

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Multiple Myeloma

A mini review for clinicians

For postgraduate residents (medical, radiation and haematology oncology, haematology, nephrology, orthopaedics, ENT, pathology, nuclear medicine, internal medicine), practising clinicians and medical students

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Updated 17 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Multiple Myeloma

Haematological cancers, part 6 · Multiple myeloma, MGUS, smoldering myeloma and solitary plasmacytoma · Diagnosis and risk · Quadruplet induction, transplant and maintenance · BCMA-directed therapy at relapse · Bone, kidney and infection care · Key points for clinicians · Last updated 17 October 2026

01 At a glance

- **Myeloma is a cancer of plasma cells in the marrow**, about 1–2% of all cancers and one in six haematological cancers. Almost every case is preceded by MGUS, a silent clone found in over 3% of people above 50 ([Landgren 2009](#)^[1]).
- **Four clinical pictures, one biology**: MGUS (watch), smoldering myeloma (watch, or treat if high risk), active myeloma (treat now) and solitary plasmacytoma (radiotherapy). The line between them is drawn by M protein size, marrow plasma cells, imaging and organ damage.
- **Active myeloma = clonal plasma cells plus a myeloma-defining event**: CRAB (calcium, renal impairment, anaemia, bone lesions) or a SLiM biomarker ($\geq 60\%$ marrow plasma cells, light-chain ratio ≥ 100 , more than one focal MRI lesion) ([IMWG 2014](#)^[2]).
- **Screen with three blood tests, not one**: serum protein electrophoresis with immunofixation and serum free light chains. A normal SPEP or a normal urine dipstick does not exclude light-chain myeloma. Image with low-dose whole-body CT, PET-CT or MRI, not X-rays or bone scans.
- **Risk is biological**: del(17p)/TP53, a high-risk translocation with chromosome 1 changes, or a high beta-2 microglobulin with normal kidneys mark the 20% who do worst ([IMS/IMWG 2025](#)^[3]).
- **First-line treatment is a four-drug combination for most** (an anti-CD38 antibody with bortezomib, lenalidomide and dexamethasone), autologous transplant for the fit, then lenalidomide-based maintenance. Where drugs are scarce, a bortezomib triplet (VTd or VCd) with transplant remains effective.
- **Relapse is expected and treatable**: BCMA-directed CAR-T cells, bispecific antibodies and belantamab now improve survival from first relapse ([CARTITUDE-4](#)^[4], [MajesTEC-3](#)^[5]).
- **Supportive care saves lives**: bone-protecting drugs, early antibiotics and antivirals, vaccines, clot prevention with IMiDs, fluids and fast treatment for kidney injury, and emergency MRI for back pain with weakness.
- **India**: patients are often younger (median 57 years in an Eastern Indian series) and present later, after months of "backache" or "kidney disease"; few receive a transplant because of cost; generic bortezomib and lenalidomide have widened access.

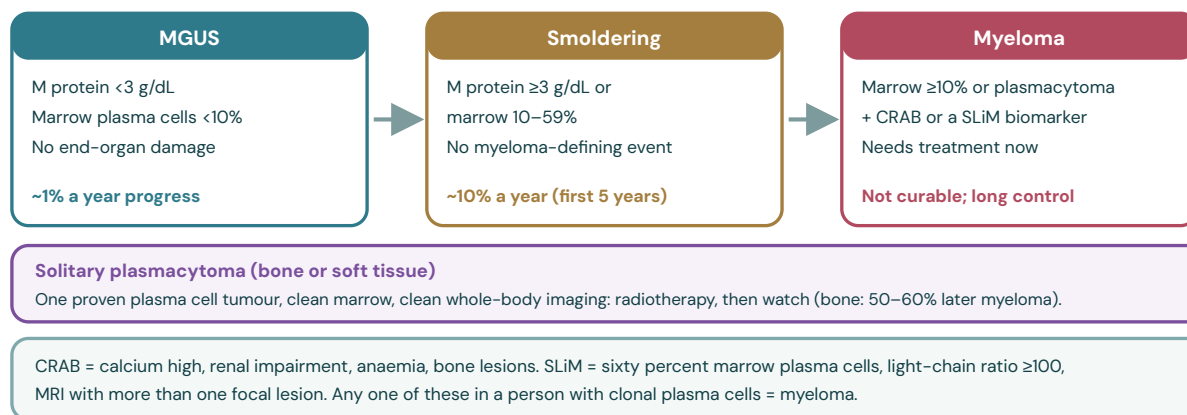
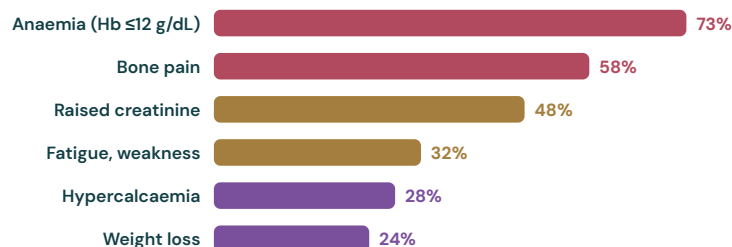
One clone, four clinical pictures: from a silent protein to active myeloma

