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The Real-World Influence of Regimen Selection Across Successive Lines of Therapy in Multiple Myeloma

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BACKGROUND

The therapeutic landscape of Multiple Myeloma has evolved substantially with novel therapeutics. Although clinical trial outcomes have improved, there remains a need to evaluate the real-world efficacy of these regimens.[1,2] **Understanding how treatment sequencing, response duration, and depth align is essential to bridge the gap between clinical trials and real-world outcomes.[3-5]**

PURPOSE

To describe the real-world treatment and response characteristics across successive lines of therapy.

METHODOLOGY

In this retrospective study, treatment regimens, duration, and clinical response data were extracted from patient records from the HealthTree Registry. Descriptive statistics were employed to identify the most frequent regimens plus steroids, treatment classes, median Time to Next Treatment (TTNT), and best responses for each line.

Table 1. Frequency, Median Age at Diagnosis, and median Time to Next Treatment by Line of Therapy.

Line of Therapy	n	Median Age at Diagnosis (Years)	Median TTNT (Days)
1	1349	61	888
2	631	61	517
3	328	60	N/A

TTNT: Time to Next Treatment; N/A: Not available.

Table 2. Regimens TTNT and Transplant Exposure Within Each Line of Therapy.

Line of Therapy	Regimen	n	Median TTNT (Days)	IQR TTNT	Transplant Exposure
1	R-VCd	19	1575	875.5 - 2293.0	Yes
1	VRd + Z	21	1338	397.0 - 1666.0	No
1	VRd + M	13	1274	610.0 - 1834.0	Yes
1	KRd	70	1242.5	775.5 - 1929.8	Yes
1	VRd	465	1197	425.0 - 1906.0	Yes
1	Dara-Vd	11	1166	437.0 - 1626.0	No
1	Vd	16	828.5	525.8 - 1461.0	No
1	Rd	18	745	415.5 - 1642.8	No
2	KRd + M	10	1353.5	692.5 - 2072.0	Yes
2	R	13	996	463.0 - 1376.0	No
2	IRd	11	504	388.5 - 1048.5	No
2	KRd	16	430.5	93.0 - 1420.2	No
2	DPd	40	428.5	178.2 - 970.8	No
2	DRd	22	298.5	122.2 - 905.2	No
2	DKd	12	216	181.5 - 685.5	No
2	DVd	11	161	84.5 - 699.0	No

TTNT: Time to Next Treatment; C: cyclophosphamide; K: carfilzomib; D: daratumumab; d: dexamethasone; I: ixazomib; M: melphalan; P: pomalidomide; R: lenalidomide; V: bortezomib; Z: zoledronic acid.

Table 3. Top 3 Regimens Characteristics Within Each Line of Therapy.

Line of Therapy	Regimen	n	Regimen Class	Treatment Intensity	Induction Class	Maintenance Class	Transplant Exposure	Median TTNT (Days)	IQR TTNT	Most Frequent Top Response
1	VRd	465	PI+IMiD	Doublet	PI + IMiD	IMiD-based	Yes	1197	425 - 1906	CR
1	KRd	70	PI+IMiD	Doublet	PI + IMiD	IMiD-based	Yes	1242.5	775.5 - 1929.75	sCR
1	R-VCd	19	PI+IMiD+Alk	Triplet	PI + IMiD	PI-based	Yes	1575	875.5 - 2293	sCR
2	DPd	40	CD38+IMiD	Doublet	NC	None/NC	No	428.5	178.25 - 970.75	CR
2	DRd	22	CD38+IMiD	Doublet	NC	None/NC	No	298.5	122.25 - 905.25	PD
2	KRd	16	PI+IMiD	Doublet	NC	None/NC	No	430.5	93 - 1420.25	SD

TTNT: Time to Next Treatment; V: bortezomib; R: lenalidomide; d: dexamethasone; K: carfilzomib; C: cyclophosphamide; D: daratumumab; P: pomalidomide; Doublet: two drug classes; Triplet: 3 classes; IMiD: immunomodulatory drug; PI: proteasome inhibitor; Alk: alkylator; CD38: CD38 monoclonal antibody; NC: not captured; sCR: stringent complete response; CR: complete response; SD: stable disease; PD: progressive disease.

