Development of a shared decision-making tool for gene therapy in hemophilia A in Italy

Giovanni Di Minno,[1] Sarah Bigi,[2] Serena Barello,[3,4] Enrico Ferri Grazzi,[5] Marco Follino,[6] Maria Francesca Mansueto,[7] Mariasanta Napolitano,[8] Rita Carlotta Santoro,[9] Giancarlo Castaman[10]

[1]Regional Reference Centre for Hemo-Coagulation Diseases, Federico II University, Naples; [2]Department of Linguistic Sciences and Foreign Literatures, Università Cattolica del Sacro Cuore, Milan; [3]WHYpsy Lab, Department of Brain and Behavioral Sciences, University of Pavia; [4]Applied Psychology Lab, IRCCS Fondazione Mondino, Pavia; [5]Federazione delle Associazioni Emofilici (FedEmo), Rome; [6]Fondazione Paracelso Onlus, Milan; [7]Azienda Ospedaliera Universitaria Policlinico Paolo Giaccone, Palermo; [8]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo; [9]Hemostasis and Thrombosis Unit, Hemato-Oncology Department, Azienda Ospedaliero-Universitaria Renato Dulbecco, Catanzaro; [10]Center for Bleeding Disorders, Department of Oncology, Careggi University Hospital, Florence, Italy

ABSTRACT

Background: Gene therapy offers a transformative treatment option for hemophilia A (HA) by restoring endogenous factor VIII production. Shared decision-making (SDM) is a collaborative process that allows patients and clinicians to weigh the risks and benefits of complex treatment options such as gene therapy. However, no SDM tools exist for the specific needs of Italian persons with HA.

Materials and Methods: An Expert Advisory Board comprising nine experts (including hematologists, a psychologist, a methodology expert, a linguist and patient advocacy group representatives) met three times between March and July 2024 to discuss gene therapy for HA in Italy, and develop an SDM tool to determine the suitability of gene therapy for HA.

Results: The resulting modular SDM tool allows for structured interactions between clinicians and patients, while remaining sensitive to each patient's level of readiness and understanding. The tool includes three components: Role Definition, Agenda Alignment, and Intention Setting, with supporting materials to guide patient-clinician dialogue and various resources (questionnaires, brochures, and visual aids).

Conclusions: Despite requiring confirmation in further studies, this SDM tool may represent a useful component of patient-centered care for HA in the Italian healthcare setting.

Key words: gene therapy, hemophilia A, Italy, patient-centered care, shared decision-making.

Corresponding author: Serena Barello, WHYpsy Lab – Department of Brain and Behavioral Sciences, University of Pavia, Piazza Botta 11, 27100, Pavia, Italy; Applied Psychology Lab, IRCCS Fondazione Mondino, Via Mondino, 2, 27100 Pavia, Italy.
E-mail: serena.barello@unipv.it

Ethical approval and consent to participate: not applicable.

Availability of data and materials: not applicable.

Competing interests: GDM was a speaker or a member of a speaker bureau for BioMarin and CSL Behring; and was an ad-hoc speaker/consultant for BioMarin and CSL Behring. SBi and SBa have acted as consultants for BioMarin. EFG participated in speakers' bureaus on behalf of a patient organization for BioMarin, CSL Behring, Novo Nordisk, Roche, and Sobi; participated in advisory boards on behalf of a patient organization for BioMarin, Pfizer, Roche, and Sobi; and participated in patient councils on behalf of a patient organization for BioMarin, Novo Nordisk, and Roche. MF has no competing interests to declare. MFM has acted as consultant and discus-sant for BioMarin, Novo Nordisk, Roche, and Sobi. MN has acted as consultant for Amgen, Bayer, CSL Behring, and Novo Nordisk; and received speaker fees from Amgen, Bayer, CSL Behring, Novartis, Novo Nordisk, Sanofi Genzyme, Sobi, and Takeda. RCS has acted as con-sultant for Bayer, Novo Nordisk, Roche, Sobi, and Takeda; and received speaker fees from Bayer, BioMarin, CSL Behring, Novo Nordisk, Kedrion, Roche, Sobi, and Takeda. GC received pay-ment or honoraria for lectures, presentations, speakers' bureaus or educational events from Bi-oMarin, Bioviiix, CSL Behring, Kedrion, LFB, Novo Nordisk, Roche, Sanofi, Sobi, and Takeda, and participated on a Data Safety Monitoring Board or Advisory Board for Bayer, BioMarin, CSL Behring, Kedrion, LFB, Novo Nordisk, Pfizer, Roche, Sanofi, and Takeda.

Funding: this project, the development of the manuscript and the open access publishing fee were supported by BioMarin, without conditions.

Contributions: GDM, SBi, SBa, and GC contributed to developing the manuscript concept and plan; EFG, MF, MFM, MN, and RCS contributed to manuscript writing and editing. All the au-thors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work. Artificial intelligence (AI)-assisted technologies were not used in the creation of the submitted work.