Figure 1. The spectrum at a glance (IMWG criteria, Rajkumar 2014; UpToDate MGUS, smoldering myeloma, myeloma diagnosis and plasmacytoma reviews).

02 Clinical presentation, common traps & causes

How myeloma shows itself: findings at diagnosis in 1027 patients



Rarely first

- Paraesthesia 5%
- Liver 4%, spleen 1%
- Nodes 1%, fever <1%
- Extramedullary mass 7%

Emergencies: back pain with leg weakness or bladder change (cord compression), oliguric kidney failure, calcium crisis (confusion, vomiting), hyperviscosity (nose bleeds, blurred vision). Total protein may be normal in light-chain myeloma.

Figure 2. Presenting features (Kyle 2003, 1027 Mayo patients; UpToDate myeloma diagnosis review). Earlier testing now finds more patients before bone damage.

Who gets it, and why

- **Myeloma:** median age 65–74 in Western series; only 10% are under 50 and 2% under 40; men slightly more than women (1.4:1); two to three times more common in people of African descent ([Kyle 2003](#)^[6]).
- **Causes:** unknown in most. Risk rises with age and body mass index; radiation, benzene and some pesticides are associated. A first-degree relative with myeloma raises the risk about 3.7-fold, but familial clusters are rare and testing relatives is not routine.
- **MGUS:** 3.2% of people at ≥50, 5.3% at ≥70 and 7.5% at ≥85 years in Olmsted County; more in men ([Kyle 2006](#)^[7]). Non-IgM MGUS (about 80%) leads to myeloma or AL amyloidosis; IgM MGUS (about 15%) leads to Waldenström or lymphoma; light-chain MGUS to light-chain myeloma or AL.
- **Smoldering myeloma:** about 10% progress each year for the first 5 years, 3% a year for the next 5, then 1–2% a year; median time to progression 4.8 years ([Kyle 2007](#)^[8]).
- **Solitary plasmacytoma:** about 5% (bone) and 3% (soft tissue) of plasma cell disorders; soft-tissue tumours sit in the nose, sinuses and nasopharynx in 45–80%, so they reach ENT surgeons first.
- **How myeloma presents:** anaemia (73%), central bone pain worse on movement (58%), raised creatinine (48%; >2 mg/dL in about 20%), fatigue, high calcium (28%) and weight loss (24%). Height loss from vertebral collapse; recurrent pneumococcal infections; occasionally a purplish skin or soft-tissue mass.
- **India:** in 696 patients at a North Indian centre (median age 66, 65% men), 5-year survival was 83%, worse with weight loss, kidney dysfunction and anaemia at diagnosis ([Yanamandra 2021](#)^[9]). In an Eastern Indian series the median age was 57 and patients with del(17p) were younger ([Jha 2023](#)^[10]).

