LONG-TERM EMICIZUMAB PROPHYLAXIS IN PEOPLE WITH HEMOPHILIA A: REAL-WORLD EXPERIENCE ACROSS ALL AGES

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Background and Aims. Emicizumab has provided people with haemophilia A (PwHA) stable bleed protection across inhibitor status and age groups. Nevertheless, a subset of patients continues to experience bleeding despite adequate treatment exposure. This study aimed to evaluate long-term laboratory and clinical outcomes in a real-world setting.

Materials and Methods. All PwHA receiving emicizumab prophylaxis regularly followed up at our Haemophilia Centre were included. Clinical data included type and number of bleeds and physical activity before and after emicizumab start. Physical activity was categorized as: no activity, light-, and moderate/high-impact physical activity. Laboratory data included emicizumab plasma concentration (r2 Diagnostics Inc., South Bend, Indiana, USA) and FVIII-like activity measured by chromogenic assay with human reagents (BiophenTM FVIII:C, Hyphen BioMed, Neuville-sur-Oise, France).

Results. Forty PwHA (97.5% severe; 40% with inhibitors; 30% children) received emicizumab prophylaxis for a median of 5.7 years (IQR 4.4–7.6). During follow-up, 12 patients (30%) were bleed-free, while 28 experienced 121 bleeding episodes (84, 69% joint bleeds; 77, 63% spontaneous). Blood samples were drawn after a median of 5 days since the last emicizumab administration (IQR 2–7; range 1-21). Median emicizumab plasma concentration was 49 µg/mL (IQR 43–59), with a corresponding median FVIII-like activity of 19.6 IU/dL (IQR 16–24). Median emicizumab concentration and FVIII-like activity were similar between bleeders and non-bleeders (47 vs 50.6 µg/ml and 20 vs 19.9 IU/dL, respectively). During emicizumab prophylaxis, the proportion of patients who performed moderate/high-impact activity increased from 15 to 33% and that of sedentary patients decreased from 48 to 25%. Overall, 15 (38%) patients reported increased physical activity intensity after switching to emicizumab.

Conclusions. In this cohort of patients followed-up for a median of 6 years, emicizumab concentration remained consistently within the therapeutic range with a median FVIII-like activity well beyond the threshold of mild haemophilia range. Only 30% of patients remained bleed free, confirming persistent heterogeneity in clinical phenotype and suggesting that emicizumab concentration and/or FVIII-like activity levels do not reflect the haemostatic potential of the drug and cannot be used to inform level of protection against bleeds. Switching to emicizumab favoured increased physical activity suggesting an important impact on patients' lifestyle and functional confidence. Further studies are warranted to investigate how individual haemostatic potential, joint status and lifestyle changes may contribute to improve treatment and monitoring individualization in PwHA on emicizumab.