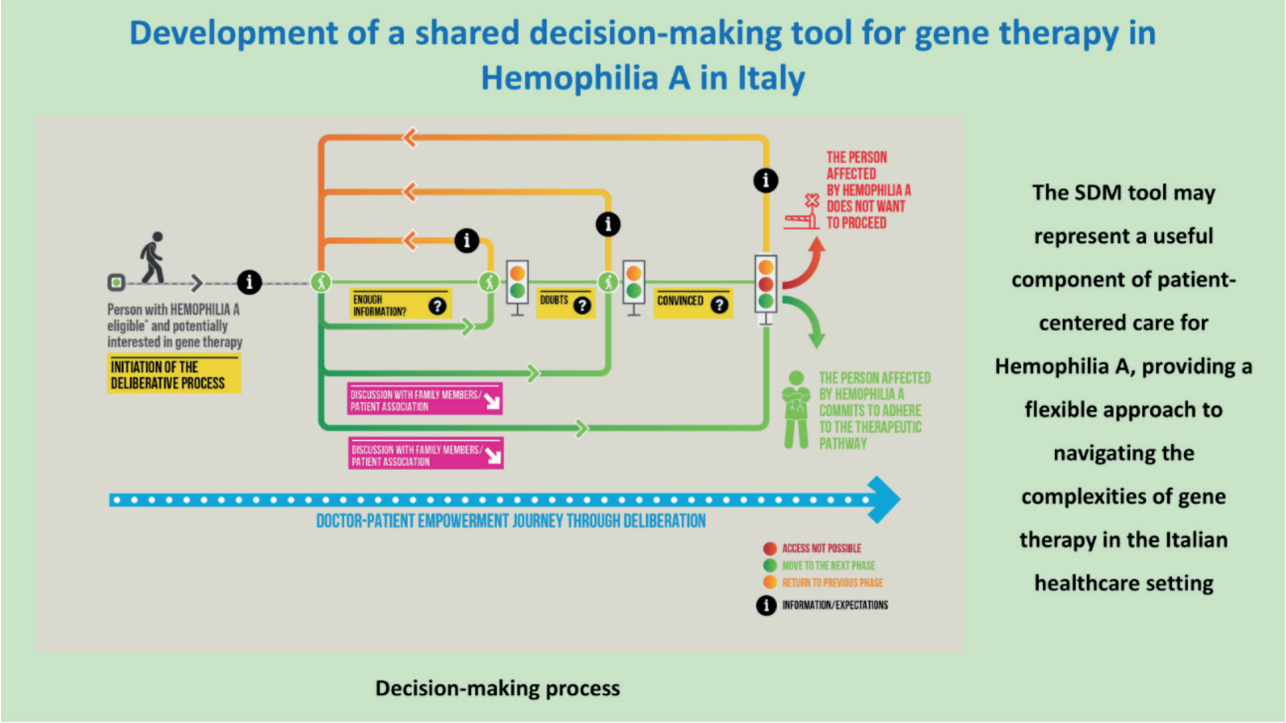
Acknowledgments: we would like to thank Georgii Filatov who assisted with the preparation of the outline and first draft of this manuscript on behalf of Springer Health+ and Nireshnee Ramchundar, PhD, of Springer Health+ who assisted with preparing the manuscript for submission and with post-submission revisions. This medical writing assistance was funded unconditionally by BioMarin.

Received: 12 December 2025.
Accepted: 29 May 2026.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Licensee PAGEPress, Italy
Bleeding, Thrombosis and Vascular Biology 2026; 5:426
doi:10.4081/btvb.2026.426

GRAPHICAL ABSTRACT



Introduction

Hemophilia A (HA) is an X-linked recessive bleeding disorder caused by a deficiency or absence of factor VIII (FVIII), a critical protein in the coagulation cascade that is produced by sinusoidal endothelial cells in the liver.[1] HA is characterized by a bleeding tendency, particularly into major joints, such as the elbows, knees, and ankles. Persons with severe HA (FVIII level <1 U/dL) commonly experience spontaneous bleeding, while those with moderate (FVIII 1-5 U/dL) or mild (FVIII 6-40 U/dL) forms typically experience bleeding in response to trauma or surgery.[1] A 2019 publication estimated the prevalence at birth of HA in six high-income countries (Australia, Canada, France, Italy, New Zealand, and the United Kingdom) to be 17.1 cases per 100,000 males, and 6.0 cases per 100,000 for severe HA.[2]

The standard treatment for HA involves intravenous administration of FVIII (replacement therapy), either prophylactically to prevent bleeding events or on-demand to manage them.[1] However, this approach requires frequent infusions, sometimes several times a week, while a residual risk of breakthrough bleeding still exists. In addition, the development of inhibitors (neutralizing antibodies against FVIII) remains a significant challenge, affecting approximately 30% of persons with severe HA and rendering replacement therapy ineffective.[1,3] Because of these issues, replacement therapy is associated with poor adherence and can impose a significant financial burden on healthcare systems. In Europe, the annual per patient cost of hemophilia care is approximately €200,000, >97% of which is attributed to clotting factor concentrates.[4]

Alternative, non-replacement treatment options include emicizumab, a monoclonal antibody that mimics the role of FVIII in the coagulation cascade by binding to activated factor IX and factor X, thereby facilitating clot formation.[1] Emicizumab has proven efficacy when administered as prophylaxis in reducing bleeding episodes, particularly in persons with FVIII inhibitors, but it cannot be used to treat acute breakthrough bleeding.[1] Thus, unmet needs remain with current treatments, including frequent infusions, inhibitor development, and high costs. As such, new therapeutic options and tools are required to better address the challenges of HA management.