CONCLUSION

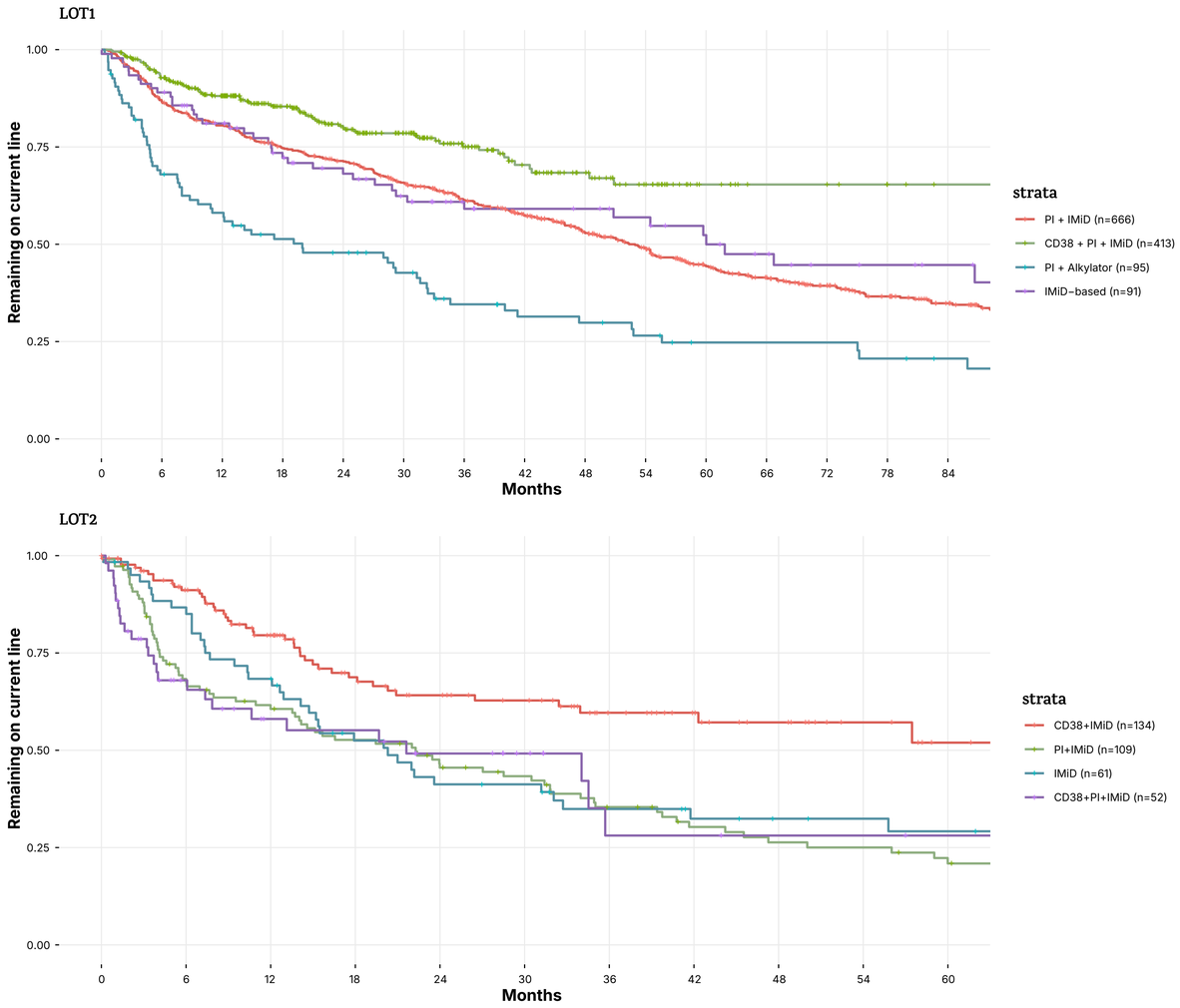
These findings highlight the decline in treated patients with each subsequent relapse, demonstrating patient outcomes in the real world and providing a foundation for understanding treatment selection, sequencing, and intensity adjustments in clinical practice, while underscoring the need for multivariate predictive models to guide personalized treatment selection and improve long-term outcomes.

For more information on clinical research collaboration, please contact research@healthtree.org

RESULTS

Time to Next Treatment by Major Treatment Backbone Across Lines of Therapy

LOT1 grouped by induction class; LOT2–3 grouped by overall regimen class. Groups restricted to n >= 20 and events >= 5.



In the HealthTree Registry, a total of 1,349 patients had records for a first line of therapy (L1), 631 for a second line (L2), and 328 for a third (L3). Across the cohort, the median TTNT was 888 days (IQR 345 - 1639) in L1 and 517 days (IQR 183.5 - 1176) in L2. The most frequent regimen for the first line of therapy (L1) was bortezomib, lenalidomide, and dexamethasone (VRd; n=465), with a median TTNT of 1197 days (IQR 425.0 - 1906.0) and complete response (CR) as the most frequent best recorded response for patients in that line.

The most common regimen for the second line of therapy (L2) was daratumumab, pomalidomide, and dexamethasone (n=40), with a median TTNT of 428.5 days (IQR 178.2 - 970.8) and CR as the most frequent best recorded response. L1 was predominantly driven by Proteasome Inhibitors (PI) + Immunomodulatory drugs (IMiD) (n=666) and Anti-CD38 monoclonal antibodies (Anti-CD38) + PI + IMiD (n=431), while L2 by Anti-CD38 + IMiD (n=134) and PI + IMiD (n=109) combinations.

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