

MYELODYSPLASTIC SYNDROMES 2023: WHAT'S NEW

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MDS 2023: Challenges in Diagnosis and Treatment - Abstract

Moshe **Mittelman**, Tel-Aviv Sourasky Medical Center, Tel-Aviv University, Israel

The myelodysplastic syndromes (MDS) are clonal bone marrow (BM) stem cell disease(s), characterized by abnormal hematopoiesis, with anemia (95%) and/or other cytopenias. The basic pathogenesis is based on genetics and inflammation of aging (inflammaging). The median age of onset is 74 yr and the incidence increases with age. Patients are classified as having a lower (LR-MDS) or higher risk disease (HR-MDS), and leukemic transformation occurs in 20%-60%.

The challenges in 2023 are: a) Diagnosis: new tools – less invasive and more accurate; earlier diagnosis; identify individuals at risks. b) Better understanding of the pathogenesis; genetics and inflammaging. c) Harmonize the various classifications. d) Treatment of LR-MDS: improve the quality of life; more effective agents for anemia, especially after failure of erythropoietin and luspatercept; effective and safe agents for thrombocytopenia. e) Treatment of HR-MDS: Hypomethylating agents (HMA) are (still) the standard 1st line treatment, but how can we improve the limit of 50% response rate lasting 2 years ?

We will focus in this symposium on some of these issues. Genetic and AI tools may help in identifying pre-MDS states, and individuals at risk, as well as establish early diagnosis, non-invasively and perhaps more accurately. Future may allow diagnostic procedures in which marrow examination can be avoided, at least in some of the suspected patients.

RBC transfusions and erythropoietin (EPO) remain the 1st line treatment for anemia. EPO is safe and might delay the need for RBC transfusions. A recent EUMDS study suggests a prolonged survival with EPO. Lenalidomide remains effective for MDS with del(5q) (50% response), but also somewhat effective (27%) in non-del(5q) patients. Luspatercept appears as an effective second-line (maybe 1st ?) agent. We will discuss it here. Several experimental agents are investigated, including oral azacytidine, imetelstat, a pyruvate-kinase activator and roxadustat. For thrombocytopenia two agents, romiplostim and eltrombopag, were shown to be effective. However, due to safety concerns their development has been stopped.

Patients with HR-MDS are offered HMA as the standard 1st line treatment. Younger patients may respond to antileukemic treatment with or without transplant. Ways to improve the HMA effect include treating the HMA-related complications; modified HMA formulation; combinations of HMA with other agents (venetoclax appears to be the frontrunner), novel agents and targeted molecules.