Gene therapy represents a groundbreaking advancement in the management of HA, offering the potential for transformative improvement by re-establishing endogenous production of FVIII through the introduction of functional genetic material into the patient's cells.[5] Valoctocogene roxaparvovec is an adeno-associated virus serotype 5 (AAV5)-based gene therapy for HA that is designed to deliver a B-domain-deleted FVIII transgene, restoring the liver's ability to produce endogenous FVIII.[6] Valoctocogene roxaparvovec is the first gene therapy approved for the treatment of persons with severe HA in Europe and has been available in Italy since August 2022.[7] The efficacy and safety of valoctocogene roxaparvovec were evaluated in the open-label, single-group, phase 3 GENEr8 trial.[6] The trial enrolled 134 men with severe HA, who were followed for up to 5 years.[8] The mean factor VIII activity level at weeks 49-52 (primary endpoint) increased by 41.9 U/dL

compared with baseline (p<0.001). In addition, valoctocogene roxaparvovec was associated with a 98.6% reduction in the annualized rate of factor VIII concentrate use and an 83.8% decrease in treated bleeding events at weeks 49–52 (p<0.001 for both).[6]

Five-year follow-up confirmed sustained FVIII expression and data showed that 77.8% of participants had no bleeding events requiring treatment; the annualized bleeding rate was reduced by 83.3%.[8] Furthermore, health-related quality of life improved significantly, with a 5.5-point increase (p<0.001) in the Haemophilia-specific health-related quality of life questionnaire for adults (Haemo-QOL-A) score after 5 years (the Haemo-QOL-A is a scale from 0 to 100, with higher scores reflecting greater impairment; differences of ≥5.5 after 5 years were considered clinically meaningful).[8] Throughout the 5-year follow-up, adverse events (AEs) occurred in all participants, the most common being alanine aminotransferase elevation (in 93.3%), which often required temporary glucocorticoid treatment.[8]

Shared decision-making (SDM) is a collaborative process in which clinicians and patients work together to make decisions based on the best available evidence, and which supports patients in considering treatment options and weighing their potential benefits and harms in order to help them express informed preferences and choose the most suitable course of action.[3,9] SDM involves reciprocal information sharing between the patient and clinician, ultimately leading to healthcare decisions that reflect the informed preferences of both parties.[3] This approach is particularly valuable in highly transformative contexts, such as gene therapy for hemophilia, where the introduction of novel treatment options requires careful consideration of the risks, benefits, and long-term implications.[10,11] In such situations, where the evidence may be unclear or evolving, SDM can help clinicians and patients to co-construct preferences and decisions through iterative dialogue, while ensuring that patient values are central to the process.[10,12] Effective SDM has been associated with improved patient satisfaction, better patient activation in the healthcare journey, enhanced treatment adherence, better health outcomes, and reduced healthcare resource utilization.[12-15]

Despite the recognized benefits of SDM, there is a significant unmet need for an SDM tool specifically designed for gene therapy in HA and tailored to the Italian cultural and linguistic context. Decision-making tools in hemophilia have been developed previously by Athale et al.,[16] Lanzel et al.,[17] Hermans et al.,[18] the Council of Hemophilia Community,[11] the Hemophilia and Thrombosis Treatment Center in San Diego (California, USA),[19] Di Minno et al.,[20] and Meade et al.[21] In addition, the GOAL-Hēm tool and the Shared Decision Making Tool For Hemophilia Treatment are available.[22,23] However, these tools tend to be designed for a single target (either clinicians or patients) and focus on providing information rather than supporting a deliberative process. As a result, these tools often lack the collaborative focus required for effective SDM.[24] Furthermore, while informative, these tools do not fully address the patient's values, expectations, priorities, and specific circumstances, which are crucial for a personalized approach, and none are tailored to the specific needs of Italian patients.[11,25]

The introduction of gene therapy as a treatment option for HA presents unique opportunities that a specially designed SDM tool can efficiently address. As a complex and potentially life-altering once-off treatment (no re-treatment required) with long-term implications, gene therapy requires a deep understanding by both patients and clinicians.[11] However, survey data indicate that most persons with hemophilia (68%) have only a basic understanding of gene therapy.[26] Furthermore, a significant proportion of healthcare professionals report having a basic or intermediate understanding of gene therapy (44%) and a limited ability to discuss gene therapy comprehensively with their patients (40%).[26,27] Importantly, the results of a survey of Italian persons with hemophilia show that, while most were reluctant to undergo gene therapy (54%), greater knowledge about it appeared to be associated with higher willingness to receive treatment.[28]

The primary objective of this paper is to present the development process and final structure of an SDM tool specifically designed for gene therapy in HA. This tool aims to support clinicians and persons with HA through the complex decision-making process associated with gene therapy in the Italian healthcare context.

Materials and Methods

The Expert Advisory Board consisted of nine members selected to ensure a comprehensive approach to the development of the SDM tool, balancing both clinical and patient-centered perspectives. The panel included four hematologists with expertise in hemophilia treatment from various regions of Italy, one psychologist, one methodology expert, one linguist and two patient advocacy group representatives. This diverse composition was intended to reflect a range of expertise, including clinical management, methodological rigor, psychological insights and patient advocacy experience, ensuring that the tool would be both scientifically robust and sensitive to patient needs.

The initial meeting of the Board took place on 19 March 2024 in Rome. The second and third meetings were held virtually and took place on 8 May 2024 and 11 July 2024, respectively.

During the initial meeting, the core objectives and framework for the SDM tool were discussed. We focused on reviewing the SDM process and its relevance in the context of gene therapy for HA, identifying key challenges and understanding patient and clinician needs specific to the Italian healthcare setting. During the second meeting, the Board panel/committee advanced the structure of the tool, emphasizing a modular design to accommodate different levels of patient readiness and clinician ability to lead an SDM dialogue. Feedback from participants helped refine the support tools for assessing patient motivation and preferences, ensuring that the tool could be effectively tailored to each patient's unique circumstances. The third meeting focused on finalizing the SDM tool.