Common traps

- **Months of painkillers for "lumbar spondylosis" or "osteoporosis".** Back pain in an adult with anaemia, a high ESR or a high total protein needs SPEP, free light chains and imaging. NSAIDs given for that pain then damage the kidney.
- **"Chronic kidney disease" in a 55-year-old with no diabetes or hypertension.** Unexplained kidney injury, especially with anaemia or bland urine with little albumin, needs serum free light chains.

- **A normal SPEP or negative urine dipstick read as "no myeloma".** Light-chain myeloma (about 15–20%) may show no spike, and the dipstick does not detect Bence Jones protein.
- **Anaemia treated with iron and B12 for months.** Normocytic anaemia with rouleaux, high ESR or high globulins: test for a monoclonal protein.
- **A vertebral collapse fixed without a biopsy.** A solitary bone lesion should never be fixed without tissue; a plasmacytoma or a metastasis changes everything.
- **An incidental small M protein turned into a cancer label.** Most MGUS never progresses; frightening patients, or repeating marrow tests in low-risk MGUS, does harm.
- **A nasal "polyp" with epistaxis sent for routine polypectomy.** Extramedullary plasmacytoma needs immunohistochemistry (CD138, light-chain restriction) and full staging.

SHARE WITH PATIENTS: SYMPTOMS AND SUSPICION

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Multiple myeloma is simply another name for bone cancer?

Persistent back pain in older adults is always due to ageing or arthritis?

Multiple myeloma occurs only in very elderly people?

If there is no bone pain, multiple myeloma is impossible?

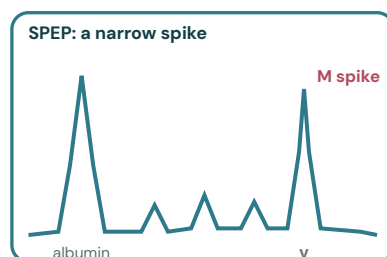
Multiple myeloma is always inherited from parents?

03 Diagnosis, workup & staging essentials

Making the diagnosis

- **Initial tests for any suspected plasma cell disorder:** CBC, calcium, creatinine, SPEP with immunofixation, serum free light chains and quantitative immunoglobulins. If a protein is found or the ratio is abnormal: 24-hour urine electrophoresis and immunofixation (baseline M protein and a check for nephrotic albuminuria).
- **Marrow aspirate and biopsy:** clonal plasma cells by CD138 staining or flow cytometry (κ/λ restriction); FISH on CD138-selected cells. Involvement can be patchy, so a low count with lytic lesions needs a lesion biopsy or a second marrow site.
- **Imaging:** whole-body low-dose CT (quick, cheap, sensitive) for new myeloma; whole-body or spine-pelvis MRI for suspected smoldering myeloma or solitary plasmacytoma; PET-CT for suspected extramedullary disease; MRI for cord compression ([Hillengass 2019^{\[11\]}](#)). Skeletal X-ray surveys and bone scans miss lesions.
- **Myeloma:** clonal marrow plasma cells $\geq 10\%$ or a biopsy-proven plasmacytoma, plus CRAB attributable to the clone (calcium > 11 mg/dL, creatinine > 2 mg/dL or clearance < 40 mL/min, haemoglobin < 10 g/dL or > 2 g/dL below normal, one or more lytic lesions on CT, PET-CT or X-ray) or a SLiM biomarker ([IMWG 2014^{\[2\]}](#)).
- **Smoldering myeloma:** serum M protein ≥ 3 g/dL or urine ≥ 500 mg/24 h and/or 10–59% marrow plasma cells, with no myeloma-defining event and no amyloidosis. **MGUS:** M protein < 3 g/dL, $< 10\%$ marrow plasma cells (if done), no end-organ damage; light-chain MGUS if only light chains are abnormal (ratio < 100).
- **Solitary plasmacytoma:** one biopsy-proven tumour of bone or soft tissue, no other lesions on MRI or PET-CT, no CRAB, and no clonal marrow plasma cells (if $< 10\%$ are present: "with minimal marrow involvement"; $\geq 10\%$ = myeloma) ([Caers 2018^{\[12\]}](#)).

