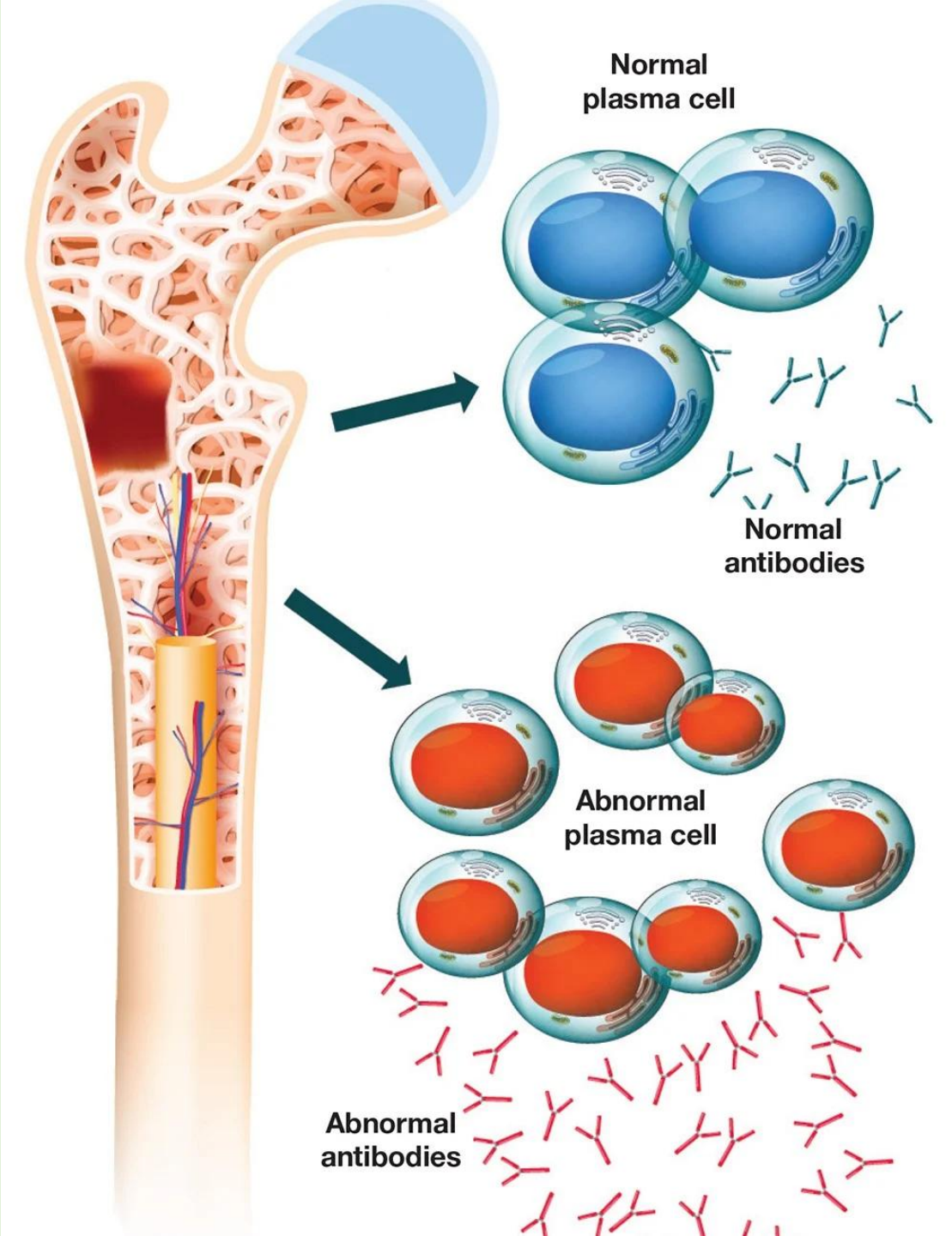
Competitive Landscape on Multiple Myeloma



Executive Summary

- Multiple Myeloma is managed as a **Chronic - Relapsing Disease**, where **Early Depth of Response**, **Transplant Utilization** and **Sequential Drug - Class Switching** drive long-term outcomes
- Treatment pathways are primarily determined by **Transplant Eligibility, Patient Fitness and Resistance Pattern**

Treatment Pathways in Multiple Myeloma

1. Treatment in **Transplant Eligible Patients (<70 yrs.)** Autologous Stem Cell Transplant (ASCT)
2. Treatment in **Non-Transplant Eligible Patients (65-75 yrs.)** (ASCT)
3. Relapsed / Refractory Myeloma

Core drugs
BTZ = Bortezomib (proteasome inhibitor)
CFZ = Carfilzomib (proteasome inhibitor)
IXZ = Ixazomib (oral PI)
LD = Lenalidomide + Dexamethasone
POM = Pomalidomide
DEX = Dexamethasone
MEL = Melphalan

CP = Cyclophosphamide
PRD = Prednisone
THAL = Thalidomide

Antibodies
DARA = Daratumumab (anti-CD38)
ELO = Elotuzumab
ISA = Isatuximab

First-Line Therapy (<70 years, Transplant-Eligible)

Step 1: Induction Therapy (Before transplant)

Goal: Reduce tumor burden as much as possible before transplant

Standard induction regimens shown:

