Study Protocol

Title	Comparison of outcomes between low dose Emicizumab and low dose factor VIII prophylaxis in clinically severe hemophilia A
Principal Investigator	Nuchanun Kessakorn, MD The Pediatric Hematology-Oncology Fellowship Program at King Chulalongkorn Memorial Hospital
Co-investigators	Prof.Dr. Darintr Sosothikul, Diplomat Professor at Pediatric Hematology-Oncology, King Chulalongkorn Memorial Hospital
Study centers & Address	Pediatric Hematology-Oncology Unit, King Chulalongkorn Memorial Hospital
Study period	12 months

Objectives:

- Primary objective: To compare outcome between Extended half-life FVIII concentrates with pharmacokinetic guided and low dose Emicizumab using Annualized bleeding rate, Annualized joint bleeding rate, and HemoQol in patient with clinically severe Hemophilia A

- Secondary objective: To study about pharmacokinetic and side effect of emicizumab

Study design: Interventional study without concurrent controls: Before-after (pre-post) studies

Population and Sample size

- Target population: patient with clinically severe Hemophilia A follow up in Pediatric Hematology-Oncology Unit, King Chulalongkorn Memorial Hospital
- Sample size: 15

Informed Consent Process Investigator give all patients about study information then contact back to investigator if one was interested to participate in the study then sign consent before enrolled and appoint for next visit

Study procedure

- Interventional study without concurrent controls: Before-after (pre-post) studies

- Pre-intervention defined as using low dose factor VIII prophylaxis. And Post-intervention defined as using low dose emicizumab (2 mg/kg/dose) Then compare Annualized bleeding rate (ABR), Annualized joint bleeding rate, AJBR, Quility of life (HemoQoL) before and after prophylaxis bleeding with low dose Emicizumab. First month, loading emicizumab 1-1.5 mg/kg/dose subcutaneous every 2 weeks then maintenance with same dose every 4 weeks for 6 months

Comparator, dosage & mode of administration

- Extended half-life FVIII concentrates intravenous using PK-based for at least 6 months

Duration of participation for each volunteer – at least 6 months

Outcome variables

- Primary: New choice of Prophylactic treatment for clinically severe Hemophilia A
- Secondary: Improve Annualized bleeding rate (ABR), Annualized joint bleeding rate (AJBR), and quality of life for clinically severe Hemophilia A

Statistical method

- Median and interquartile range (percentile 25-75) for continuous variables
- Frequency and percentage for discrete variables
- Wilcoxon Signed rank test: to compare outcome between before-after low dose emicizumab
- Pearson's correlation coefficiency: to find correlation factor affect emicizumab levels
- Paired t test : to compare ABR, AJBR between before-after low dose emicizumab
- $P<0.05$ is statistic significant

Ethical Consideration: Respect of person, Beneficence/Non-malefience, and Justice: Study protocol have been approved by Institutional review board, Faculty of medicine, Chulalongkorn University

Approved by Institutional review board COA No 08-0/2023

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