MDS Foundation
The Myelodysplastic Syndromes Foundation, Inc.

2025 MDSF Friday Satellite Symposium

Patient Discussion Session

High-Risk MDS

The patients will be presented by:
Howard Oster MD, PhD
Tel-Aviv Sourasky Medical Center

Patient RY:

A 70-year-old woman presented in mid-2024 with weakness, fatigue and weight loss (10 Kg within a year) as well as mild anemia (Hb 11.4 gr/L).

Her past medical history (PMH) was remarkable for stable ischemic heart disease, hypertension (ramipril), hyperlipidemia (atorvastatin) and heavy smoking (60 packyears).

On physical examination she was skinny-cachectic (poor general condition), pale with evidence of mild obstructive lung diseases. Hb 11.4 gr/dL, MCV 104 Fl, WBC $3.5x10^9$/L, ANC $1.5x10^9$/L, PLT $445x10^9$/L. Routine chemistry was normal.

Her bone marrow (BM) was hypercellular with trilinear dysplasia and 10% blasts. The karyotype was del(5q). NGS failed to detect myeloid mutations.

Course: She was classified as HR-MDS and azacitidine (vidaza^R) was initiated. We considered adding venetoclax but due to her poor general condition and difficulties in getting the insurance approval, it was decided to postpone it. The tolerance was quite poor with decreased counts, requiring dose modification and treatment delays, infections requiring hospital admission and supportive care (RBC transfusions).

After 6 cycles, her symptoms subsided, she put on weight, and the BM had 3% blasts. Yet, she remained anemic (8.5-9 g/dL). rounds she was classified as CR with 3% blasts, she had put on weight. Hematopoietic stem cell transplant (HSCT) was considered but the decision was postponed.

While we were considering the next step, symptoms returned (weight loss, fatigue, erythromelalgia) and Hb dropped (7.3 gr/dL). This time BM had 7% blasts.

Three more modified (dose and intervals) vidaza cycles were administered, with difficulties in tolerance and supportive treatment.

After cycle 8, the situation is similar: She is mildly symptomatic but active, requiring RBC transfusion about every 3-4 weeks. Hb is maintained on the 6.6-8 g/dL level, other counts unchanged, and 6-7% BM blasts. Karyotype again shows the del(5q) anomaly.

What now?

Patient SD:

An 81-year-old man presented in 2017 with mildly symptomatic macrocytic anemia (Hb 11.3 gr/dL). His PMH included coronary artery disease (S/P CABG), diabetes, hypertension, hyperlipidemia, and remote Whipple surgery (2005), for pancreatic tumor (later found to be benign). The workup, including BM examination and cytogenetics (normal) established a diagnosis of very low / low-risk MDS, and follow up was recommended, with no intervention.

In early 2023, he complained of weakness and fatigue and the counts declined: Hb 9.9, WBC $3x10^9$/L, ANC 1.8 $x10^9$/L, PLT $95x10^9$/L. MCV rose from 80 to 104Fl. BM picture was similar.

In early 2024, the symptoms became significant, and the counts continued to drop. This time BM examination demonstrated hypercellularity, erythroid and myeloid dysplasia, and 11% blasts! NGS detected a TET2 mutation (VAF 35%).

Course: Vidaza was initiated, with difficult tolerance (dose modification, supportive treatment). After 6 cycles, the patient reported on stabilization and improvement of symptoms. He continued to require supportive treatment. BM showed 6% blasts. Aza treatment was continued. After 10 cycles, the patient is "relatively stable" but mildly symptomatic, active and says that he "feels good". His last counts are: Hb 7.7 g/dL, MCV 96 Fl, WBC 3.0 $x10^9$/L, ANC 0.8 $x10^9$/L, PLT 16 $x10^9$/L, requiring frequent RBC transfusion units (1/week), G-CSF and occasional PLT transfusions. The BM morphology has unchanged (7% blasts), Repeated NGS was remarkable for *TET2* (VAF 44%) and *EZH2* (50%) mutations.

What now?

Low-Risk MDS

The patients will be presented by:
Albert Kolomansky MD, PhD,
Assuta Ashdod Medical Center

Patient AU:

A 65-year-old male presented in July 2021 with mildly symptomatic (weakness and fatigue) anemia. His medical history was remarkable for stable ischemic heart disease, peptic disease, osteoarthritis and sleep apnea syndrome requiring CPAP. Physical examination was unremarkable, and the relevant lab results were macrocytic (MCV 98 Fl) anemia (Hb 10.5 g/dL), serum iron 175 micg/dL, transferrin 143 mg/dL and ferritin 800 ng/ml. The remaining CBC and chemistry were normal. Bone marrow (BM) examination showed slight hypercellularity, dyserythropoiesis, 1% blasts and ringed sideroblasts. The karyotype was 20q- and NGS detected several myeloid mutations, including RUNX1, TET-2, SF3B1 (all>40% VAF), and also DNMT3A. MDS, RARS type, IPSS-R low score was diagnosed and follow up was recommended.

In 11/2022 the anemia became symptomatic, he underwent a serious COVID episode and also symptomatic angina pectoris (underwent PCI). Hb declined (6-7g/dL), requiring RBC transfusions. Other labs and BM picture remained the same. ESAs were initiated (Epoetin-α, 30,000-60,000 IU/w; Aranesp 150-300 µg/wk), but with no response, continuing to require 2-3 RBC units/week, to maintain Hb level at 6-7.5 g/dL.

The recommendation at that time (mid 2023) was to switch to luspatercept. However, the drug was not approved at that time, so hematopoietic stem cell transplant (HSCT) was considered, and a donor search was launched.

In July 2023, the patient managed to be reimbursed by private insurance for luspatercept. The response was dramatic: In November 2023, he was asymptomatic, Hb 12.5, and obviously, with a complete abolition of the need for RBC transfusions.

Over the last couple of years, the patient has been relatively stable, with Hb level of 12-12.5 g/dL, with no need for transfusions. Following some articular symptoms and a nasal lesion, a biopsy was performed, and seronegative vasculitis was diagnosed. He continues to be followed by rheumatologists, who administered a course of rituximab, with a good response of the vasculitis.

Over the last 6 months, there is a tendency towards minimal symptoms associated with a mild decrease of Hb (11.5 g/dL). BM shows a similar picture, except for 100% cellularity.

What now?

Patient DE:

A 78-year-old male was referred for evaluation of anemia, found in routine checkup. He is asymptomatic and denies any bleeding. His past medical history, as well as the physical examination, are unremarkable. Hb is 8.6 gr/dL, MCV 106 Fl, while other CBC parameters and routine chemistry are normal.

The BM was mildly hypercellular, with bi-lineage erythroid and megakaryocyte dysplasia, blasts 0-1%, no ringed sideroblasts, normal karyotype and NGS detected a DNMT3A mutation.

A diagnosis of low-risk MDS (low blasts) was established, with IPSS-R score 2.3.

What's the recommended approach?