-up (post-treatment monitoring). If centers are only able to complete 1 or any combination of two tasks, they would partner with another center to complete the necessary work needed for gene therapy.[1] Based on level of experience with gene therapy, the process of implementation will differ in timing and complexity between HTCs.

Although there has not been a clearly defined pathway at this time, organizations such as European Association for Hemophilia and Allied Disorders (EAHAD) and European Hemophilia Consortium (EHC) recommend a highly coordinated integrated model (ex. hub and spoke). EAHAD and EHC describe this model as prescribed and managed exclusively by expert hemophilia comprehensive care centers (as the national hubs), and monitored, by hemophilia treatment centers in close communication with the primary expert hub (as spokes linking into that hub).[3]

Miesbach[2] describes the hub and spoke model for gene therapy using two broad scenarios:

> 1- The 'Hub' is a HTC experienced in both comprehensive care and gene therapy (GT) and the 'Spoke' is another HTC with no or minimal GT experience, which will be the home center for the patient. The Hub in this scenario will take the lead in all aspects of GT delivery pre infusion and post infusion. Although the patient may be managed locally (visits, routine bloods, MDT review), decisions relating to GT will remain a collaborative discussion between the Hub and Spoke staff to ensure optimum patient outcomes.
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> 2- In this scenario the 'hub' is a dosing center (GT delivery experienced) and the 'Spoke' is a management center (also GT experienced). To offer a full range of gene therapy platforms, patients may need to go to other sites for infusion, as it is possible that not all centers will have all platforms open, but return to their 'home' center for subsequent management.

In case that the patient was referred for dosing by another HTC, tests for the gene therapy program and existing antibodies against AAV need to be planned. After the referred patient has been dosed, the 'home' HTC and spoke center would remain responsible for patient follow-up, which should be done in close cooperation with the dosing center.[2]

Both centers would have key roles in both short and long term follow ups. From a short-term perspective, the "hub" would provide counseling/collaboration, perform further regular follow ups and provide immunosuppression as guided from studied protocol, where as the "spoke" can perform regular weekly to monthly follow ups and initiate immunosuppressive treatment. Long term follow up from year two suggests the "hub" to provide counseling about long-term risks and follow up can expand occasional reviews, and the "spoke" perform regular follow up every 3 to 6 months and liver health review.[2]

As multidisciplinary teams are identified certain educational requirements will need to be addressed. HTCs will require key resources and protocols for successful implementation of gene therapy, such as how to coordinate care and develop a follow up plan. These resources will have to be developed in coordination with key partners within the hemophilia community, such as, organizations and industry. Physicians and nurses will need to educate about gene therapy, develop standards for gene therapy eligibility, and screen candidates. Pharmacists will need to develop processes for ordering, storing, handling and reconstituting gene therapy products. Hepatologists may be required to monitor the liver health of gene therapy recipients, particularly in the first months. Follow-up centers ensure incorporation of monitoring into standard operating procedures.[1]

As new therapies become available and standard of care and guidelines are updated periodically, there is a need for continuing medical education for health care providers to maintain, develop, or increase their knowledge, skills, and professional performance and relationships to provide services for patients, the public, or the profession.

References:

1. Miesbach W, Pasi KJ, Pipe SW, et al. Evolution of haemophilia integrated care in the era of gene therapy: Treatment centre's readiness in United States and EU. Haemophilia. 2021;27(4):511-514.
2. Miesbach W, Chowdary P, Coppens M, et al. Delivery of AAV-based gene therapy through haemophilia centres—A need for re-evaluation of infrastructure and comprehensive care: A Joint publication of EAHAD and EHC. Haemophilia. 2021;1–7.
3. EAHAD-EHC Joint Statement on: Promoting hub-and-spoke model for the treatment of haemophilia and rare bleeding disorders using gene therapies. May 2020.

Program Requirements:

The Program must be accredited and fully compliant with the ACCME standards for commercial support.

CSL Behring's grant in support of the Program is not subject to any condition or restriction regarding the content or execution of the Program or the selection of Program presenters or faculty members. The grant recipient will be solely responsible for the selection of the Program venue, faculty and/or educational methods, and for the quality and scientific integrity of the Program. CSL Behring will not influence the grant recipient's exercise of these responsibilities, even if asked by the recipient to do so.

The grant recipient must ensure that: (i) the Program is free of commercial bias; (ii) the Program presents objective information about any product(s) based on scientific methods generally accepted in the medical community; (iii) if CSL Behring products, or other products used to treat or being investigated to treat the same indications, are featured in the Program, featured data is objectively selected and presented, with both favorable and unfavorable information in respect of the products fairly represented, and that there is a balanced presentation and, if applicable, interactive discussion of the prevailing body of scientific information in respect of the products and alternative treatment options; (iv) there is meaningful disclosure during the Program of any limitations on information presented in the Program; and (v) if the Program addresses unapproved (unlabeled) uses of any product, or an investigational use not yet approved for any purpose, the Program includes disclosure that

the product is not approvedin the United States for the use under discussion or, as may be applicable, that the product isstill under investigation in respect of such unapproved use.

The grant recipient also must ensure meaningful disclosure in Program announcements and materials, and to the audience during the Program, that (i) CSL Behring is funding the Program, and (ii) a relationship exists between the grant recipient and CSL Behring and, if applicable, between the Program presenters or faculty and CSL Behring.

Additional requirements will be included in the Grant Agreement between CSL Behring and the grant recipient to be executed following award of the grant.