ASH 2025: MDS Highlights

Abstract Summaries: Clinical

Israel MDS Group – 26-02-2026

Moshe Mittelman

Higher-Risk MDS

Attempt to change the disease course

VERONA: Subgroups benefit from V + V

- **Background:** HMA – 1st line for HR-MDS, but:
  - <50% ORR; < 2yr; no cure
- **VERONA:** Phase 3 RCT; Vidaza vs Vidaza + Venetoclax (V+V)
  - **Primary EP:** Overall survival (OS)
  - **Results** (6/2025): No OS advantage – 22 vs 21m
- **Abs 235 (GGM):** A post hoc subgroup analysis
  - Some subgroups: benefit from the combination
  - **Younger** patients
  - Patients with **higher blast > 5%**
  - 19% proceeded to transplant
    - Suggest: V + V – bridge to SCT ?
- My comment: Venetoclax dose – high!

Garcia-Manero G, ASH 2025; # 235; D. **Lavie** – co-author

HR-MDS with TP53: Bexmarilimab

- **Background:**
  - HMA – The 1st line for HR-MDS
  - TP53 – poor risk; APR-246- still ?
- **Bexmarilimab** (Faron):
- A novel macrophage checkpoint inhibitor targeting Clever-1, a scavenger receptor expressed on malignant blasts and monocytes in MDS
- **BEXMAB Study**: phase 1/2 in TP53 mutated HR-MDS
  - Treatment: Aza and Bexmarilimab
  - Treatment-naïve patients
  - **70% CR !**
  - OS in the RR - 14.5m (vs historical 5-6m)
  - 50% of the frontline TP53 proceeded to transplant

Zeidan A ASH 2025; # 236

Lower-Risk MDS: Anemia

Focus on Quality of Life and Anemia

LR-MDS: HMA - Shorter Durations ?

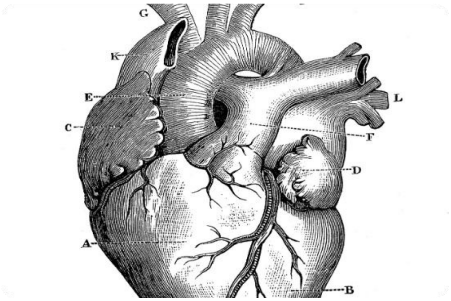
- **Background:**
  - HMA used in LR-MDS (dose ? Duration ?)
  - Standard dose (used in HR-MDS) - toxic
- **Trial:** Can lower doses and/or shorter periods effective in LR ?
- 247 LR-MDS: Dec (3d) vs Aza (3d) vs Aza (5d)
- **Aza-5d – best**
  - ORR (transfusion independent) – 70% (vs 50% vs 17%)
  - ORR (transfusion dependent) – 48%
  - Better EFS, OS
- My comments:
  - We do it
  - Possible, but still questionable

MD Anderson

Bouligny I , ASH 2025 # 487

Luspatercept – What's new ?

- **Background**:
  - **MEDALIST**: Effective after ESAs *(Fenaux NEJM 2020)*
  - **COMMANDS**: Better as 1st line *(Dela Porta LH 2024)*
- **Santini** (Abs 792): **Post hoc** analysis of COMMANDS
  - Early treatment - more beneficial
- **Zeidan** (Abs 789): MAXILUS trial - **High-Dose** Luspa
  - Starting luspa (1.75 mg/kg) rather than titrating up
  - Well-tolerated; Faster transfusion independence; Safe
- **Hassan** (Abs 233):
  - Preclinical study in TET2-mutated mouse models
  - Luspa **improved cardiac function**
  - Reduced inflammatory signaling and cardiac stress
  - Suggests benefit beyond treating chronic anemia



IMERGE: Cytopenia is not a bad sign !

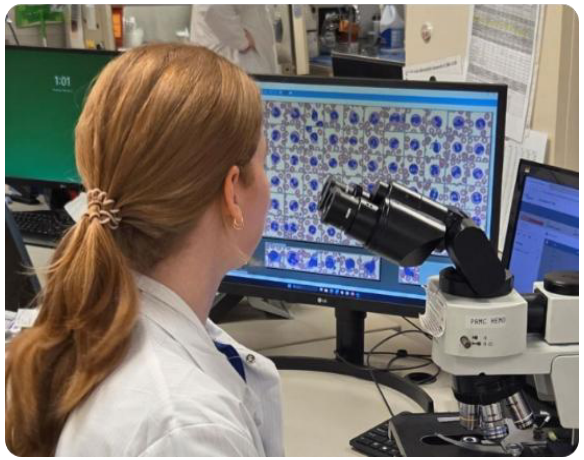
iMERGE

- **Background:**
  - Imetelstat – A telomerase inhibitor
  - **IMERGE**: A phase 3 RCT: Im vs placebo in EPO-resistant TD LR-MDS
  - Approved (as 2nd/3rd line)
  - Problem: **Cytopenias** (Toxicity ??)
- **Abs 490 (Zeidan)**: A post hoc analysis of iMERGE
  - Grade 3-4 neutropenia or thrombocytopenia – transient and manageable
  - Associated with better erythroid response
  - **Conclusion**: Not off-target adverse effects - **effect on stem cells**
  - Cytopenia serves as a response biomarker

Zeidan A et al. ASH 2025; # 490

Elritercept (Ker-050) for anemia

- **Background:**
  - TGF-β superfamily ligand
  - Previous successful phase 1, 2 trials in LR-MDS
- **Abs 787** (**Chee**, Melbourne):
  - International group; Phase 2
  - ORR 50%
  - Duration (median) – 40 wk
  - Several patients: "multilineage" improvements
    - increases in ANC and PLT also
- My comment: “Second generation luspa”



Chee et al. ASH 2025; # 787

Lower-Risk MDS: Low PLT

Hetrombopag – another thrombomimetic ?