Finding the monoclonal protein: four tests, each with a blind spot



SPEP	Finds and measures the spike Misses small and light-chain-only proteins
Immunofixation	Confirms clonal; names it (IgG κ ...) Does not measure the amount
Serum free light chains	κ/λ ratio (normal 0.26–1.65); light-chain myeloma Ratio drifts up in kidney disease
24-h urine PEP + IFE	Bence Jones protein; baseline Urine dipstick does not detect it

Screen with SPEP + immunofixation + serum free light chains (+ quantitative immunoglobulins, CBC, calcium, creatinine). If a protein is found or the ratio is abnormal, add 24-hour urine electrophoresis and immunofixation. Follow a patient on the same free-light-chain assay throughout: results differ between manufacturers.

Figure 3. Monoclonal protein tests (UpToDate laboratory methods for monoclonal proteins review). Schematic drawing, not to scale.

From a suspicious finding to a named disorder

Clues: anaemia + back pain, raised protein or ESR, unexplained kidney injury, high calcium, lytic lesion, recurrent infections, neuropathy
Order: CBC, calcium, creatinine, SPEP + immunofixation, serum free light chains, quantitative immunoglobulins

Protein found → marrow aspirate + biopsy (clonal plasma cell %, FISH) and whole-body low-dose CT, PET-CT or MRI
Marrow and imaging may be skipped in low-risk MGUS: IgG <1.5 g/dL, normal ratio, no anaemia, calcium or kidney problem

MGUS

- M <3 g/dL
- Marrow <10%
- No CRAB, no SLiM

Smoldering

- M ≥3 g/dL or 10–59%
- No CRAB, no SLiM
- MRI to be sure

Myeloma

- ≥10% or plasmacytoma
- Plus CRAB or SLiM
- Treat now

Plasmacytoma

- Single tumour
- No clonal marrow cells*
- Imaging clean

*Clonal cells <10% = minimal marrow involvement. Not myeloma: IgM protein with lymphoplasmacytic cells (Waldenström), nephrotic albuminuria or heart failure with λ light chains (AL amyloidosis), neuropathy with sclerotic bone lesions (POEMS), ≥5% plasma cells in blood (plasma cell leukaemia), lytic lesions with an unrelated MGUS (metastatic carcinoma: biopsy the lesion).

Figure 4. Work-up of a suspected plasma cell disorder (IMWG criteria, Rajkumar 2014; IMWG imaging consensus, Hillengass 2019; UpToDate MGUS and myeloma diagnosis reviews).

Not myeloma: the differentials to exclude

- **AL amyloidosis:** often <10% marrow plasma cells and a small λ protein, with nephrotic albuminuria, heart failure with thick walls, neuropathy, macroglossia or periorbital bruising: tissue biopsy with Congo red (separate module later).
- **Waldenström macroglobulinaemia:** an IgM protein (seen in <1% of myeloma), lymphoplasmacytic cells (CD19, CD20), MYD88 L265P in >90%; IgM myeloma needs lytic lesions or t(11;14) (indolent B-cell module).
- **POEMS syndrome:** polyneuropathy, sclerotic bone lesions, organomegaly, endocrinopathy, skin changes and a small λ protein; high VEGF.
- **Plasma cell leukaemia:** ≥5% clonal plasma cells on the blood smear; aggressive, treated in specialised centres.
- **Metastatic carcinoma with an unrelated MGUS:** lytic lesions plus a small protein are not always myeloma; biopsy the lesion. **Polyclonal increase** (infection, liver disease, autoimmunity): a broad band, not a spike.
- **MGRS:** kidney damage from a small, non-malignant clone (deposition disease, cryoglobulinaemia, light-chain tubulopathy); diagnosed by kidney biopsy and treated against the clone.

