EMICIZUMAB VERSUS IMMUNOSUPPRESSION FOR ACQUIRED HEMOPHILIA A (AHA) (#2612)

C. HART[1], R. KLAMROTH[2], U.J. SACHS[3], R. GREIL[4], P.N. KNÖBL[5], J. OLDENBURG[6], W. MIESBACH[7], C. PFREPPER[8], K. TRAUTMANN-GRILL[9], I. PEKRUL[10], K. HOLSTEIN[11], H. EICHLER[12], C. WEIGT[13], D. SCHIPP[13], S. WERWITZKE[14] and A. TIEDE[14]

1. University Hospital Regensburg, Germany. 2. Vivantes Clinic Friedrichshain, Berlin, Germany. 3. Justus Liebig University, Giessen, Germany. 4. University Hospital Salzburg, Austria. 5. Medical University of Vienna, Austria. 6. University Clinic Bonn, Germany. 7. Goethe University Frankfurt, Germany. 8. University Hospital Leipzig, Germany. 9. University Hospital Carl Gustav Carus, Dresden, Germany. 10. Hospital of Ludwig Maximilian University Munich, Germany. 11. University Medical Center Hamburg-Eppendorf, Germany. 12. Saarland University, Homburg, Germany. 13. GWT-TUD GmbH, Dresden, Germany. 14. Hannover Medical School, Germany.

German, Austrian and Suisse Association on Thrombosis and Haemostasis Research

INTRODUCTION

- AHA is a serious autoimmune bleeding disorder, caused by neutralizing antibodies against factor VIII (F VIII), predominately affecting people at advanced age
- Standard of care is immunosuppressive therapy (IST)
- Infection and mortality due to IST is a major risk in AHA, as shown in the GTH-AH 01/2010 study
- Emicizumab (EMI) can be used to effectively prevent bleeding in AHA (GTH-AHA-EMI trial)*

AIM

- Comparison of treatment outcomes (bleeding, infections, thromboembolic events, overall survival) between patients treated with IST in the GTH-AH 01/2010 study and patients treated with EMI in the recently published GTH-AHA-EMI study
- The current analysis was prospectively planned as an exploratory analysis of the GTH-AHA-EMI trial (NCT04188639; registered at www.clinicaltrials.gov)

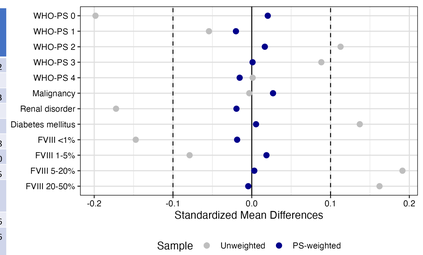
METHOD

- Individual patient data were retrieved from the
  - **GTH-AHA-EMI** study:
    n=47; treatment with EMI (dosage: 6 mg/kg/bw s.c. on day 1 and 3 mg/kg/bw s.c. on day 2, followed by 1,5 mg/kg/bw s.c. weekly until week 12)
  - **GTH-AH 01/2010 study**
    n=101; treatment with IST (prednisolone, stepwise escalation to prednisolone +/- cyclophosphamide +/- rituximab until remission was reached
- Propensity score (PS) matching was used to account for covariates (F VIII activity, diabetes mellitus, renal disease, malignancy, WHO-status at baseline) that influenced bleeding risk and overall survival in the GTH-AH 01/2010 study

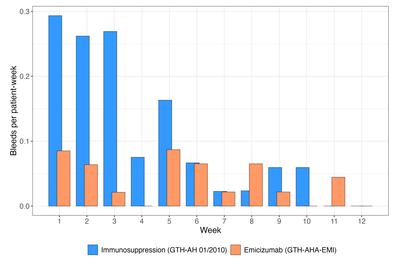
RESULTS

Variable	Emicizumab (GTH-AHA-EMI) N = 47	Immunosuppression (GTH-AH 01/2010) N = 101	SMD	P
Age, median (IQR) - years	76 (66-80)	74 (62-81)	0.071	0.682
Sex – no. (%)				
Female	23 (49)	43 (43)	0.128	0.483
Male	24 (51)	58 (57)		
Underlying conditions – no. (%)				
Autoimmunity	7 (15)	20 (20)	0.130	0.648
Malignancy	6 (13)	13 (13)	0.003	1.000
Postpartum period	1 (2)	5 (5)	0.153	0.665
Selected concomitant disorders – no. (%)				
Diabetes mellitus	16 (34)	28 (28)	0.137	0.446
Renal disorders (excl. urogenital)	13 (28)	36 (36)	0.172	0.356
Cardiac disorders	13 (28)	38 (38)	0.214	0.269
WHO performance status – no. (%)			0.230	0.825
0	4 (9)	15 (15)		
1	11 (23)	26 (26)		
2	13 (28)	23 (23)		
3	12 (26)	22 (22)		
4	7 (15)	15 (15)		
Factor VIII activity, median (IQR) – IU/dl	1.4 (0.3-5.6)	1.4 (0.0-3.4)	0.250	0.318
Factor VIII inhibitor, median (IQR) – BU/ml	12.2 (4.0-47.2)	19.0 (7.5-71.1)	0.036	0.089

