**ESA- Still the 1st line for LR-MDS**

**Abstract – Yes**

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Erythroid stimulating agents (ESA) have been the linchpin of therapy in early myelodysplastic syndromes (MDS), and for good reason. Decades of experience with ESA have shown their safety, tolerability and effectiveness in alleviating myelodysplastic syndrome induced anemia. It has been repeatedly shown that ESA do not increase the likelihood of AML transformation and that side effects are well manageable. A recent study (the COMMANDS trial [1]) implies that luspatercept is superior to ESA in improving anemia in MDS patients with or without ring sideroblasts. However, this study is based on assumptions that do not reflect the clinical reality: The vast majority of patients with lower risk myelodysplastic syndromes will be diagnosed before they become transfusion dependent. Hence, the treating physician will most often be confronted with a patient suffering from anemia, but not necessarily from transfusion dependent anemia. In a seminal study published by Fenaux et al. It was shown that ESA work best in patients with non-transfusion dependent anemia and an endogenous erythropoietin level of <200 U/L [2]. However, it was precisely this patient population that did not feature in the COMMANDS trial.

The inclusion criteria of that trial stipulated transfusion dependence of 2-6 U per 8 weeks prior to baseline. Still, ESA were more effective in achieving the primary endpoint of red blood cell transfusion independence for at least 12 weeks with a concurrent mean hemoglobin increase of at least 1.5 g/dL during weeks 1–24 in the non-ring sideroblastic subgroup (46% for ESA vs 41% for luspatercept, respectively). Given that it is anticipated that patients with EPO levels of >200 U/L do not respond well to treatment (only 12% primary response rate in the COMMANDS trial) and that transfusion dependent patients also have a low response rate to ESA, the target population for ESA treatment should consist of non-transfusion dependent patients with an EPO level of <200 U/L. In this population, response rates close to 70% can be achieved which reflects the efficacy of ESA if the patient selection is sensible. Therefore, ESA remain my favorite drug in the first line treatment of MDS patients that are not transfusion dependent and display an EPO level of <200 U/L.

**Literature**
