NOVEL THERAPIES IN INTERMEDIATE AND HIGH-RISK SMOLDERING MULTIPLE MYELOMA: A SCOPING REVIEW

Authors M. HAMEED[1], Z. SHAH[2] and T. NISHIHORI[3]
1. Florida State University Sarasota, FL, USA
2. Roswell Park Comprehensive Cancer Center, NY, USA
3. Moffitt Cancer Center, FL, USA

Introduction

Smoldering multiple myeloma (SMM) is an asymptomatic precursor to active multiple myeloma (MM), with **intermediate/high-risk patients having up to a 50% chance of progression within two years.**

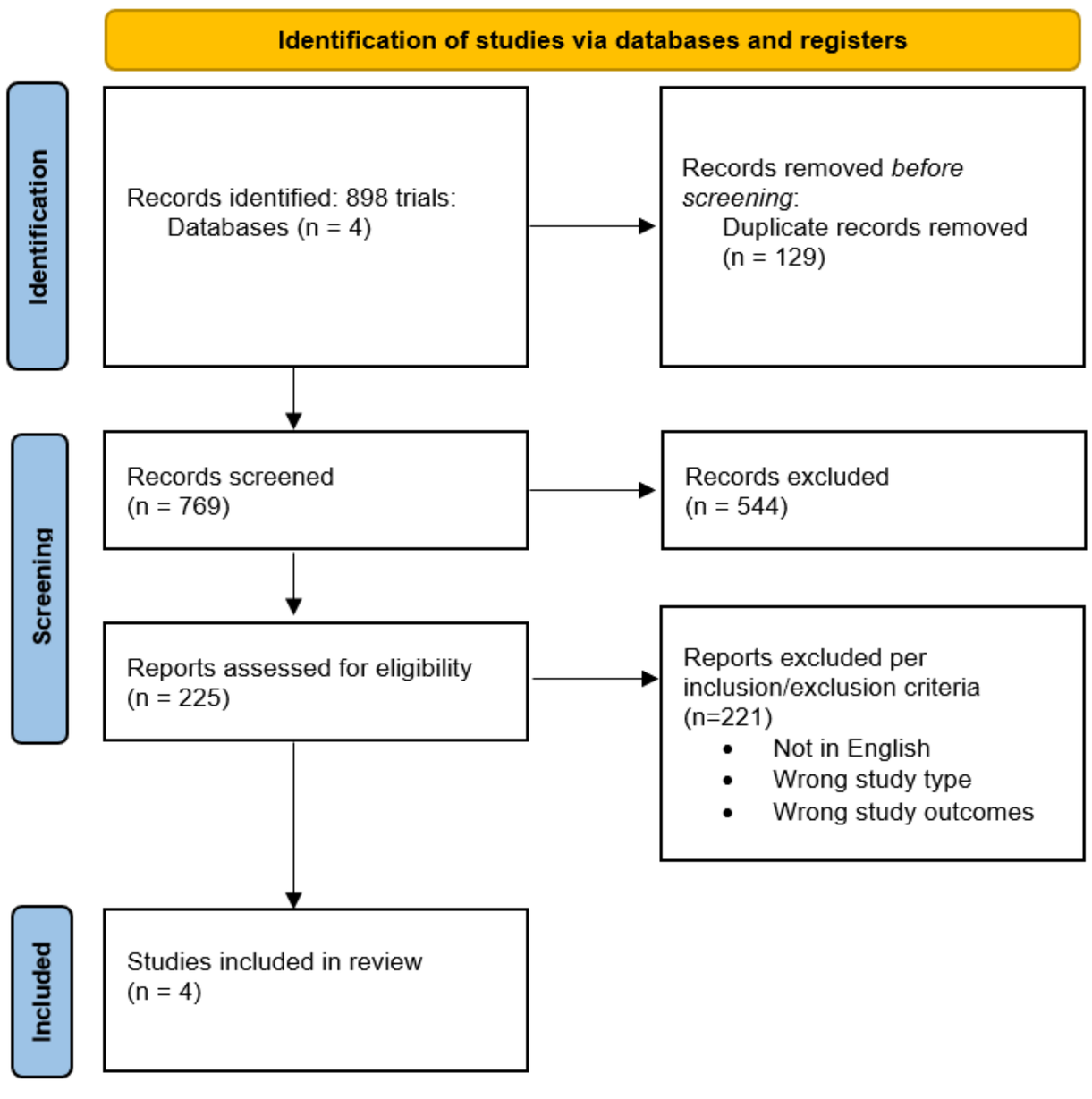
The current standard of care remains **observation until clinical progression**, and no FDA-approved therapies exist for intermediate/high-risk SMM despite the growing interest in early intervention.

Aim

This review aimed to evaluate **efficacy and safety outcomes** of **novel single-arm treatment strategies for intermediate/high-risk SMM.**

Methods

A **systematic review** was conducted following PRISMA guidelines. A total of **898 studies** were screened from Medline, Embase, Cochrane, and ClinicalTrials.gov.



Four single-arm clinical trials met inclusion criteria, reporting outcomes for novel treatments in intermediate/high-risk SMM.

Conclusion

Evidence from single-arm trials suggests that **early treatment of intermediate/high-risk SMM with novel agents may significantly improve ORR, PFS, and OS, supporting** the potential role of **early intervention** in delaying progression to symptomatic MM.

Results

Across the four studies, 357 patients were treated with daratumumab **(d; n=123),** lenalidomide-dexamethasone **(Rd; n=125),** carfilzomib-lenalidomide-dexamethasone **(KRd; n=54),** and ixazomib-lenalidomide-dexamethasone **(IxaRD; n=55),** with a median follow-up of 67.6 months.

Table 1. Single-Arm Study Outcomes

Outcome	Single-Arm Study			
	d*	Rd	KRd	IxaRD
OS	Not reached in any dosage arm	10.5 years	100%	Not reached
ORR	58.5%, 53.7%, 37.5%	Not reported	96 months	93%
PFS	Not reached, 84.4 and 74.1 months	5%	77%	Not reached
Median TTP	Not reported	114.1 months	Not reported	23 months
Grade 3 AE	0%	Not reported	38.9%	63%
Grade 4 AE	0%	Not reported	0%	9%
Median follow up	85.2 months	150.1 months	31.9 months	50 months

*With long-intense, intermediate and short-intense dosage arms

Key: d: Daratumumab; Rd: Lenalidomide-Dexamethasone; KRd: Carfilzomib-Lenalidomide-Dexamethasone; IxaRD: Ixazomib-Lenalidomide-Dexamethasone; OS: Overall survival; ORR: Overall Response Rate; PFS: Progression Free Survival; TTP: Time To Progression; AE: Adverse Event

KRd demonstrated the most favorable outcomes, including 100% overall survival (OS) and overall response rate (ORR) at 96 months, 77% progression-free survival (PFS), **and no reported deaths.**

IxaRD also showed high efficacy (93% ORR), though median OS and biochemical PFS were not reached; **however, 100% of patients experienced adverse events**, including 63% with grade 3 and 9% with grade 4 toxicities.

Contact

References

1. Landgren, O et al. (2025).
2. Mateos, M. V. et al. (2022)
3. Kazandjian, D. et al. (2021)
4. Nadeem, O. et al. (2025)