Results

Overview of the shared decision-making tool for hemophilia A

The final tool developed by the members of the Expert Advisory Board is designed for use in clinical settings where gene therapy is being considered as a treatment option for persons with HA. Its primary purpose is to facilitate structured interactions between healthcare professionals and patients, thereby helping patients understand the potential benefits, risks, and long-term implications of gene therapy.

Tool structure and components

The SDM tool was organized into three primary components: (1) role definition, (2) agenda alignment, and (3) intention setting.

The Role Definition component was designed to assess the patient's readiness and willingness to engage in the decision-making process (Figure 1). Clinicians can use the Control Preference Scale to gauge the patient's preferred level of involvement (Supplementary Figure S1).[29] This form presents various options for the patient, ranging from full participation in decision-making to preferring the clinician to lead the process.[29] If the patient is hesitant to take an active role, the clinician is advised to guide the dialogue more explicitly, adjusting the approach as necessary to match the patient's preferred level of involvement.

The Agenda Alignment component was designed to ensure that the patient has a comprehensive understanding of gene therapy to treat HA (Figure 2). Several tools can be used to support this task. The Informative Brochure provides detailed, clear explanations of the application of gene therapy specifically to HA. The Assessment Questionnaire for Evaluating Priorities in Therapy Choice is a custom-developed instrument that prompts the patient to list aspects such as daily activity levels, treatment frequency, and physical impacts in order of priority (Supplementary Figure S2). The Assessment Questionnaire for Evaluating Willingness to Change Therapy is another custom-developed instrument designed to assess the patient's readiness to transition to a new treatment, with responses rated on a 10-point scale (Supplementary Figure S3). An adapted version of the Assessment Questionnaire of the Motivation to Manage Disease/Therapy was used to assess the patient's self-awareness and confidence in managing HA (Supplementary Figure S4);[30] patients are asked to rate 10 statements on a 10-point scale. The Questions/Doubts Support section allows the patient to document any concerns they have, ensuring that these are discussed during the consultation.

The final component, Intention Setting, was designed to help the patient clarify their intentions regarding gene therapy (Figure 3). The Assessment Questionnaire for Evaluating Expectations Towards Gene Therapy, developed on the basis of the Treatment Expectation Questionnaire (TEX-Q),[31] can be used to support this task (Supplementary Figure S5). It assesses the patient's level of agreement with statements related to their expectations for symptom management, energy levels, and overall treatment outcomes. Many of the tools included in the other components, such as the Informative Brochure, Assessment Questionnaire for Evaluating Priorities in Therapy Choice, and the Questions/Doubts Support materials can also be used here.

The SDM tool follows an iterative and flexible decision-making process (Figure 4). Patients and clinicians move together through stages of information gathering, addressing doubts and eventually committing to receiving or declining gene therapy. Throughout the process, participants can revisit previous components and patients are encouraged to involve their family members and patient associations for additional support, ensuring that their decision is fully informed and aligned with their values and preferences.

