

(PB3109) HOTSPOT GENE MUTATIONS AND TREATMENT RESPONSE IN MYELODYSPLASTIC SYNDROMES (MDS): PREDICTIVE BIOMARKERS AND TARGETED STRATEGIES

Topic: 10. Myelodysplastic syndromes - Clinical

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Background

MDS response to HMAs/chemotherapy is unpredictable; genomic biomarkers are missing

Aims

Identify hotspot mutations that predict response to HMAs, chemotherapy or targeted agents and translate them into precision choices.

Methods

Systematic review of 2020-2025 literature; 1,600+ MDS cases; response defined by 2018 IWG criteria; multivariate Cox for survival.

Results

HMAs:ASXL1mut → HMA resistance (ORR 32 %), but VEN+HMA rescue (ORR 87 %);TET2mut/ASXL1wt → best HMA response (ORR 62 %); dual TET2-ASXL1 loses benefit (19 %);DNMT3A-R882 decitabine hypersensitivity via hemi-methylated enhancer trapping; median PFS 20.3 vs 50 mo WT;Chemotherapy:RUNX1, BCOR, EZH2 mutations independently cut response to cytarabine/anthracycline (ORR ≤19 %);Targeted therapyTP53 multi-hit: eprenetapopt + AZA ORR 73 %, median OS not reached at 12 mo; IDH1/2 mut: ivosidenib 83 % ORR, mOS 35.7 mo; enasidenib 53 % ORR, mOS 16.9 mo.

Summary/Conclusion

ASXL1, TET2, DNMT3A, RUNX1, BCOR, EZH2, TP53, IDH1/2 mutations are actionable predictors; genotyping should guide front-line therapy and trial selection.

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