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Continuing Medical Education (CME) Questions

C5 inhibition in aHUS

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Brocklebank V, Walsh PR, Smith-Jackson K, Hallam TM, Marchbank KJ, Wilson V, Bigirumurame T, Dutt T, Montgomery EK, Malina M, Wong EKS, Johnson S, Sheerin NS, Kavanagh D, for the NRCTC aHUS Research Consortium. Atypical hemolytic uremic syndrome in the era of terminal complement inhibition: an observational cohort study. *Blood.* 2023;142(16):1371-1386.

1. **Your patient is a 24-year-old woman with suspected complement-mediated atypical hemolytic uremic syndrome (CaHUS). Based on the national observational cohort study using National Renal Complement Therapeutics Centre (NRCTC) data by Brocklebank and colleagues, which of the following statements about clinical and genetic characteristics of individuals with suspected CaHUS treated with eculizumab is correct?**
   - ☐ One-quarter of patients with confirmed CaHUS treated with eculizumab had an inherited and/or acquired complement abnormality
   - ☐ *CFI* mutations were the most common among patients with CaHUS treated with eculizumab
   - ☐ Mean systolic blood pressure was 150 mm Hg and varied significantly among mutation types
   - ☐ In the eculizumab-treated CaHUS cohort, a trigger was identified in 31% of patients, most commonly infection (16%) and pregnancy (10%)
2. **According to the national observational cohort study using NRCTC data by Brocklebank and colleagues, which of the following statements about outcomes of individuals with suspected CaHUS treated with eculizumab is correct?**
   - ☐ The 5-year cumulative estimate of end-stage kidney disease (ESKD)–free survival improved from 33.5% in a control cohort to 55.5% in the eculizumab-treated cohort
   - ☐ Underlying genotype was not linked to outcome after eculizumab treatment
   - ☐ The relapse rate after stopping eculizumab was 1 per 9.5 person-years (PY) with a pathogenic mutation and 1 per 10.8 PY with a variant of uncertain significance
   - ☐ The rate of meningococcal infection in the treated cohort was 250 times greater than the background rate in the general population
3. **According to the national observational cohort study using NRCTC data by Brocklebank and colleagues, which of the following statements about clinical implications of real-world experience of treating individuals with suspected CaHUS with eculizumab is correct?**
   - ☐ Biallelic pathogenic mutations in *EXOSC3* and other genes encoding an essential part of the RNA exosome may cause non-eculizumab-responsive atypical hemolytic uremic syndrome (aHUS)
   - ☐ Recessive *HSD11B2* mutations causing mineralocorticoid deficiency may present with a thrombotic microangiopathy
   - ☐ The study definitively proved that stopping eculizumab does not cause relapses in patients without a rare complement genetic variant
   - ☐ The study proved that endothelial accumulation of aberrant RNA species activates proapoptotic pathways secondary to ribosomal dysfunction

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