Selinexor in RRMM: Addressing Unmet Needs with a Unique MoA

Evolving Landscape and Unmet Needs

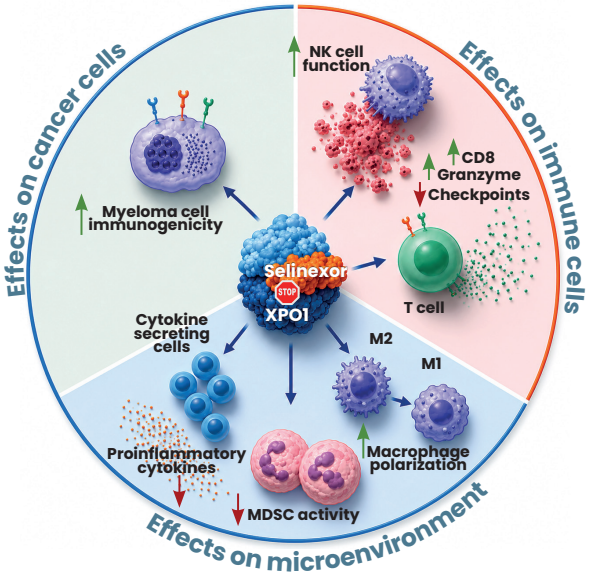
Despite novel therapeutics in RRMM, unmet needs continue to exist

- **Refractory Pressures:** Increasingly common 2L/3L Len and anti-CD38 refractory patients
- **Strategic Sequencing:** The need for distinct MoAs to overcome resistance and preserve future T-cell-directed therapies

Unique MoA

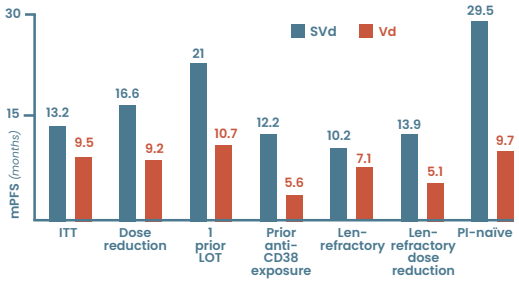
- **First-in-Class:** Selinexor is a selective, oral XPO1 inhibitor with a unique MoA and a direct effect on tumor cells
- **Antigen-Independent:** Selinexor's activity is independent of BCMA or T-cell fitness

Selinexor's XPO1 inhibition MoA

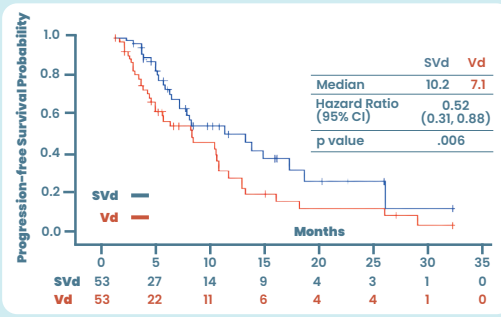


Selinexor's Efficacy in Difficult-to-Treat Populations

SVd in Boston Trial, mPFS across subgroups

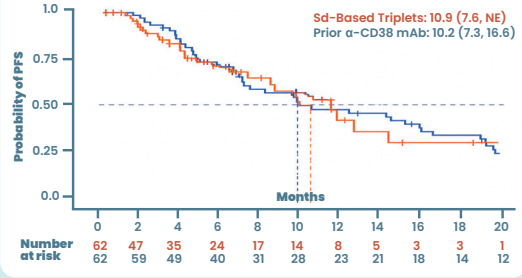


PFS in lenalidomide-refractory population



In the BOSTON trial, SVd had longer mPFS vs Vd across all difficult-to-treat subgroups, including *Len-refractory, 1 Prior LoT, and Dose Reduction* populations

Sd-Based Triplets vs. Prior α-CD38 mAb



Efficacy of selinexor triplets in anti-CD38 refractory population (STOMP/BOSTON) was comparable to that of prior anti-CD38 containing regimen (10.9 vs 10.2 mos mPFS)

Selinexor's Safety Profile

Selinexor AEs are predictable, reversible, and non-cumulative; non-hematological AEs are limited to 2-3 cycles and effectively managed with double anti-emetic prophylaxis and dose reductions

Optimising Sequencing with T-Cell Based Therapies

BCMA-directed therapies cause **T-cell exhaustion** and could **deplete** cell surface **BCMA**

UPREGULATION OF BCMA:
Selinexor increased BCMA cell surface density and gene expression, while maintaining cell viability

T-CELL FITNESS:
Selinexor reduced markers of T-cell exhaustion and promoted T-cell fitness

potentially enhancing efficacy of subsequent BCMA-directed therapies

KEY CLINICAL TAKEAWAYS

Selinexor addresses the unmet needs of difficult-to-treat RRMM patients by providing a unique therapeutic option in early relapse settings

Selinexor's non-BCMA dependant MoA reserves BCMA-targeted therapies for later lines of treatment, while its immunomodulatory effects potentially improve their efficacy

Selinexor has a predictable safety profile and manageable AEs

Initiate **selinexor** at 80 to 100 mg to balance efficacy and tolerability

References

Dimopoulos et al. Ann Oncol. 2021;32:309-22; Kastritis et al. Blood. 2022;139:2904-17; Costa et al. Leukemia. 2025;39:543-54; Mateos et al. Hemasphere. 2022;6:24-25; Kapoor et al. Blood. 2025;146:2281; Grosicki et al. Lancet. 2020;396:1563-73; Schiller et al. Clin Lymphoma Myeloma Leuk. 2023;23:e286; Firestone et al. Blood. 2024;144:402-7; Tasbihi et al. Cells. 2025;14:430. Verbruggen et al. Blood. 2025;146:6102

Abbreviations

2L/3L: Second-/third-line of treatment; BCMA: B-cell maturation antigen; Len: Lenalidomide; LoT: Line of treatment; MM: Multiple myeloma; MoA: Mechanism of action; mo/mos: Month(s); mPFS: Median progression-free survival; MDSC: Myeloid-derived suppressor cells; NK: Natural killer; RRMM: Relapsed/refractory multiple myeloma; SVd: Selinexor, bortezomib, and dexamethasone; XPO1: Exportin 1

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