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Update on Predictors of Progression in Smoldering Multiple Myeloma: A Systematic Review

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INTRODUCTION

Smoldering multiple myeloma (SMM) is an asymptomatic state of proliferation of plasma cells.

Currently, predictors of progression in patients with SMM to multiple myeloma (MM) remain uncertain. Identifying these factors is crucial for developing improved risk models.

AIM

The aim of this study is to identify predictors associated with progression of SMM to overt MM.

METHOD

- A Systematic review was conducted following PRISMA guidelines.
- A literature search was performed utilizing the following databases: PubMed, Embase, and clinicaltrial.gov.
- MeSH terms were “smoldering multiple myeloma”, "smoldering myeloma", and "asymptomatic multiple myeloma".
- The inclusion criteria were defined as studies published in English from 2017 that reported risk factors for the progression of SMM.

RESULTS

- A total of 1,303 studies were identified with the MeSH terms.
- Eleven clinical trials met inclusion criteria.
- Several predictors were identified. Refer to Table 1.

Table 1- Predictors of progression to Multiple Myeloma

Author, Year	Predictors of progression	Findings
Visram et al., 2022	Urine monoclonal proteinuria and serum free light chain ratio	≥200 mg/24 h and ≥100
Jamet et al., 2020	PET/CT	Presence of focal bone lesion without underlying osteolysis
Lakshman et al., 2018	Serum M protein	>2g/dL
Gonsalves et al., 2017	Circulating tumor cells and clonal plasma cells	Flow cytometry
Visram et al., 2021	Serum B-cell maturation levels	Mean increased by 2.7-fold
Mussetti et al., 2019	PD-L1, LAG3, and HLA-DR	Expression on plasma cells
Kumar et al., 2024	Three-dimensional telomere profiling	Genomic instability, and exhausted cytotoxic plasma cells
Termini et al., 2022	Circulating tumor cells	Patients with >0.015 of CTCs at baseline
Gonzalez et al., 2017	Bence Jones proteinuria	⩾ 500 mg
Isola et al., 2021	Gene expression analysis of bone marrow cells	Upregulation of TNF and inhibitory immune checkpoints

CONCLUSIONS

- The use of PET/CT scans, urine monoclonal protein excretion, free light chain ratio, BCMA levels, serum M protein and circulation clonal plasma cells are predictors associated with progression of SMM to MM.
- Three-dimensional telomere profiling and the identification of markers such as PD-L1, LAG3, and HLA-DR are also associated and are currently under study.
- Further research is warranted to support their inclusion in current risk models.

REFERENCES

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