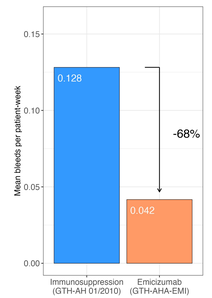
Baseline characteristics of the unmatched study populations.
➔ Baseline characteristics of the study populations were very similar before matching.
BU: Bethesda units; IQR: interquartile range; SMD: standardized mean difference; WHO: world health organization
In bold: Covariates that influenced bleeding risk, remission status and overall survival in der GTH-AH 01/2010 study



PS-Matching accounting for covariates that were previously established to influence bleeding risk and overall survival (Y-axis).
➔ Baseline characteristics further improved after PS matching.



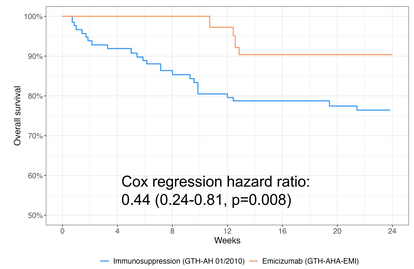
Bleeding risk in the unmatched patient population depicted as clinically relevant new bleeds (CRNB) per patient-week.
➔ IST treated patients had a high risk of bleeding in the first 3 weeks (0.25-0.3 CRNB) per patient-week
➔ EMI treated patients were largely protected from bleeding during the study period (<0.1 CRNB per patient-week)



Negative binominal modelling of bleeding rate after PS-matching.
➔ Bleeding rate of EMI treated patients was 68% lower compared to IST treated patients (incident ratio 0.325, 95% CI 0.182-0.581, p<0.001).

Infections	EMI (GTH-AHA-EMI) N = 47	IST (GTH-AH 01/2010) N = 101	Thromboembolic events	EMI (GTH-AHA-EMI) N = 47	IST (GTH-AH 01/2010) N = 101
All events			All events		
Patients, n (%)	10 (21)	29 (29)	Patients, n (%)	1 (2)	7 (7)
Events, n	11	36	Events, n	1	7
Fatal events			Fatal events		
Patients, n (%)	–	11 (11)	Patients, n (%)	–	4 (4)
Events, n	–	11	Events, n	–	4

Infection and thromboembolic events during week 1 to 12.
➔ Infections were less often fatal in EMI versus IST treated patients.
➔ Thromboembolic events were less frequent and less often fatal.



PS-matched overall survival until week 24. Kaplan-Meier curves were drawn using weighted individual patient data.
➔ Risk for a fatal event is 56% lower in EMI-treated patients compared to IST.

CONCLUSIONS

Our analysis showed:

- Better bleed protection and improved overall survival in patients on EMI prophylaxis compared to patients treated with IST
- These observations suggest a change of clinical practice
- EMI prophylaxis should be offered to patients with AHA to reduce the risk for bleeding
- EMI offers the chance to postpone IST until clinical stabilization and improvement of the general health status is reached

REFERENCES

Tiede A et al. Emicizumab prophylaxis in patients with acquired heamophilia A (GTH-AHA-EMI): an open-label, single arm, multicentre, phase 2 study. *Lancet Haematol, published online October 16, 2023.*

Holstein K et al. Bleeding and response to hemostatic therapy in acquired hemophilia A: results from the GTH-AH 01/2010 study. *Blood; 2020; 136; 279-287.*

Tiede A et al. Prognostic factors for remission of and survival in acquired hemophilia A (AHA): results from the GTH-AH 01/2010 study. *Blood; 2015; 125; 1091-1097.*

*Use of EMI in AHA is off-label except for Japan where it was recently approved as a preventive treatment in patients with AHA

ACKNOWLEDGEMENTS

The GTH-AHA-EMI and GTH-AH 10/2010 trials were conducted by the German, Austrian and Suisse Society on Thrombosis and Haemostasis Research (GTH e.V.). The authors acknowledge the contribution to all study sites.

CONTACT INFORMATION

Prof. Andreas Tiede, Hannover Medical School,
30625 Hannover, Germany
Email: tiede.andreas@mh-hannover.de

Dr. Christina Hart, University Hospital Regensburg,
93052 Regensburg, Germany
Email: christina.hart@ukr.de

Poster Session Online
American Society of Hematology
Helping hematologists conquer blood diseases worldwide
322. Disorders of Coagulation or Fibrinolysis: Clinical and Epidemiological: Poster II
Christina Hart
SUN-2612
ASH2023