anos (DP = 15,9). A prevalência de tabagismo, elitismo e obesidade foi 13,8%, 12,5% e 24,6%, respectivamente. A prevalência de eventos trombóticos foi 9,6% (n = 17). Entre os fatores associados ao evento trombótico, pacientes com histórico de trombose venosa profunda apresentaram percentual superior para evento trombótico quando comparados com aqueles sem histórico (50 *vs* 8,2%; p < 0,001 – RR = 2.14). Das características clínicas, pacientes com tumores de grau III e IV, e IDH não mutante tiveram maiores percentuais para eventos trombóticos, porém sem associação significativa (p > 0,050). Ao analisar a terapêutica pós-cirúrgica, pacientes que realizaram radioterapia e quimioterapia apresentaram RR = 1,14 (IC95% 1,07 – 1,21) e RR = 1,11 (IC95% 1,02 – 1,20), respectivamente. Quanto ao óbito dos pacientes, 17,9% apresentaram evento trombótico enquanto entre os vivos, 8,5% apresentaram o evento (p = 0,247 – RR = 1,11; IC95% 0,93 – 1,33). O tempo de seguimento mediano entre o evento trombótico e o status final foi de 2,8 meses (1 dia a 9 meses) e 3,84 meses (1 dia a 12 meses), respectivamente, para os pacientes que vieram a óbito e vivos (p > 0,050). **Discussão:** Nesta amostra preliminar, o estudo indica que pacientes com evento trombótico apresentam maior risco de evoluir a óbito em, aproximadamente, 3 meses pós-evento. Quanto ao histórico de saúde, a presença de trombose venosa profunda prévia e as terapêuticas pós-cirúrgicas associaram-se ao evento trombótico pós-diagnóstico. Embora a associação entre o evento trombótico e a demais características clínicas (i.e., grau tumoral, IDH, dentre outras) não tenha sido significativa, tais achados podem ser atribuídos ao tamanho amostral. **Conclusão:** Em pacientes com neoplasia maligna do sistema nervoso central, os fatores associados ao evento trombótico foram históricos de trombose venosa profunda, realização de radioterapia e quimioterapia.

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SOCIAL RETURN OF INVESTMENT ANALYSIS OF GENE THERAPY FOR HEMOPHILIA IN BRAZIL: STUDY PROTOCOL

DV Pachito [a], J Balardin [b], L Piton [a], R Feitoza [a], PHRF Almeida [a], S Lima [a], F Vicente [a]

