The myelodysplastic syndromes (MDS) are a heterogeneous group of bone marrow disorders characterized by cytopenias and risk of progression to acute myeloid leukemia (AML). Survival and AML risk are predicted by the International Prognostic Scoring System (IPSS), which takes into account the number of cytopenias, marrow blast count, and cytogenetic abnormalities. Most MDS patients eventually develop symptomatic anemia with a regular requirement for transfusion of red blood cells (RBC). As RBC contains iron in hemoglobin and the body has no mechanism to excrete the excess, iron overload develops, which may impact on organ function and survival.

Mechanisms of iron toxicity include deposition into tissues and organs. The liver, heart and endocrine organs are particularly susceptible and clinical results include hepatic dysfunction, fibrosis and cirrhosis, congestive heart failure and arrhythmias, and glucose intolerance and diabetes. In addition, non-transferrin-bound iron (NTBI) may form, resulting in oxidative stress, which can damage lipids, proteins, and nucleic acids, and potentially lead to apoptosis or mutagenesis and malignant progression, both features of MDS.

Guidelines recommend iron chelation therapy in patients with lower-risk MDS and a reasonable life expectancy, where retrospective studies show a survival benefit. Chelation is also considered for patients with higher risk MDS eligible for disease modifying therapies such as hypomethylating agents or stem cell transplantation (SCT). In SCT, decreased survival and increased treatment-related mortality with iron overload is seen, a sharp increase in NTBI occurs, and lower infection risk, delayed leukemic transformation and improved outcome with chelation are suggested. In this presentation, pre-clinical and clinical data regarding iron overload and iron chelation therapy in MDS will be reviewed.