prophylaxis and expectations for future therapies. **Objectives:** To understand the physical, emotional, and systemic challenges related to current hemophilia care in Brazil and stakeholders' hopes for less burdensome, equitable treatment options. **Material and methods:** A targeted thematic analysis was conducted on semi-structured interviews with 43 participants: 23 PwH, 10 family members, and 10 HCPs. Participants were purposively sampled across Brazil to capture geographic and socioeconomic diversity. Interviews were conducted virtually, transcribed verbatim, and analyzed using the framework method. **Results:** Three overarching themes emerged: (1) Burden of current treatment: Participants emphasized the logistical and emotional toll of regular intravenous prophylaxis, including difficult venous access, time-consuming infusion preparation, cold-chain storage, treatment-related waste, and limitations on mobility and daily activities. The need to self-infuse or depend on caregivers led to stress and fatigue, while some PwH skipped doses when in pain or emotionally overwhelmed. (2) Systemic barriers and healthcare inequities: Despite centralized provision of CFCs, participants reported recurrent medication stockouts at treatment centers, long travel distances to treatment centers, limited access to mental health support, and lack of awareness about hemophilia among non-specialist providers. These challenges were especially acute in remote or low-resource settings, where travel and treatment costs strained families despite the medication being free. (3) Expectations for future therapies: Stakeholders expressed high hopes for long-acting, subcutaneous, and gene therapies to reduce the frequency and burden of treatment. HCPs emphasized the importance of ensuring equitable access, infrastructure for monitoring novel therapies, and education to support adherence. Participants also highlighted the need for individualized treatment plans and stronger psychosocial support. **Discussion and Conclusion:** While prophylactic CFC therapy improves clinical outcomes, it imposes a daily burden that undermines quality of life and adherence. Stakeholders' narratives emphasize the urgent need to expand access to simplified therapies and reinforce health literacy strategies. Addressing structural barriers, enhancing patient-centered care, and ensuring equitable implementation of innovations are critical steps for advancing hemophilia care in Brazil.

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FACTOR-VIII MIMETIC BISPECIFIC ANTIBODIES FOR THE TREATMENT OF HEMOPHILIA A: AN UPDATE

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Introduction: Hemophilia A is an inherited bleeding disorder resulting from the deficiency or dysfunction of coagulation Factor VIII (FVIII). Standard treatment with FVIII replacement has improved outcomes but remained limited by frequent intravenous administration and the risk of inhibitor development in People with Hemophilia A (PwHA). In this context, FVIII-mimetic bispecific antibodies have emerged as prophylactic agents for PwHA, both with or without inhibitors. These drugs can bind Factor IX (FIX) and Factor X (FX), allowing the coagulation process to continue normally. **Objectives:** This review aimed to update and discuss the FVIII-mimetic bispecific antibodies in hemophilia A. **Material and methods:** We reviewed the current literature and checked scientific event proceedings about the subject. **Discussion and Conclusion:** Emicizumab is currently approved FVIII-mimetic bispecific antibody for hemophilia A prophylaxis. It is administered subcutaneously and has a half-life around 30 days, enabling weekly to monthly regimens. Real-life reports corroborated the clinical trials, demonstrating reductions in bleeding rates associated with enhanced quality of life and improved joint health. Safety profiles mainly concerned the association between emicizumab and increased doses of bypassing agents, but were particularly rare when reduced bypassing agent doses were prescribed. Clinically active anti-emicizumab antibodies are even rarer, although they remain an important issue for emicizumab discontinuation. Alternative emicizumab prophylaxis regimens are under investigation in several countries worldwide to reduce waste and possible futility. Novel FVIII- mimetic bispecific antibodies were developed with modified molecules to improve pharmacokinetics/pharmacodynamics compared to emicizumab. Mim8 (denecimig) has a favorable pharmacokinetics (half-life = 26–35 days) and safety profile in phase I/II studies, with no thrombotic events or anti-Mim8 antibodies reported. In addition, in vitro data suggested that Mim8 might be effective in the presence of anti-emicizumab antibodies. NXT007 is another promising candidate, designed to be more potent than emicizumab. NXT007 half-life may reach more than 2 months. Phase I study with healthy individuals showed no dose-related adverse event, but 30% of participants developed anti-NXT007 antibodies that promoted faster clearance. Ongoing innovation continues beyond these agents. Inno8 is a single-chain bispecific antibody developed for orally delivery and then albumin-bound, having an increased half-life. In animal models, oral Inno8 had a half-life of 113h. In vitro studies showed its hemostatic effect. A phase I trial is ongoing. A single- chain fragment of the FIX-binding emicizumab was fused with the membrane-binding C2-domain of factor V, generating VH9/VL+C2. Compared to emicizumab, the in vitro FVIII-mimetic cofactor activity of VH9/VL+C2 was 3× greater, without inhibitor interference. SS315 was developed with four paratopes composed of symmetric anti-FX and anti-FIX arms. In preclinical assays, SS315 was more potent than emicizumab. NVG-444 was developed by inserting thrombin-sensitive peptides into the structure of emicizumab, providing a negative autoregulation. FVIII-mimetic bispecific antibodies represent a shift in hemophilia A prophylaxis. Emicizumab has redefined the standard-of-care, and newer agents may offer even greater hemostatic improvements. Continued research will refine their role in personalized therapy, especially for PwHA with challenging clinical profiles.

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