[a] *Pfizer Brasil, São Paulo, Brazil*
[b] *Cerner Enviza, São Paulo, Brazil*

Objectives: To estimate the social return of investment (SROI) of gene therapy (Tx) for hemophilia A and B in Brazil, and to discuss a framework for measuring social and long-term value of advanced therapy medicinal products (ATMPs). **Methods:** SROI forecast analysis. A conceptual logical model was developed as a first step by a multi-disciplinary team to map (i) main stakeholders; (ii) inputs and outputs expected along the implementation of gene Tx for hemophilia in the Brazilian public health system; and (iii) short-, medium-, and long-term outcomes. This conceptualization is the foundation of the Theory of Change that will underpin the SROI analysis. Patients, family members, and health care professionals (HCPs) were mapped as main stakeholders. Study protocol will be submitted to an Institutional Research Board and participation will be voluntary and conditioned to informed consent. Patients and family members will be enrolled from patients' associations. One-to-one semi-structured interviews will be carried out using an online platform. Forty stakeholder interviews are planned, with participation of at least 20 patients. Family members and HCPs will account for the other 20 interviews. Theoretical saturation will be assessed through a saturation table and a pre-defined codebook. Questions will address the impact of disease and its treatment on the ability of performing daily life activities and social interactions. The impact of gene Tx on the number of bleedings will be derived from pivotal randomized controlled trials and extrapolated over time. Reduction of health care expenditures related to prophylaxis and complication management will be estimated, as well as the reduction of social security expenditures. Financial proxies will be applied for valuing intangible outcomes. Social value will be calculated by the amount of tangible and intangible earnings multiplied by the respective financial values, with adjustments for attribution, deadweight, and drop off. SROI per dollar invested will be presented as the main study outcome. **Results:** Results are expected to be obtained and presented in scientific Journals by the end of 2024. **Discussion:** There are challenges for valuing ATMPs, including lack of definition and valuation of cure for chronic diseases, approach for qualifying cost-savings compared with current treatments, and choice of perspective. Some frameworks have been developed to address limitations of traditional health technology assessments (HTA) methods, considering the specificities of ATMPs and the limitations of using quality-adjusted life years (QALYs) in some situations. The ISPOR Value Flower accounts for novel value elements, such as severity of illness, value of insurance, value of hope. The generalized risk-adjusted cost-effectiveness (GRACE) approach was developed to account for the adjustment of a willingness-to-pay threshold to untreated illness severity or pre-existing permanent disability, and the differentiation between life expectancy and quality of life across health states. SROI is a comprehensive, well-described method of cost-benefit analysis that considers tangible and intangible outcomes, allowing for the measurement of long-term value from the societal perspective **Conclusion:** This study will provide evidence on the social value of gene Tx for hemophilia, advancing the methods for valuing ATMPs. Results may support future HTA, along with cost-effectiveness analysis and budget impact analysis.

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WHAT ARE THE PERCEPTIONS AND MOST RELEVANT TREATMENT OUTCOMES REGARDING GENE THERAPY ACCORDING TO PEOPLE WITH HEMOPHILIAS IN BRAZIL? STUDY PROTOCOL FOR A QUALITATIVE PATIENT PREFERENCE STUDY

F Vicente [a], J Balardin [b], L Piton [a], R Feitoza [a], S Lima [a], DV Pachito [a]

[a] *Pfizer Brasil, São Paulo, SP, Brasil*
[b] *Cerner Enviza, São Paulo, SP, Brasil*

Introduction: Gene therapies for hemophilias present a new reality for patients and their families. Gaining a better understanding of patient perceptions regarding these therapies may provide insights regarding their willingness to accept them. Moreover, as gene therapies will likely be soon available for hemophilias, health technology assessment decision-making needs to be tailored towards patients'preferences and needs. **Objectives:** To describe a study protocol aimed at understanding patient preferences among people with hemophilias, and their opinions and concerns regarding gene therapies. **Methods:** The protocol for this qualitative study was designed following the general steps described in the PAVING Study (Patient Preferences to Assess Value IN Gene Therapies in Hemophilia). The protocol consisted of (i) a target literature review and (ii) patient relevant information needs and (treatment) attributes identification and ranking. A target literature review of attributes and previous published preference studies will be performed. Participants will be recruited through purposive sampling. Relevance of attributes will be investigated in online one-to one interviews with up to 20 people with hemophilia A and B. An interview guide for semi-structured interviews was designed. Prior to any questions about gene therapy, participants will receive information regarding the disease, standard of care and gene therapy using an educational tool validated in previous studies to ensure comprehension of the attributes and the gene therapy context. We will translate the educational tool and pilot them with Brazilian participants. Interviews will also cover opinions and concerns of people with hemophilias regarding gene therapies. The selected attributes (from the literature review and interviews) will be included in an exercise, in which participants will rank their top six attributes. Data from answers to open questions will be organized using NVivo and analyzed following framework analysis. Data saturation will be assessed by a saturation table and a documented codebook. Details on the methods and results of the interviews will be reported according to the consolidated criteria for reporting qualitative research (COREQ) checklist. **Results:** Results are expected to be obtained and presented in conferences and scientific peer-reviewed journals by the end of 2024. **Discussion:** This protocol describes the methodological steps to qualitatively elicit and study patient preferences and perspectives in hemophilias. These findings will inform future quantitative patient preference studies (discrete choice and best-worst scaling experiments). **Conclusion:** Results will provide evidence on patient preferences regarding alternatives of care for hemophilias in Brazil. Patient preferences should be considered for decision making related to individual care and to reimbursement and coverage decisions in health systems, along with traditional cost-effectiveness and budget impact analysis. **Acknowledgements:** All authors contributed to the abstract conception and design. All authors read and approved the final manuscript.