BTZ-DEX-IMiD

= Bortezomib + Dexamethasone + Lenalidomide/Thalidomide

CURRENT GOLD STANDARD

BTZ-CP-DEX Used when IMiDs not suitable

BTZ-THAL-DEX-DARA Quadruplet therapy

Deeper responses but higher cost/toxicity

Orange boxes = experimental / not yet approved

CFZ-LD-DEX → under trials, high responses

BTZ-LD-DEX-DARA → Phase II data

Key insight: Trend is moving from **triplets → quadruplets**

Step 2: High-Dose Melphalan + ASCT

High-dose **melphalan** kills myeloma cells

Patient's own stem cells reinfused (**ASCT**)

This step gives **longest first remission**

Step 3: Consolidation Therapy

Short re-treatment after transplant

Especially important in **high-risk disease**

Tandem ASCT = back-to-back transplants

Step 4: Maintenance Therapy

Goal: delay relapse

Options: **LD** → most common

BTZ → high-risk cytogenetics

IXZ → oral option

Myeloma is now treated like a **chronic disease**

First-Line Therapy Patients NOT Eligible for ASCT (65-75 years)

Regimens shown:

BTZ-CP-PRD

BTZ-LD-DEX

BTZ-MEL-PRD

LD-DEX-DARA

BTZ-MEL-PRD-DARA

These patients:

- **Older**
- **Have comorbidities**
- **Cannot tolerate transplant**

Clinical principle

- Lower intensity
- Balance **efficacy vs tolerability**
- Often **continuous until progression**

Relapse & Refractory Disease

First Branch: Frail vs Non-Frail at Relapse

Frail patients

Doublets only

- **DEX-LD**
- **DEX-BTZ**
- **DEX-CFZ**

Non-Frail patients

Prefer **triplet regimens**

Choose based on prior drug exposure

- 4 × LD-based triplets
- 3 × BTZ-based triplets
- 2 × CFZ-based triplets
- 2 × POM-based triplets
- **mAb - based regimens**

Second & Subsequent Relapses

If refractory to LD + BTZ

Use:

POM-DEX-DARA

POM-DEX-ELO

POM-DEX-ISA

If refractory to:

BTZ / CFZ / IXZ

IMiDs

DARA

→ **SEL-DEX** (Selinexor)

Market Sizing

Population Group	% of Population	Estimated Number
Total US population	100 %	348 Million
People living with cancer	5.4 %	18.8 Million
People living with Multiple Myeloma	0.058 % (of total Population)	0.20 Million
Diagnosed & Treated Patients (Symptomatic)	87.5 % (of total MM)	0.17 Million

Therapy		Percentage	Total Patient on Therapy
Transplant-Eligible Patients	Induction Therapy (Quadruplets)	43 %	**76,000**
	Stem Cell Transplant (ASCT)	37.6 %	**66,000**
Transplant-Ineligible Patients	Standard Triplet Therapy (Triplets)	40 %	**70,000**
	Gentle Therapy (Doublets)	12 %	**21,000**
Relapsed or Advanced Therapy	Immunotherapies	10 %	**17,000**

Therapy Type	Typical Cost Range (US* per treated patient)	India Equivalent Context
CAR-T cell therapy	~$400k–$700k+ (one course, multiyear value)	~₹30 L–₹75 L ($37k–$85k)
Bispecific antibodies	~$300k–$550k per year	Generally unavailable locally (specialty import costs vary)
Monoclonal Abs	$150k+ per year typical (combo dependent)	~₹20 L–₹50 L+ per year

A) Anti-CD38 monoclonal antibodies (backbone immunotherapy)

Target	Generic	Brand	Company	Route	Where used
CD38	Daratumumab	Darzalex / Darzalex Faspro	Janssen (J&J)	IV / SC	Frontline + Relapse combinations
CD38	Isatuximab	Sarclisa	Sanofi	IV	Relapsed / Refractory

SLAMF7 Antibody

Target	Generic	Brand	Company	Route	Where used
SLAMF7	Elotuzumab	Empliciti	BMS + AbbVie	IV	Relapsed / Refractory

CAR-T Cell Therapies

Target	Generic	Brand	Company	Route	Where used
BCMA	Idecabtagene vicleucel	Abecma	BMS	IV (one-time)	R/R MM (≥4 prior lines)
BCMA	Ciltacabtagene autoleucel	Carvykti	Janssen (J&J)	IV (one-time)	R/R MM (≥4 prior lines)

Bispecific Antibodies

Target	Generic	Brand	Company	Route	Where used
BCMA × CD3	Teclistamab	Tecvayli	Janssen (J&J)	SC	R/R MM (≥4 prior lines)
BCMA × CD3	Elranatamab	Elrexfio	Pfizer	SC	R/R MM (≥4 prior lines)
BCMA × CD3	Linvoseltamab	Lynozyfic	Regeneron	IV	R/R MM (≥4 prior lines)
GPRC5D × CD3	Talquetamab	Talvey	Janssen (J&J)	SC	R/R MM (≥4 prior lines)

Antibody–Drug Conjugate (ADC)

Target	Generic	Brand	Company	Route	Where used
BCMA (ADC)	Belantamab mafodotin	Blenrep	GSK	IV	Relapsed / Refractory (combo use)