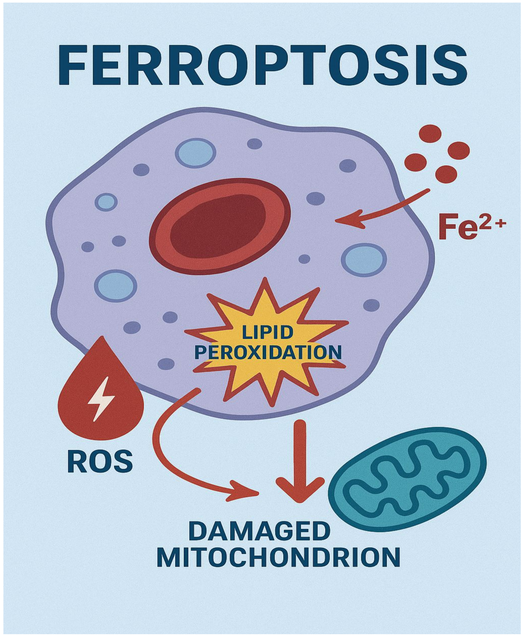
Systematic Review Of Ferroptosis - Inducing Therapies in TP53-Mutant Acute Myeloid Lukemia and Myelodysplastic Syndrome

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Introduction

TP53 mutations in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are associated with poor responses to standard therapies and limited survival. Ferroptosis, an iron-dependent, non-apoptotic form of regulated cell death driven by lipid peroxidation, has emerged as a promising therapeutic target in TP53- mutant hematologic malignancies.



Aim

To systematically review and synthesize preclinical and clinical evidence evaluating ferroptosis-inducing therapies in TP53-mutant AML and MDS.

Methods

A systematic literature search was conducted across PubMed, Scopus, Web of Science, and ClinicalTrials.gov from 2010 to 2025. Search terms included “ferroptosis,” “TP53 mutation,” “AML,” “MDS,” “APR-246,” “erastin,” and “GPX4 inhibitors.” I

Inclusion criteria included original preclinical or clinical studies involving ferroptosis-targeting agents in TP53-mutant AML or MDS. Exclusion criteria included review articles, non-hematologic malignancies, and studies not focused on ferroptosis.

Results

Phase II Trials (n=100, TP53-mutant AML/MDS):

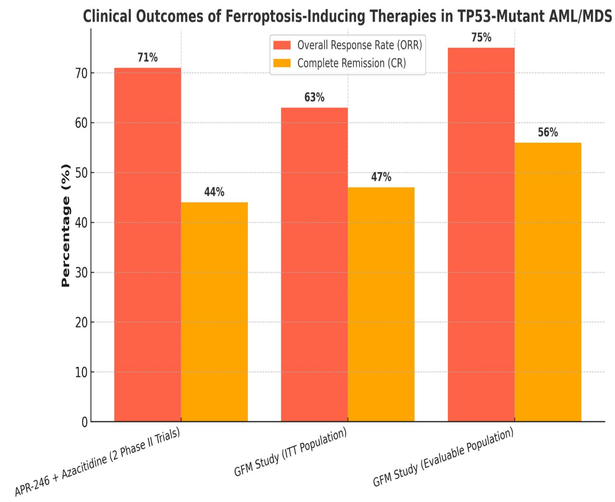
- ORR **71%**, CR **44%**
- Median response: **10.3 mo**
- Median OS: **11.6 mo**

GFM Study:

- ORR **63% (ITT)**, **75% (evaluable)**
- CR **47% (ITT)**, **56% (evaluable)**
- **78%** cytogenetic remission
- **100%** TP53 mutation clearance (<2% VAF)

Preclinical Models:

- APR-246 triggers **ferroptosis**, increases chemosensitivity, and may overcome resistance.



Conclusion

Ferroptosis-inducing agents, particularly APR-246, show encouraging clinical efficacy and strong mechanistic rationale in TP53-mutant AML and MDS. These therapies represent a novel and potentially transformative strategy for a historically treatment-refractory patient population.