IT'S NOT "ONE SIZE FITS ALL":

Addressing Complications and Barriers to Unlock Individualized Treatment and Management for Patients With Hemophilia A

SUGGESTED READINGS

MODULE 1: *Selecting and Dosing Clotting Factors to Individualize Treatment for Patients With Hemophilia A*

Collins PW. Personalized prophylaxis. *Haemophilia*. 2012;18(suppl 4):131-135. doi:10.1111/j.1365-2516.2012.02838.x

Konkle BA, Shapiro AD, Quon DV, et al. BIVV001 fusion protein as factor VIII replacement therapy for hemophilia A. *N Engl J Med*. 2020;383:1018-1027. doi:10.1056/NEJMoa2002699

Mahlangu J, Young G, Hermans C, et al. Defining extended half-life rFVIII: a critical review of the evidence. *Haemophilia*. 2018;24:348-358. doi:10.1111/hae.13438

Oldenburg J. Optimal treatment strategies for hemophilia: achievements and limitations of current prophylactic regimens. *Blood*. 2015;125:2038-2044. doi:10.1182/blood-2015-01-528414

Peyvandi F, Mannucci PM, Garagiola I, et al. A randomized trial of factor VIII and neutralizing antibodies in hemophilia A. *N Engl J Med*. 2016;374:2054-2064. doi:10.1056/NEJMoa1516437

Warren BB, Thornhill D, Stein J, et al. Young adult outcomes of childhood prophylaxis for severe hemophilia A: results of the Joint Outcome Continuation Study. *Blood Adv.* 2020;4:2451-2459. doi:10.1182/bloodadvances.2019001311

Young G, Mahlangu JN. Extended half-life clotting factor concentrates: results from published clinical trials. *Haemophilia*. 2016;22(suppl 5):25-30. doi:10.1111/hae.13028

MODULE 2: *Clinical Complications, Challenges, and Comorbidities Associated With Hemophilia and Its Treatment*

Carcao M, Goudemand J. *Inhibitors in Hemophilia: A Primer*. 5th ed. World Federation of Hemophilia; 2018. Accessed January 3, 2022. https://www1.wfh.org/publication/files/pdf-1122.pdf

Centers for Disease Control and Prevention. Data and statistics on hemophilia. Accessed January 3, 2022. https://www.cdc.gov/ncbddd/hemophilia/data.html

DiMichele DM. *Inhibitors in Hemophilia: A Primer*. 4th ed. World Federation of Hemophilia; 2008.

Jaffray J, Young G, Ko RH. The bleeding newborn: a review of presentation, diagnosis, and management. *Semin Fetal Neonatal Med*. 2016;21:44-49. doi:10.1016/j.siny.2015.12.002

Konkle BA, Huston H, Fletcher SN. Hemophilia A. 2000 [Updated 2017]. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews®* [Internet]. University of Washington, Seattle; 1993-2021. Accessed January 3, 2022. https://www.ncbi.nlm.nih.gov/books/NBK1404/pdf/Bookshelf_NBK1404.pdf

MedlinePlus. Hemophilia: inheritance. Accessed January 3, 2022. https://ghr.nlm.nih.gov/condition/hemophilia#inheritance

MedlinePlus. Hemophilia: resources. Accessed January 3, 2022. https://ghr.nlm.nih.gov/condition/hemophilia#resources

Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: diagnosis, treatments, and its complications. *Lancet.* 2016;388:187-197. doi:10.1016/S0140-6736(15)01123-X

White GC, DiMichele D, Mertens K, et al. Utilization of previously treated patients (PTPs), noninfected patients (NIPs), and previously untreated patients (PUPs) in the evaluation of new factor VIII and factor IX concentrates. Recommendation of the Scientific Subcommittee on Factor VIII and Factor IX of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. *Thromb Haemost.* 1999;81:462.

