

REGISTRY STUDIES ON MYELOYDYSPLASTIC SYNDROME AND SECONDARY ACUTE MYELOID LEUKEMIA. European and Swedish perspectives.

Akademisk avhandling

Som för avläggande av medicinsk doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i M106 K Isaksson, Medicinargatan 16 den 4 Maj 2018, klockan 13:00-16:00

av **HEGE KRISTIN GRAVDAHL GARELIUS**

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Avhandlingen baseras på följande delarbeten

- I. **Garelius HK**, Johnston WT, Smith AG, Park S, de Swart L, Fenaux P, Symeonidis A, Sanz G, Čermák J, Stauder R, Malcovati L, Mittelman M, van de Loosdrecht AA, van Marrewijk CJ, Bowen D, Crouch S, de Witte TJ, Hellström-Lindberg E. Erythropoiesis-stimulating agents significantly delay the onset of a regular transfusion need in nontransfused patients with lower-risk myelodysplastic syndrome. *J Intern Med.* 2016 Dec 7. doi: 10.1111/joim.12579.
- II. Hulegårdh E, Nilsson C, Lazarevic V, **Garelius H**, Antunovic P, Rangert Derolf Å, Möllgård L, Uggla B, Wennström L, Wahlin A, Höglund M, Juliusson G, Stockelberg D, Lehmann S. Characterization and prognostic features of secondary acute myeloid leukemia in a population-based setting: a report from the Swedish Acute Leukemia Registry. *Am J Hematol.* 2015 Mar;90(3):208–14. doi: 10.1002/ajh.23908.
- III. Nilsson C, Hulegårdh E, **Garelius HK**, Möllgård L, Brune M, Wahlin A, Lenhoff S, Frödin U, Remberger M, Stockelberg D and Lehmann S. The role of allogeneic hematopoietic stem cell transplantation in patients with secondary acute myeloid leukemia: A nationwide population-based study from the Swedish AML Registry. Manuscript.
- IV. **Garelius HK**, Nilsson C, Hulegårdh E, Genell A, Antunovic P, Ejerblad E, Höglund M, Jerkfält M, Juliusson G, Lorentz F, Nilsson L, Rangert Derolf Å, Uggla B, Lehmann S, Stockelberg D, Hellström-Lindberg E and Möllgård L. *Acute myeloid leukemia secondary to myelodysplastic syndrome. Results from merging of the Swedish AML and MDS Registries 2009-14.* Manuscript.

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Registry studies on myelodysplastic syndrome and secondary acute myeloid leukemia

European and Swedish perspectives

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Abstract

The aims were (I) to describe a European lower risk MDS population and the use of erythropoietin stimulation agents (ESA), (II) to describe the AML population in Sweden 1997-2006 with emphasis on secondary AML (s-AML) and therapy-related AML (t-AML), (III) to investigate the use and effect of allogeneic hematopoietic stem cell transplantation (HSCT) in the AML population in Sweden 1997-2013, and (IV) to merge patients from the Swedish AML Registry 2009-14 with patients from the Swedish MDS Registry 2009-14 in order to describe the patients with s-AML after MDS from time of MDS diagnosis and AML diagnosis. **Patients, methods and results:** (I) ESA treatment were given to 45.6% patients with lower risk MDS, median duration 27.5 months. A propensity model, comparing ESA-treated and untreated was used. Median time to first post-ESA treatment transfusion was 6.1 months in patients transfused before ESA treatment compared to 23.3 months in non-transfused patients ($p < 0.0001$), showing that ESAs can significantly delay the onset of a regular transfusion need in patients with lower-risk MDS. (II) Of 3,363 AML patients with induction therapy, 73.6% were de novo AML, 18.7% had antecedent hematological disease (AHD-AML), and 7.7% had t-AML. S-AML-patients were older compared to de novo AML and had higher cytogenetic risk scores. Multivariate analysis showed that AHD-AML and t-AML were independent risk factors for inferior survival in the younger age groups. (III) Of 3337 intensively treated patients, 21% underwent HSCT at any stage of the disease. Five-year survival without and with allogeneic HSCT were 0% vs 50% for MPN-AML, 3% vs 39% for MDS-AML, 8% vs. 48% for t-AML and 24% vs. 57% for *de novo* AML-patients. Presence of any chronic graft versus host disease (cGvHD) compared to no cGvHD and a GvHD grade 1 or lower was significantly associated to better survival in a multivariable analysis. Allogeneic HSC is the only option for cure in S-AML. (IV) We found 257 patients with sufficient information from both AML and MDS registries for further examination. 72.2% had high risk cytogenetics and 66.8%, had performance status 0-1 at AML diagnosis. Median time from MDS diagnosis to AML diagnosis was 10.8 months. Median survival time for S-AML was 4.93 months. Allogeneic HSCT improves survival significantly in the younger age groups. **Keywords:** Myelodysplastic syndromes, secondary acute myeloid leukemia, erythropoietin stimulating agents