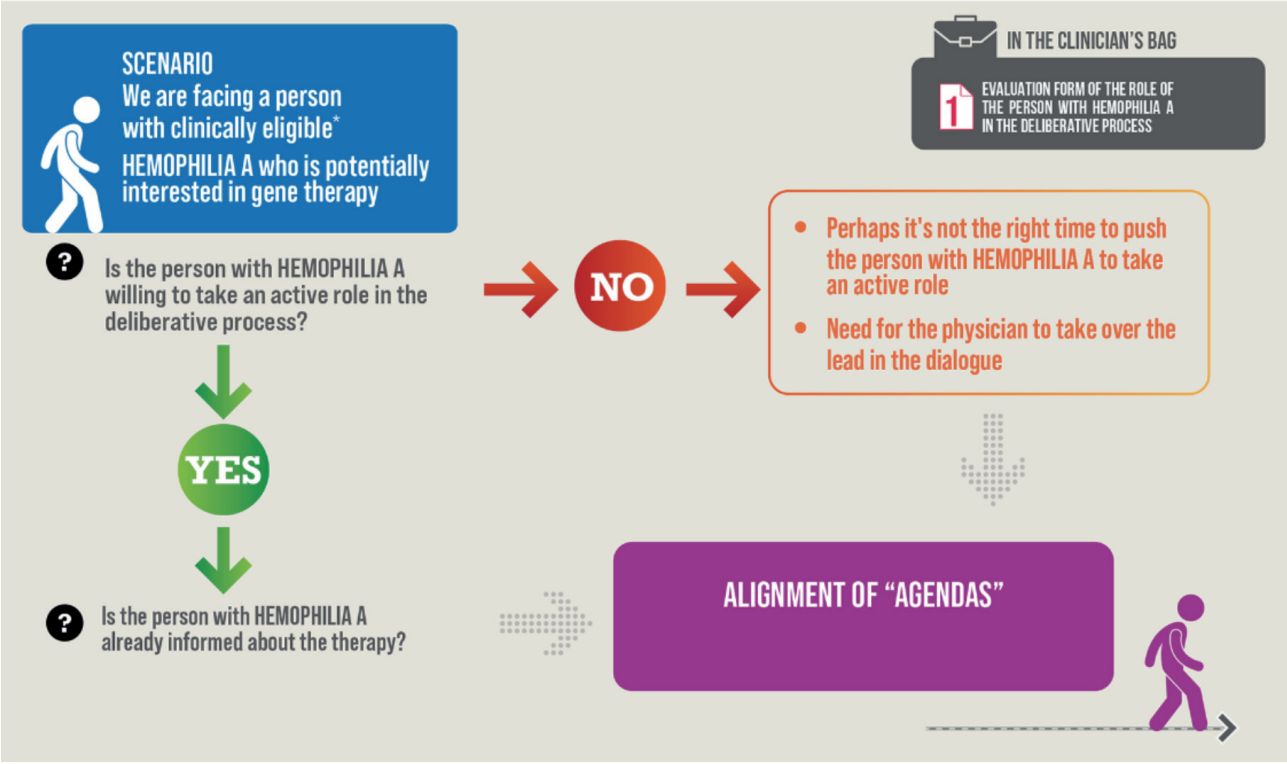


Figure 1. Component 1: Role definition when considering gene therapy for hemophilia A. According to the criteria of the Summary of Product Characteristics of valoctocogene roxaparvovec.[7]

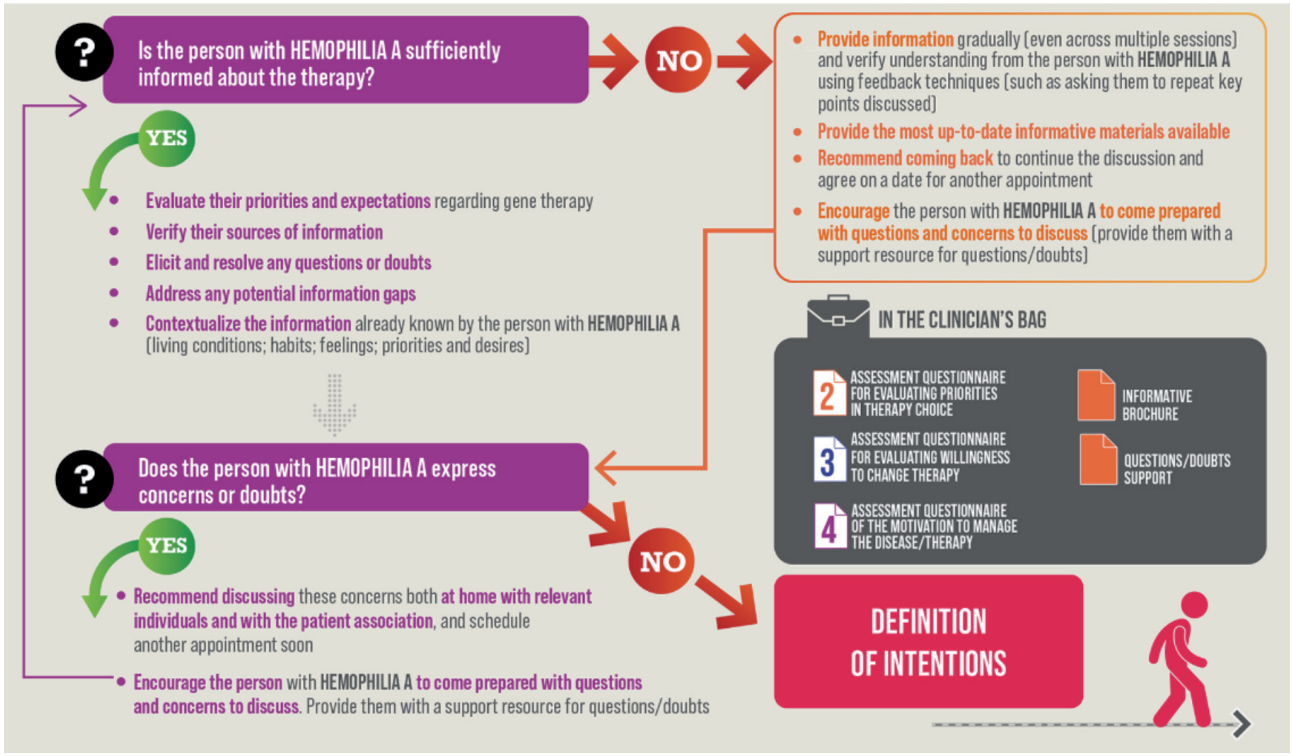


Figure 2. Component 2: Agenda alignment when considering gene therapy for hemophilia A.

