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508.BONE MARROW FAILURE: ACQUIRED

Analysis of the Impact of Body Mass Index (BMI) on the Durability of Response in Patients with Aplastic Anemia Treated with Weight-Adjusted Horse Anti-Thymocyte Globulin (hATG)

Jeanette Walter[1,2], *Benjamin Rolles, MD*[1,2,3,4], *Yannic Schumacher*[1,2], *Frauke Theis, MD*[5], *Leo Hansmann, MD*[6,7], *Daniel Heudobler, MD*[7], *Markus Radsak, MD*[8], *Michael Heuser, MD*[9], *Julia-Annabell Georgi, MD*[10], *Jörg Chromik, MD*[11], *Beatrice Drexler, MD*[12], *Jörg Schubert, MD*[13], *Kim Kricheldorf*[1,2], *Susanne Isfort*[2,1], *Jens Panse, MD*[1,2], *Tim H. Brümmendorf*[2,1], *Fabian Beier, MD*[1,2]

[1] Department of Hematology, Oncology, Hemostaseology and Stem Cell Transplantation, Medical Faculty, RWTH Aachen University, Aachen, Germany
[2] Center for Integrated Oncology - Aachen Bonn Cologne Duesseldorf (CIO-ABCD), Aachen, Germany
[3] Division of Hematology, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
[4] Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA
[5] Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany
[6] Department of Hematology, Oncology, and Tumor Immunology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany
[7] Department of Internal Medicine III, Hematology and Oncology, University Hospital Regensburg, Regensburg, Germany
[8] Department of Medicine III, Johannes Gutenberg University Medical Center, Mainz, Germany
[9] Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[10] Department of Medicine I, University Hospital Carl Gustav Carus, Dresden, Germany
[11] University Hospital Frankfurt, Frankfurt, Germany
[12] Department of Hematology, University Hospital Basel, Basel, Switzerland
[13] Department of Internal Medicine II, Elblandklinikum Riesa, Riesa, Germany

Introduction: Immunosuppressive therapy (IST) with anti-thymocyte globulin (ATG), cyclosporine A (CsA) and Eltrombopag (Epag) has recently been established as standard of care in adult patients (pts.) with severe (sAA) or very severe (vsAA) aplastic anemia > 40-50 years or ineligible for transplant for other reasons. ATG works via immunosuppressive properties including T-cell depletion and induction of immune tolerance. Horse ATG (hATG) is applied for 4 days with 40 mg/kg/day based on the patient's *current* body weight. Thus, obese pts., defined by a body mass index (BMI) ≥ 30, receive higher absolute hATG dosages than non-obese pts. (BMI < 30). To date, it is unknown whether increased hATG dosages in obese pts. might have beneficial or adverse effects on AA treatment. To address the role of obesity in AA, we investigated (1) the prevalence of obesity in 334 pts. with (suspected) AA and (2) compared the overall survival (OS) and response of 89 obese and non-obese AA pts. to the treatment with hATG/CsA ±Epag.
Methods: Retrospective analysis of data from pts. enrolled in the German Registry for Aplastic Anemia and Bone Marrow Failure (AA-BMF). 334 pts. with (suspected) AA and available BMI data (49% (n=164) male/ 51% (n=170) female, 83% (n=278) BMI < 30, 17% (n=56) BMI ≥ 30) were identified of which 89 pts. (43 male/ 46 female, mean age 50 ± 17 years, 75 BMI < 30/ 14 BMI ≥ 30 at hATG administration) with confirmed diagnosis of AA (4 mAA/ 49 sAA/ 18 vsAA/ 14 AA not otherwise specified/ 4 AA-PNH Overlap) and treatment with hATG/CSA were analyzed in detail. 14 pts. received hATG/CSA/Epag (all BMI < 30). Follow-up data were compiled over 35 ± 38.5 months between 2000 and 2023, whereby follow-up data of 12 pts. were incomplete. Results are given as mean ± standard deviation.
Results: Analysis of the age distribution of the 343 pts. with (suspected) AA showed a mean age of 50 ±17 years with a biphasic peak at age approx. 25 and 65 years. The average BMI stratified by age (20-30y: 22.9, 31-40y: 24.5, 41-50y: 26.8, 51-60y: 26.4, 61-70y: 27.5, >70y: 27.8) corresponded to the BMI distribution of the German population surveyed by the German Federal Statistical Office. In accordance with the expected survival rates, the 89 AA pts. treated with hATG/CSA (including 14 pts. with Epag) revealed a 5-year overall survival (OS) of 93%/ 86%/ 67 % at < 40/ 40-60/ > 60 years. Regarding BMI, no significant difference was observed in 5-year OS between obese (BMI ≥ 30, 5y-OS 67%) and non-obese pts. (BMI < 30, 5y-OS 85%, p =

0.51). In pts. responding to IST, hematological response at six months after ATG was reached in 67 % (n=7/11) of the obese and 63 % (n=21/33, in 9 pts. exact timepoint not available) of the non-obese pts. (p = 0.85). The proportion of primary IST refractory pts. was numerically lower in obese (21 %, n=3/14) than in non-obese pts. (32 %, n=21/65, p=0.53). Among all 53 responders (2 pts. had incomplete follow-up to assess relapse), a significantly lower relapse rate of 9 % (n=1/11) in obese (median follow-up: 16 months, range 3 to 120 months) compared to 55 % (n=22/40) in non-obese pts. was observed (median follow-up: 19 months, range 1 to 87 months, p=0.008).

Conclusion: BMI distribution of AA pts. by age is comparable to that of the general population with a higher rate of obesity in older pts.. Pts. with a BMI $\geq$ 30 thus receiving higher ATG dosages do appear to have comparable OS and hematological response rates compared to pts. with BMI <30. However, pending validation in a larger patient cohort, we hypothesize, based on our analysis, that a higher cumulative total ATG dose may have a beneficial impact on relapse rates in pts. with BMI $\geq$ 30 compared to those with BMI < 30.

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