Before treatment

Area	What to do	Why
Disease burden	SPEP, immunofixation, free light chains, 24-h urine; marrow with FISH (± NGS for TP53)	Baseline for response; IMS/IMWG risk
Staging	Albumin, beta-2 microglobulin, LDH	R-ISS; high-risk B2M (≥5.5 mg/L with normal creatinine)
Bones	Low-dose whole-body CT (PET-CT or MRI as needed); DXA if no lesions	Bone drug, RT, fixation, cord risk
Kidneys	Creatinine, urine albumin, 24-h urine; biopsy if albuminuria or light chains not very high	Cast nephropathy vs AL/MIDD/MGRS; drug choice

Area	What to do	Why
Infection and blood bank	HBV, HCV, HIV; varicella status; type and screen before daratumumab	Prophylaxis; anti-CD38 interferes with cross-matching
Fitness	Performance status, comorbidity, frailty; heart and lung tests if transplant considered	Transplant eligibility; dose adjustment
Teeth	Dental examination before a bone drug	Jaw osteonecrosis prevention

SHARE WITH PATIENTS: TESTS AND DIAGNOSIS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A normal calcium level rules out multiple myeloma?

A normal X-ray means the bones are healthy and myeloma is excluded?

A normal routine blood test excludes myeloma?

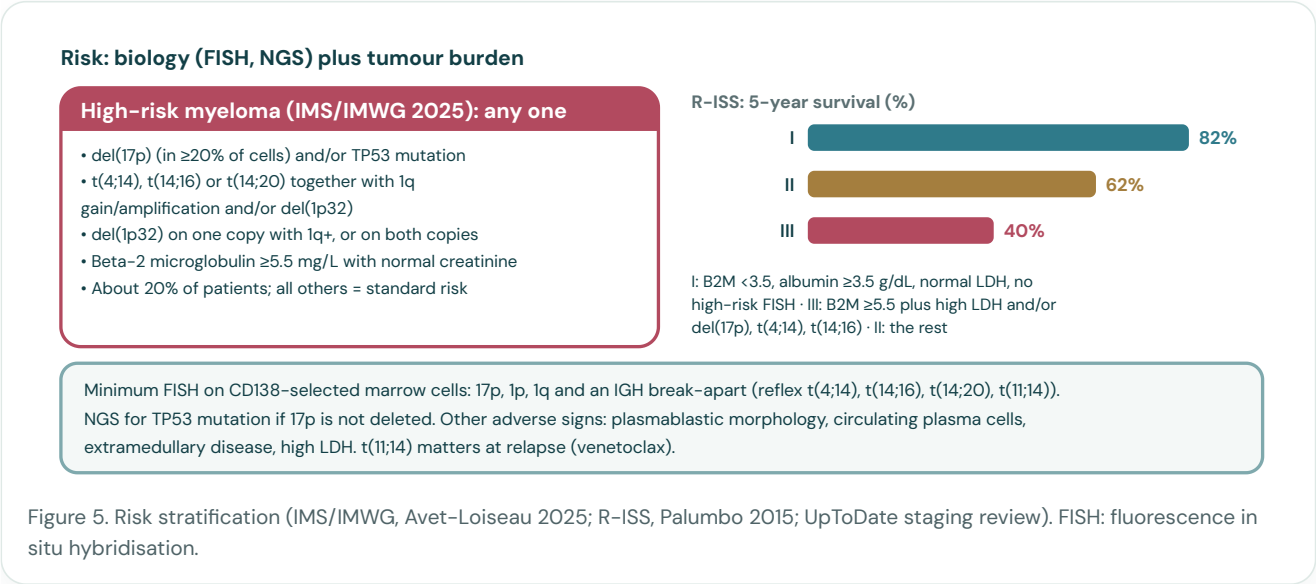
Finding an abnormal protein in the blood always means cancer that needs treatment?

A bone marrow biopsy is unnecessary if blood tests suggest myeloma?