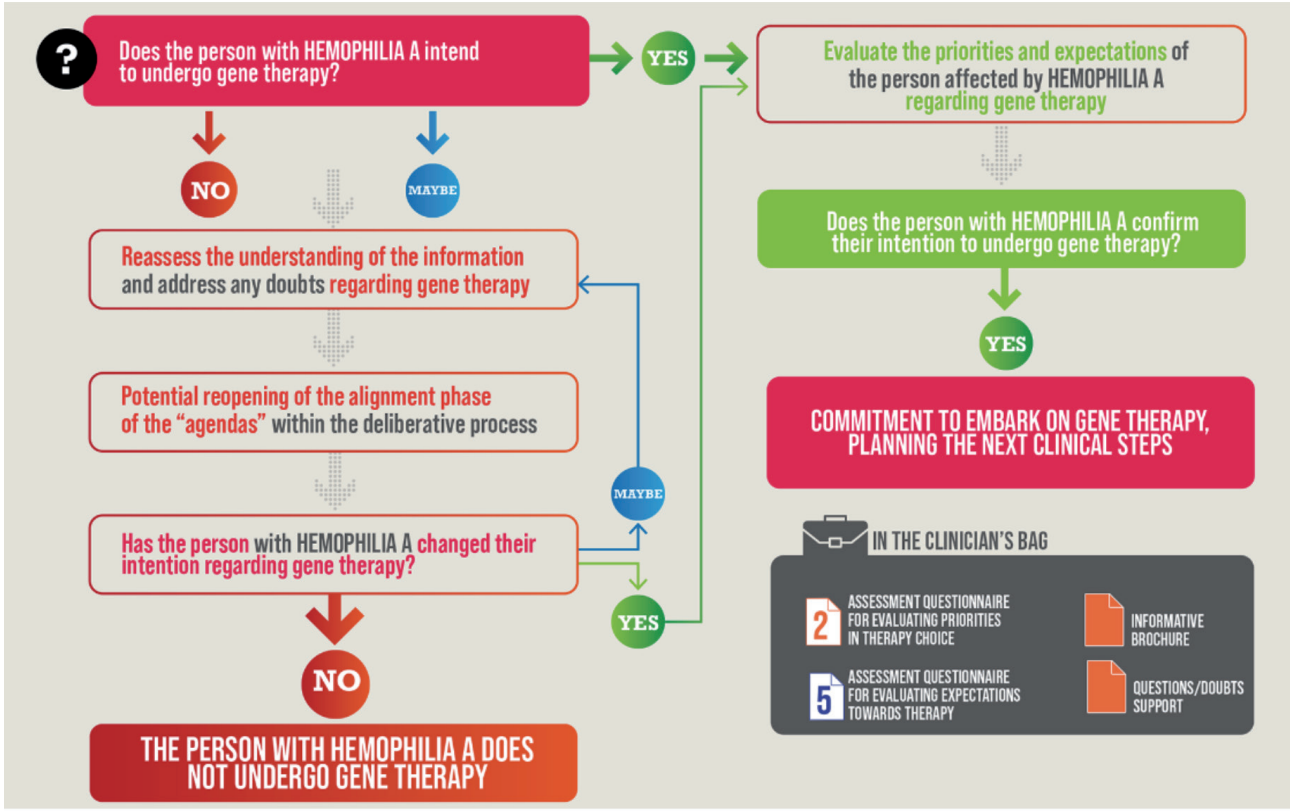


Figure 3. Component 3: Intention setting for gene therapy to treat hemophilia A.

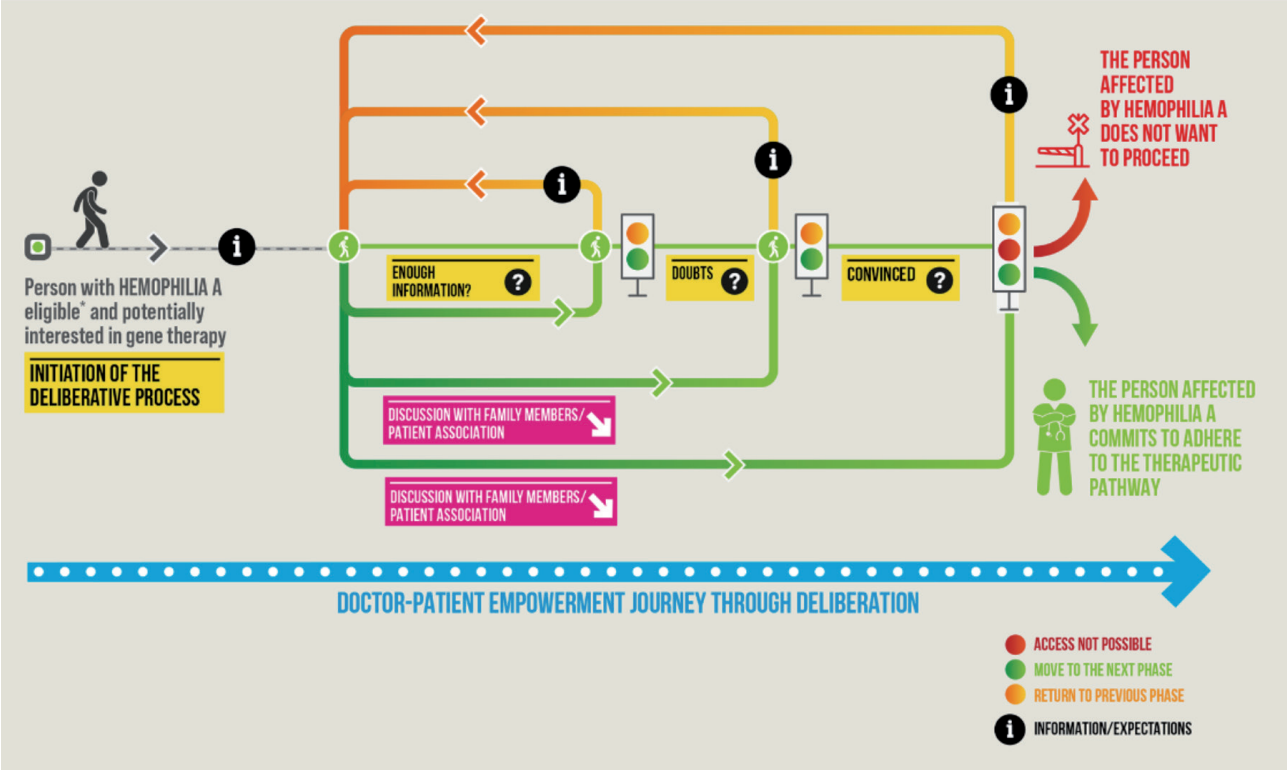


Figure 4. Diagram of the decision-making process when considering gene therapy for hemophilia A. According to the criteria of the Summary of Product Characteristics of valoctocogene roxaparvovec.[7]

Discussion

The development of the SDM tool for gene therapy in HA successfully addressed the primary objective of creating a tailored, patient-centric resource to guide informed decision-making. The modular design facilitates structured interactions between clinicians and patients, ensuring that patient values, preferences, and concerns are central to the deliberative process.