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HEMOFILIA A GRAVE: RELATO DO 1CASO DE ARTROPLASTIA TOTAL DE TORNOZELOS REALIZADO EM PORTO ALEGRE

AC Luz, CBF Dametto, GFC Diaz, MLS Paula, CS Barros, PEB Correa, SC Frichembruder

Hemocentro do Estado do Rio Grande do Sul (HEMORGS), Porto Alegre, RS, Brasil

Introdução: A Hemofilia A (HA) é um distúrbio hereditário da coagulação ligado ao cromossomo X. Caracteriza-se pela redução do fator VIII da coagulação, podendo ser classificada em leve (FVIII 5-50%), moderada (FVIII 1-5%) e grave (FVIII < 1%). Nos casos de HA grave (HAG), os sangramentos podem se manifestar espontaneamente, sendo 80% no sistema musculoesquelético, como os sangramentos intra-articulares (hemartroses) e as hemorragias musculares (hematomas). As hemartroses ocorrem com mais frequência nos joelhos, cotovelos e tornozelos. O tratamento indicado é a reposição de FVIII profilática ou sob demanda para tratar os sangramentos. O sangramento recorrente provoca uma hipertrofia sinovial, levando a uma sinovite crônica e consequente degeneração articular. **Objetivo:** Relatar caso de um portador de HAG com artropatia hemofílica nos tornozelos que realizou Artroplastia Total de Tornozelos (ATT) em Porto Alegre, atendido no Hemocentro. RELATO DO CASO: Paciente DPP, masculino, 25 anos, HAG, inibidor negativo, diagnóstico psiquiátrico de TOC, prescrição de profilaxia secundária 3 vezes por semana desde 05/2014, sem adesão adequada, com história de hemartrose de repetição nos cotovelos e tornozelos desde a infância. Em 2008 consulta com ortopedista que avaliou os tornozelos e diagnosticou estágio I de Arnold, amplitude de movimento (ADM) do tornozelo direito (TD): dorsiflexão (DF) 25°e flexão plantar (FP) 30°, tornozelo esquerdo: DF 30°e FP 22°, indicou fisioterapia por 90 dias, se não apresentar boa evolução, encaminhar para radiossinoviórtese. Não aderente ao tratamento fisioterapêutico, não retornou no ortopedista. Em decorrência dos problemas psiquiátricos o paciente nunca teve acompanhamento regular com a equipe multidisciplinar do Hemocentro, com o passar do tempo e sem realizar a profilaxia regularmente, os tornozelos apresentaram piora, aumento da dor, limitação da amplitude de movimento e dificuldade na marcha. Em 2018 nova consulta com ortopedista várias infiltrações de corticoide (CTC) nos tornozelos e teve indicação de ATT direito, reiniciou a fisioterapia. Procurou outros médicos, fez tratamento com medicina regenerativa com células tronco nos 2 tornozelos. Em janeiro de 2022 realizou artroplastia no tornozelo direito, prótese tíbio-talar, osteotomia do calcâneo e alongamento de tendão, 30 dias imobilizado com tala gessada, substituída por robofoot por mais 1 mês, em março reinicia a fisioterapia diária, ADM de DF 21°e FP 10°, mas ainda referia dor na região do calcâneo D e na articulação subtalar, ortopedista prescreve pregabalina e indica terapia por ondas de choque, realizadas 3 aplicações. Em agosto nova cirurgia para retirada dos parafusos do calcâneo D, ainda apresentando dor na subtalar, já com indicação de realizar artrodese no futuro, nova infiltração