MODULE 3: *Evaluating Emerging Gene Therapies to Further Treatment for Patients With Hemophilia A*

American Society of Gene + Cell Therapy. Hemophilia. Accessed January 3, 2022. https://patienteducation.asgct.org/disease-treatments/hemophilia

George L, Eyster E, Ragni M, et al. Phase I/II trial of SPK-8011: stable and durable FVIII expression for >2 years with significant ABR improvements in initial dose cohorts following AAV-mediated FVIII gene transfer for hemophilia A. *Res Pract Thromb Haemost*. 2020;4(suppl 1):10. Accessed January 3, 2022. https://abstracts.isth.org/abstract/phase-i-ii-trial-of-spk-8011-stable-and-durable-fviii-expression-for-2-years-with-significant-abr-improvements-in-initial-dose-cohorts-following-aav-mediated-fviii-gene-transfer-for-hemophilia-a

Ginn SL, Amaya AK, Alexander IE, et al. Gene therapy clinical trials worldwide to 2017: an update. *J Gene Med.* 2018;20:e3015. doi:10.1002/jgm.3015

High KA, George LA, Eyster ME, et al. A phase 1/2 trial of investigational Spk-8011 in hemophilia A demonstrates durable expression and prevention of bleeds. *Blood.* 2018;132(suppl 1):487. Accessed January 3, 2022. https://ash-publications.org/blood/article/132/Supplement%201/487/262202/A-Phase-1-2-Trial-of-Investigational-Spk-8011-in

Kuzmin DA, Shutova MV, Johnston NR, et al. The clinical landscape for AAV gene therapies. *Nat Rev Drug Discov.* 2021;20:173-174. doi:10.1038/d41573-021-00017-7

Leebeek FWG, Miesbach W. Gene therapy for hemophilia: a review on clinical benefit, limitations, and remaining issues. *Blood.* 2021;138:923-931. doi:10.1182/blood.2019003777

Rangarajan S, Walsh L, Lester W, et al. AAV5-factor VIII gene transfer in severe hemophilia A. *N Engl J Med.* 2017;377:2519-2530. doi:10.1056/NEJMoa1708483

Pasi J, Rangarajan S, Tavakkoli F, et al. Achievement of normal factor VIII activity following gene transfer with valoctocogene roxaparvovec (BMN 270): long-term efficacy and safety results in patients with severe hemophilia A. World Federation of Hemophilia 2018 World Congress. Abstract T–FPMED01–001 (153). Accessed January 3, 2022. https://elearning.wfh.org/resource/achievement-of-normal-fviii-activity-following-gene-transfer-with-valoctocogene-roxaparvovec-bmn-270-long-term-efficacy-and-safety-results-in-patients-with-severe-hemophilia-a

MODULE 4: *Expanding Patient Engagement to Advance Hemophilia A Treatment Adherence and Outcomes*

Agency for Healthcare Research and Quality (AHRQ). Overcoming barriers to shared decision making. Accessed January 3, 2022. www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecision-making/webinars/sharewebinar518-slides.pdf

AHRQ. The SHARE approach. Accessed January 3, 2022. https://www.ahrq.gov/health-literacy/professional-training/shared-decision/index.html

Antun A, Monahan PE, Manco-Johnson MJ, et al. Inhibitor recurrence after immune tolerance induction: a multicenter retrospective cohort study. *J Thromb Haemost.* 2015;13:1980-1988. doi:10.1111/jth.13143

Carcao MD, Iorio A. Individualizing factor replacement therapy in severe hemophilia. *Semin Thromb Hemost.* 2015;41:864-871. doi:10.1055/s-0035-1552563

Department of Health and Human Services. Basic concepts of hemophilia: a self-study and planning workbook for families with a new diagnosis of hemophilia. Accessed January 3, 2022. https://www.cdc.gov/ncbddd/hemophilia/documents/ProviderGuide.pdf

Dolan G, Hermans C, Klamroth R, et al. Challenges and controversies in haemophilia care in adulthood. *Haemophilia.* 2009;15(suppl 1):20-27. doi:10.1111/j.1365-2516.2008.01949.x

Eckhardt CL, van Velzen AS, Peters M, et al. Factor VIII gene (F8) mutation and risk of inhibitor development in nonsevere hemophilia A. *Blood.* 2013;122:1954-1962. doi:10.1182/blood-2013-02-483263

Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab prophylaxis in hemophilia A with inhibitors. *N Engl J Med.* 2017;377:809-819. doi:10.1056/NEJMoa1703068