- **Background:**
  - Low PLT – a problem
  - Romiplostim & eltrombopag – effective (40% response) but
  - Not approved ! (Disease progression ?)
- **Abs 492 (Mei, China):**
  - Hetrombopag:
    - Novel oral thrombopoietin receptor agonist (TPO-RA)
  - Prospective: Hetrombopag (15 mg/day) in LR-MDS
  - **Platelet response: 42% %**
  - Long-term safety data still collected
- **My comment**: Still too early to say

Mei et al. ASH 2025; # 492

CMML (MDS/MPN)

Approach: Similar to HR-MDS

CMML: Decitabine ? ASTX ?

- **Abs 791 (Itzykson):**
  - **DACOTA**: Decitabine vs HU - Similar outcomes
  - Post hoc analysis: Severe **neutropenia** - better survival (both arms)
- **Abs 488 (Wiseman):**
  - **ASTX 727**: Oral combo – LD decitabine + cedazuridine
    - Cedazuridine: A cytidine deaminase inhibitor
  - **AMMO trial**: ASTX 727 vs. HU or supportive in CMML
  - **ASTX727 superior**:
    - ORR 53% vs 30%; CR 8.2 vs 4.2%
- **Abs 790 (G-Manero):** Phase 2 ASTX727 – LD vs standard dose
  - Similar effect: Median OS – 24m vs 26m
  - Conclusion: **Low dose ASTX effective**, less toxic

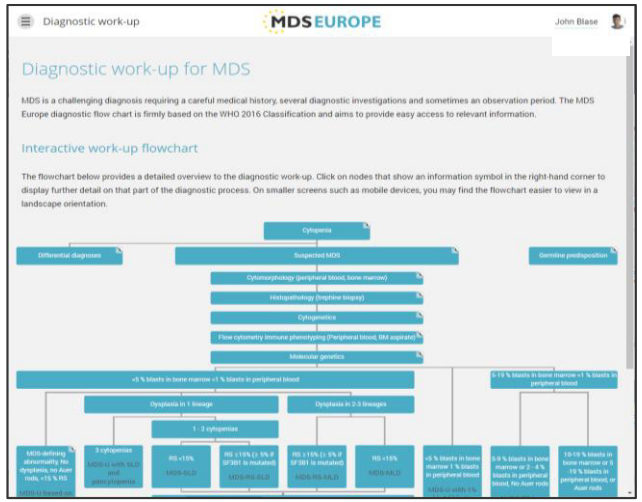
MDS EUROPE

mds-europe.eu

Endorsed by EHA EUROPEAN HEMATOLOGY ASSOCIATION

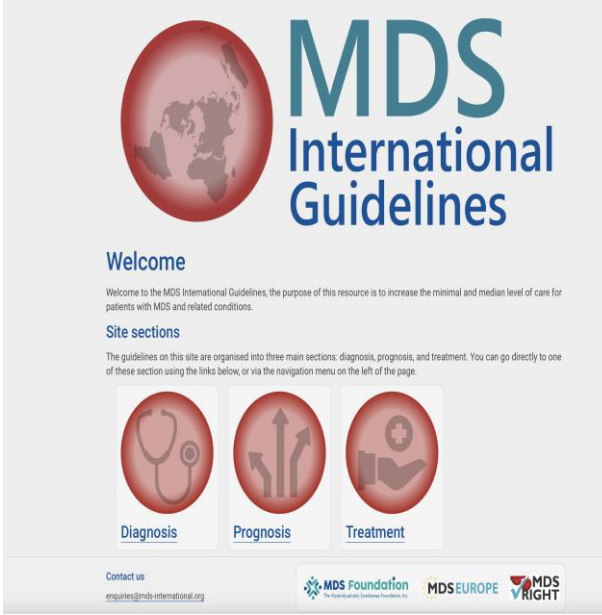
Inspired by the MDS-RIGHT project

diagnosis **prognosis** **treatment**



EHA Endorsement of the European **Guidelines** for MDS, **MDS**-RIGHT. Blum S, Malcovati L. **Hemasphere**. 2021 Aug 30;5(9):e631.

New MDS Guidelines



- **Background:**
  - Time to update
  - Based on EUMDS guidelines
  - International group: E. Hellstrom & L. Malcovati
- **R. Buckstein (FSS):** The new guidelines
- Updated – integrating molecular data (IPSS-M)
  - Can be applied into daily practice
- Serves for diagnosis, treatment, prognosis
- Easy to use – online and printed (soon)
- Dynamic – will be updated

https://mds-international-guidelines.org/

- Still a work in progress but hope to finalize by EHA
- Please bookmark and share with your colleagues/student/staff
- Please provide feedback for refinements and improvements
- This is living/breathing online tool that will evolve over time
- Contact: eva.hellstrom-lindberg@ki.se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