Unlike previous SDM tools, which were often limited in scope or lacked a comprehensive focus on patient-clinician collaboration,[24] this tool was developed through a unique, multidisciplinary process that involved Italian experts from a range of fields, including clinical hematology, psychology, methodology, and patient advocacy. This collaborative approach ensured that the tool not only reflects diverse perspectives but was specifically designed to meet the needs of patients and healthcare professionals in Italy. While its implementation in Italian clinical settings is expected to enhance patient engagement and to improve decision-making outcomes, the modular and adaptable structure of the tool could serve as a valuable framework for developing similar SDM tools in other countries when gene therapy for HA becomes available.

While there are still uncertainties related to the long-term durability of the effects of gene therapy for HA, the transformative nature of this therapy represents a significant shift, offering the possibility of an almost hemophilia-free lifestyle. The implementation of SDM is crucial for aligning treatment decisions with patient values and goals, as gene therapy can drastically reduce or even eliminate the need for regular treatments and the associated logistical burdens, allowing patients to achieve greater freedom in their daily lives.[11] Given the complexity and irreversible nature of gene therapy, SDM is essential in addressing patient concerns, providing clarity on treatment implications and ensuring that both patients and clinicians have a shared understanding of the treatment process and expectations.[3,11]

The process leading to the development of the SDM tool for gene therapy in HA in Italy yielded several important insights and led to key adjustments that enhanced its final design. Feedback received from the experts during the meetings prompted significant refinements to the tool's design, particularly in terms of user-friendliness. Refinements also focused on encouraging clinicians to seek out continuous education to maintain up-to-date knowledge of gene therapy, in order to be able to provide potential recipients with the most up-to-date and relevant information. Moreover, visual aids and clear instructions were integrated into the tool to improve clarity and accessibility, particularly when addressing the complexities of gene therapy. These adjustments ensured the SDM tool was practical, patient-centered, and suitable for a wide range of clinical settings where persons with HA are routinely managed.

One of the primary takeaways was the necessity for a flexible and modular structure, allowing the tool to adapt to persons with varying levels of readiness and understanding. In addition, the tool design ensures that clinicians and patients

can revisit earlier components as necessary, aligning the decision-making process with the patient's evolving journey. The tool also provides a set of resources that clinicians can utilize to facilitate structured discussions and patient-centered decision-making, particularly in situations where additional support is needed to ensure that patient values and preferences are fully addressed. Cultural sensitivity and contextual relevance were also integral to the tool's structure, which has been designed to seamlessly fit into the patient journey in the Italian healthcare context.

Several limitations associated with the SDM tool should be considered. First, although the tool is designed to be adaptable to different levels of patient readiness, there is still potential for variability in patient engagement, particularly among individuals with low health literacy or a limited understanding of gene therapy. In addition, the complexity of gene therapy itself poses a challenge, as even with simplified language and visual aids, some patients may struggle to fully understand the long-term implications of this novel treatment. Given the rarity of HA and the highly innovative nature of the treatment, it is difficult to recruit patients to validate the use of the tool extensively. Finally, the SDM process has historically been time-intensive, which is critical in busy clinical environments.[3] However, this tool has been designed with flexibility in mind, where specific steps were implemented to minimize the impact on day-to-day clinical management by ensuring that the tool is modular and adaptable. This flexibility allows the tool to be revisited at different stages and ensures that it can be applied even in the busiest clinical settings.

Conclusions

The development of an SDM tool for gene therapy in HA represents a useful advancement in patient-centered care in Italy. The tool offers a structured yet adaptable approach to navigating complex treatment decisions. By incorporating feedback from the experts on the Advisory Board and addressing the unique challenges of gene therapy, this SDM tool provides both clinicians and persons with HA the resources needed for informed, collaborative decision-making in managing gene therapy. Validation studies, continued refinement, and real-world testing will be essential to confirm its long-term effectiveness and applicability in diverse clinical settings.

