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Treatment-Limiting On-Target Toxicity With Talquetamab/GPRC5D-Directed Therapy in Relapsed/Refractory Multiple Myeloma: A Systematic Review and Meta-Analysis

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BACKGROUND & METHODS

Background

GPRC5D-directed therapy has expanded RRMM treatment options, but oral, dermatologic, nail, and nutritional toxicities may affect tolerability, dose intensity, and persistence.

Aim

Quantify treatment-relevant, largely nonhematologic toxicity with talquetamab/GPRC5D-directed therapy in RRMM.

Search strategy

PubMed/Medline, Cochrane Library, ClinicalTrials.gov, and major hematology/oncology meetings, including ASH, ASCO, EHA/HemaSphere, and SOHO, from 2022 to 2026.

Analysis

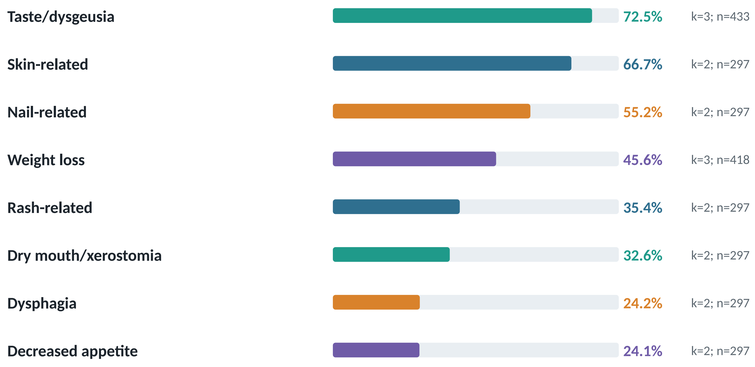
Random-effects logit-transformed pooled proportions were estimated.

POOLED TOXICITY BURDEN

72.5%	66.7%	55.2%
Taste/dysgeusia	**Skin-related AEs**	**Nail-related AEs**
95% CI 68.1-76.5	95% CI 51.9-78.8	95% CI 49.5-60.8

Treatment-relevant on-target/off-tumor toxicities were common across pooled talquetamab cohorts.

Pooled incidence of selected adverse events



Taste, skin, nail, and weight-related toxicities represented the dominant toxicity pattern.

TOXICITY DOMAINS

Talquetamab/GPRC5D-directed therapy produced a broad pattern of nonhematologic toxicity relevant to daily function and treatment persistence.

Most prominent domains

Less frequent but clinically relevant symptoms included xerostomia, dysphagia, and decreased appetite.

Adverse event-related discontinuation appeared comparatively uncommon.

STUDY SET & SYNTHESIS

Included cohorts

Four unique talquetamab cohorts/arms met inclusion criteria for quantitative synthesis.

Primary analysis

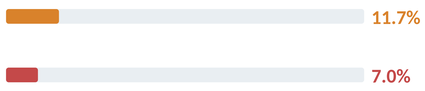
Two pivotal MonumenTAL-1 prior T-cell redirection-naïve dose cohorts plus one German multicenter real-world cohort.

A prior T-cell redirection cohort was analyzed separately as a sensitivity cohort.

TREATMENT-LIMITING OUTCOMES

11.7%	7.0%
Dose reduction	**AE discontinuation**
95% CI 6.4-20.5; k=2; n=297	95% CI 3.8-12.6; k=2; n=297

Treatment-limiting outcomes were less frequent than the most common on-target toxicities.



Sensitivity analyses including the prior T-cell redirection cohort produced similar estimates.

CONCLUSIONS

Talquetamab/GPRC5D-directed therapy in RRMM is associated with a high burden of taste, skin, nail, and weight-related on-target/off-tumor toxicities.

Adverse event-related discontinuation appears comparatively uncommon.

Findings support proactive counseling, early nutritional and supportive care, dose-modification strategies, and standardized reporting of treatment-limiting toxicity in future GPRC5D-directed therapy studies.

Abbreviations: AE, adverse event; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; CI, confidence interval; EHA, European Hematology Association; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma; RRMM, relapsed/refractory multiple myeloma; SOHO, Society of Hematologic Oncology.