The Future of Care for Myelodysplastic Syndromes (MDS): An AI-Driven Multidisciplinary Virtual Clinical Panel

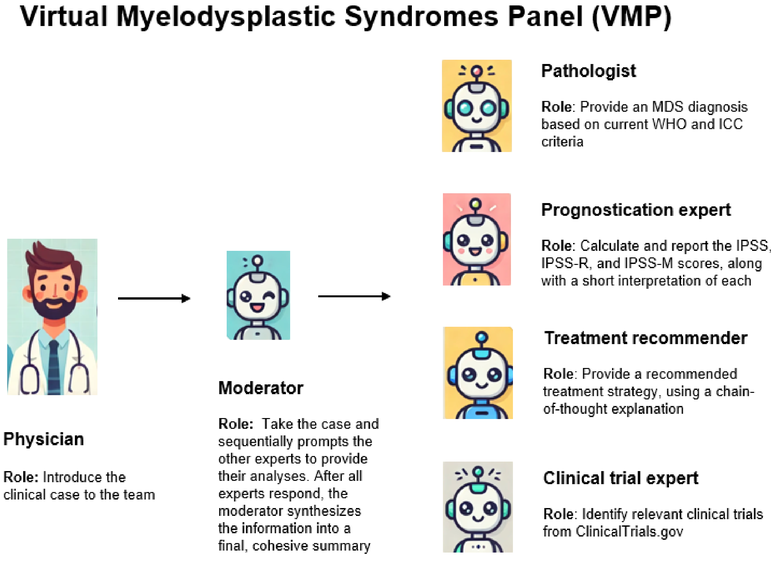
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Introduction

- MDS presents a diagnostic and therapeutic challenge requiring multidisciplinary expertise.
- To improve diagnostic accuracy, prognostication, and provide comprehensive personalized treatment recommendations, additional tools are needed
- We developed a Virtual MDS Panel (VMP), composed of five specialized artificial intelligence (AI) agents — Moderator, Pathologist, Prognostication Expert, Treatment Recommender, and Clinical Trial Expert.

Figure



Methods

- The VMP was trained to simulate domain-specific expertise using the latest WHO and ICC diagnostic criteria, IPSS/IPSS-R/IPSS-M scoring systems, and evidence-based treatment guidelines
- Each virtual expert operates within a structured framework: the Pathologist provides MDS subtyping, the Prognostication Expert interprets risk scores, the Treatment Recommender applies reasoning for therapy selection and provides publications and evidence to support treatment selection, and the Clinical Trial Expert identifies targeted trials from clinicaltrials.gov.
- The system's performance was benchmarked against ChatGPT and other generative AI models in a blinded evaluation of 30 de-identified MDS cases by three board-certified MDS specialists.

Example Response

FINAL SUMMARY:

Key Clinical Features:
- 60-year-old male
- Pancytopenia (Hb 7 g/dL, platelets 80 ×10⁹/L, ANC 1.3 ×10⁹/L)
- 20% ring sideroblasts, 2% blasts
- Normal cytogenetics
- SF3B1 mutation (VAF 29%) and mono-allelic TP53 mutation (VAF 15%)

Diagnosis:
- WHO 2022: MDS with low blasts and SF3B1 mutation (MDS-SF3B1)
- ICC 2022: MDS with mutated SF3B1

Prognosis:
- IPSS-R: Low Risk (score 3.0)
  * Median survival: 5.3 years
  * AML evolution risk: 10.8 years
- IPSS-M: Moderate Low Risk (score -0.32653)

Treatment Recommendations:
1. First-line: Luspatercept-aamt (Category 1, preferred)
   - Strong indication given SF3B1 mutation and RS ≥15%
   - Expected response rate ~65% in RS-positive disease

Clinical Trial Approach:
- Priority focus on:
  * First-line trials for SF3B1-mutated MDS
  * Novel erythroid maturation agents
  * Splicing modulator studies
  * Early intervention trials for TP53 mutation
- Consider trials with luspatercept combinations

Case Example

- A 60-year-old male presents with anemia (Hb 7 g/dL), thrombocytopenia (platelets 80 ×10⁹/L), and mild neutropenia (ANC 1.3 ×10⁹/L). Bone marrow biopsy reveals dysplasia in neutrophils and red cells, 20% ring sideroblasts, and 2% blasts. Cytogenetics are normal, but molecular testing shows SF3B1 mutation (29% VAF) and mono-allelic TP53 mutation (15% VAF).

Discussion

- The VMP demonstrated superior diagnostic precision, achieving 97% agreement with expert adjudication versus 82% for ChatGPT.
- Prognostication scores matched expert calculations in 96% of cases, and treatment plans aligned with evidence-based guidelines in 92% of cases, outperforming ChatGPT's 75%.
- Clinical trial matching was accurate in 89% of cases, significantly higher than ChatGPT's 60%.
- Specialists highlighted the VMP's domain-specific reasoning and structured approach as key advantages.

Conclusion

- We developed an advanced, MDS-focused AI system that increased accuracy and alignment with expert practice, outperforming current state-of-the-art general AI models.
- By emulating a virtual tumor board, the system offers structured, evidence-based guidance that can aid hematologists in optimizing their precision care.

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