References

1. Berntorp E, Fischer K, Hart DP, et al. Haemophilia. Nat Rev Dis Primers 2021;7:45.
2. Iorio A, Stonebraker JS, Chambost H, et al. Establishing the prevalence and prevalence at birth of hemophilia in males: a meta-analytic approach using national registries. Ann Intern Med 2019;171:540-6.
3. Valentino LA, Blanchette V, Negrier C, et al. Personalising haemophilia management with shared decision making. J Haem Pract 2021;8:69-79.
4. O'Hara J, Hughes D, Camp C, et al. The cost of severe haemophilia in Europe: the CHESS study. Orphanet J Rare Dis 2017;12:106.
5. Hermans C, Gruel Y, Frenzel L, et al. How to translate and implement the current science of gene therapy into haemophilia care? Ther Adv Hematol 2023;14:20406207 221145627.
6. Ozelo MC, Mahlangu J, Pasi KJ, et al. Valoctocogene roxaparvovec gene therapy for hemophilia A. N Engl J Med 2022;386:1013-25.
7. European Medicines Agency. Roctavian: EPAR - Product Information. European Medicines Agency; 2022. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/roctavian (accessed: October 8, 2024).
8. Leavitt AD, Mahlangu J, Raheja P, et al. Durability of efficacy, safety, and quality of life 5 years after valoctocogene roxaparvovec gene transfer for severe hemophilia A: final phase 3 GENEr8-1 trial results. Res Practice Thrombosis Haemostasis 2026;10:103416.
9. Elwyn G, Laitner S, Coulter A, et al. Implementing shared decision making in the NHS. BMJ 2010;341:c5146.
10. Epstein RM, Gramling RE. What is shared in shared decision making? Complex decisions when the evidence is unclear. Med Care Res Rev 2013;70:94s-112s.
11. Wang M, Negrier C, Driessler F, et al. The hemophilia gene therapy patient journey: questions and answers for shared decision-making. Patient Prefer Adherence 2022;16:1439-47.
12. Stiggelbout AM, Pieterse AH, De Haes JC. Shared decision making: concepts, evidence, and practice. Patient Educ Couns 2015;98:1172-9.
13. Hughes TM, Merath K, Chen Q, et al. Association of shared decision-making on patient-reported health outcomes and healthcare utilization. Am J Surg 2018;216:7-12.
14. Anderson G, Rega ML, Casasanta D, et al. The association between patient activation and healthcare resources utilization: a systematic review and meta-analysis. Public Health 2022;210:134-41.
15. Muscat DM, Shepherd HL, Nutbeam D, et al. Health literacy and shared decision-making: exploring the relationship to enable meaningful patient engagement in healthcare. J Gen Intern Med 2021;36:521-4.
16. Athale A, Giguere A, Barbara A, et al. Developing a two-sided intervention to facilitate shared decision-making in haemophilia: decision boxes for clinicians and patient decision aids for patients. Haemophilia 2014;20:800-6.
17. Lanzel AF, Soucie JM, Meeks SL, et al. Ethical decision making framework in previously untreated severe hemophilia A patients. Blood 2017;130:5583.
18. Hermans C, Noone D, Benson G, et al. Hemophilia treatment in 2021: choosing the"optimal" treatment using an integrative, patient-oriented approach to shared decision-making between patients and clinicians. Blood Rev 2022;52:100890.
19. Limjoco J, Thornburg CD. Development of a haemophilia A gene therapy shared decision-making tool for clinicians. Haemophilia 2023;29:1184-90.
20. Di Minno G, Spadarella G, Maldonato NM, et al. Awareness of individual goals, preferences, and priorities of persons with severe congenital haemophilia A for a tailored shared decision-making approach to liver-directed gene therapy. A practical guideline. Blood Rev 2023;62:101118.
21. Meade L, Klaassen R, Sun HL, et al. Enhancing engagement to support shared decision-making within haemophilia. Haemophilia 2023;29:196-7.
22. Roberts JC, Richardson S, Miles ME, et al. The GOAL-Hēm

journey: shared decision making and patient-centred outcomes. Haemophilia 2022;28:784-95.
23. Coffin D, Skinner MW, Thornburg CD, et al. Development of the World Federation of Hemophilia Shared Decision-Making Tool. Haemophilia 2024;30:1298-308.
24. Sun HL, Klaassen RJ, Anger DL, et al. Shared decision-making related to treatment of haemophilia: a scoping review of influential factors and available support tools. Haemophilia 2024;30:880-93.
25. Di Minno G, Spadarella G, Calcaterra IL, et al. The evolving landscape of gene therapy for congenital severe hemophilia: a 2024 state of the art. Bleeding Thromb Vasc Biol 2024; 3:144.
26. Pierce GF, Coffin D. The 1st WFH Gene Therapy Round Table: understanding the landscape and challenges of gene therapy for haemophilia around the world. Haemophilia 2019;25:189-94.
27. Peyvandi F, Lillicrap D, Mahlangu J, et al. Hemophilia gene therapy knowledge and perceptions: results of an international survey. Res Pract Thromb Haemost 2020;4: 644-51.
28. Cutica I, Mortarino M, Garagiola I, et al. Knowledge and attitudes toward gene therapy of a cohort of Italian patients with hemophilia. J Thromb Haemost 2024;22:1001-8.
29. Solari A, Giordano A, Kasper J, et al. Role preferences of people with multiple sclerosis: image-revised, computerized self-administered version of the control preference scale. PLoS One 2013;8:e66127.
30. Arnett GW, Worley CM, Jr. The Treatment Motivation Survey: defining patient motivation for treatment. Am J Orthod Dentofacial Orthop 1999;115:233-8.
31. Shedden-Mora MC, Alberts J, Petrie KJ, et al. The Treatment Expectation Questionnaire (TEX-Q): validation of a generic multidimensional scale measuring patients' treatment expectations. PLoS One 2023;18:e0280472.

Online supplementary material:

Supplementary Figure S1. Control Preference Scale regarding the decision to start gene therapy for Hemophilia A in A) English, and B) Italian.

Supplementary Figure S2. Assessment Questionnaire for Evaluating Priorities in Therapy Choice to treat Hemophilia A in A) English, and B) Italian.

Supplementary Figure S3. Assessment Questionnaire for Evaluating Willingness to Change Therapy for Hemophilia A in A) English, and B) Italian.

Supplementary Figure S4. Adapted version of the Assessment Questionnaire of the Motivation to Manage Disease/Therapy for Hemophilia A in A) English, and B) Italian.

Supplementary Figure S5. Assessment Questionnaire for Evaluating Expectations Towards Gene Therapy for Hemophilia A in A) English, and B) Italian.