The Official Journal of the Italian Society for the Study of Hemostasis and Thrombosis
SISET
Società Italiana per lo Studio dell'Emostasi e della Trombosi
Corso Nazionale SISET
Bergamo | 23-25 ottobre 2025

29TH NATIONAL CONFERENCE OF THE ITALIAN SOCIETY FOR THE STUDY OF HEMOSTASIS AND THROMBOSIS, 2025

ABSTRACT N. CO31

MALATTIE EMORRAGICHE CONGENITE E ACQUISITE

# IMMUNE SYSTEM PROFILING IN FVIII-TREATED AND EMICIZUMAB-TREATED PEDIATRIC HA PATIENTS.

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**Background:** Prophylactic treatments to prevent bleeding are considered the standard therapy in Hemophilia A (HA) and inhibitor formation is the main complication of FVIII infusion. Another option for HA with or without inhibitors is represented by Emicizumab, whose use has shown encouraging results in terms of efficacy and safety in adult patients. However, due to restricted reported experience, administration of Emicizumab in neonates and children is limited and still under investigation.

**Aim:** To study the circulating immune population and plasma cytokine profiles in pediatric HA patients in FVIII or Emicizumab prophylaxis.

**Methods:** After informed consent, blood samples from patients affected by HA, HB and healthy subjects were collected and analyzed by flow-cytometry for percentage and number of immune populations. Cytokine profiling was evaluated using a Multiplex approach. Monocyte-derived macrophages from blood samples were obtained in vitro, stimulated with FVIII and lysed for RNA extraction.

**Results:** FVIII-treated patients had more circulating CD11c+ cells than Emicizumab ones. However, when evaluating HLA-DR expression on CD11c+ cells, Emicizumab-treated patients showed a higher expression compared to FVIII-treated ones. Likewise, HLA-DR expression on CD14+ cells was higher in HA patients compared to healthy subjects. Cytokines associated with CD14+ cells activity, such as IL12p40, CCL22, IL18, CCL4 and TNFα, were higher in HA plasma samples. Gene expression analysis of HA patient-derived macrophages showed a stronger tendency in shifting to M1 phenotype following FVIII-stimulation in vitro, delineating a different gene-pattern between FVIII and Emicizumab treatment.

**Conclusions:** These results suggest a difference in the myeloid compartment of HA patients and, possibly, a different interaction with adaptive immune system between Emicizumab-treated and FVIII-treated patients. Our data show a higher recall or activation of HA monocytes-macrophages in vitro and in vivo. Eventually, this work helps to get additional information of pediatric HA patients increasing knowledge to maximize the therapeutic effect, reducing or avoiding adverse side effects.

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