04 Biology and biomarkers that change treatment

Biology in brief

- **Two starting routes:** about half of MGUS begins with an IgH translocation at 14q32 (t(11;14) in about 25%, t(4;14) 15%, t(14;16) 5%, t(6;14) 3%, t(14;20) 2%) and most of the rest with trisomies of odd-numbered chromosomes (hyperdiploid). These early events happen decades before diagnosis.
- **Progression** to myeloma adds secondary hits: MYC rearrangement, 1q gain, 1p and 17p loss, TP53 and RAS/MAPK mutations, NF-κB activation and APOBEC mutagenesis, helped by a supportive marrow niche.
- **Bone destruction** comes from osteoclast activation (high RANKL, low osteoprotegerin) with suppressed osteoblasts (DKK1): lesions are purely lytic and do not light up on bone scans; they rarely heal fully.



Marker or feature	What it tells you	What it changes
del(17p) (≥20% of cells) or TP53 mutation	High risk (IMS/IMWG 2025)	Quadruplet induction, early HCT, two-drug maintenance; trials
t(4;14), t(14;16) or t(14;20) with 1q+ and/or del(1p32)	High risk	As above; a proteasome inhibitor in maintenance
1q gain or amplification; del(1p32)	Adverse; combined they define high risk	As above
B2M ≥5.5 mg/L with creatinine <1.2 mg/dL	High risk (tumour burden)	As above
t(11;14)	Standard risk; BCL-2 dependence	Venetoclax option at relapse (off-label)
R-ISS I / II / III	5-year OS 82% / 62% / 40% (Palumbo 2015 ^[13])	Prognosis; trial comparison
Circulating plasma cells; plasmablastic morphology; extramedullary disease	Aggressive biology	Fast, intensive therapy; ≥5% on smear = plasma cell leukaemia
Frailty and comorbidity	Tolerance	Dose-reduced, dexamethasone-sparing regimens

- **Testing needed:** FISH for 17p, 1p, 1q and an IGH break-apart with reflex partners; NGS for TP53 mutation (reasonable to reserve it for cases without del(17p) when resources are limited). Older systems (R-ISS, [R2-ISS^{\[14\]}](#)) remain useful for comparing trials.

05 Local therapy: radiotherapy, surgery & procedures

Radiotherapy for solitary plasmacytoma

Solitary plasmacytoma: bone versus soft tissue

Solitary plasmacytoma of bone

- ~5% of plasma cell disorders; spine, pelvis, ribs
- Pain or fracture; small M protein in 30–75%
- RT 35–50 Gy (≥ 2 cm margin; one vertebra above and below)
- Local control >80–90%; best <5 cm
- 50–60% later develop myeloma, most within 4 years

Solitary extramedullary plasmacytoma

- ~3% of plasma cell disorders; median age 55–60
- 45–80% in nose, sinuses, nasopharynx
- Incomplete excision → RT 40–50 Gy
- Complete excision → observe (some give RT)
- 10–15% later develop myeloma; OS >10 years

Before calling it solitary: biopsy the lesion, marrow aspirate + biopsy, PET-CT (and MRI for bone), CRAB tests.

Clonal plasma cells <10% in marrow = "minimal marrow involvement": bone lesions progress far faster (67% vs 30% at 2 years).

An M protein that persists one year after RT also predicts myeloma. No routine bisphosphonate; no adjuvant chemotherapy.

Figure 6. Solitary plasmacytoma (Caers 2018; ILROG, Tsang 2018; Paiva 2014; UpToDate SPB and SEP reviews).

- **Bone (SPB):** involved-site RT 35–50 Gy over about 4 weeks, lower end for tumours <5 cm, higher for larger; field covers the lesion with a margin of at least 2 cm and one uninvolved vertebra above and below for spinal lesions; give RT even after complete excision. Local control exceeds 80–90% ([ILROG 2018](#)^[15]).
- **Soft tissue (SEP):** after incomplete excision or biopsy alone, RT 40–50 Gy (doses below 40 Gy did worse); after complete excision, observation is reasonable (some give RT). Fewer than 7% recur locally; 10–15% develop myeloma ([Ozsahin 2006](#)^[16]).
- **No adjuvant chemotherapy and no routine bisphosphonate** for either; the role of systemic therapy for minimal marrow involvement is being studied.

Palliative radiotherapy in myeloma

- **Indications:** uncontrolled bone pain, cord or root compression, impending or actual fracture, and after fixation of long bones. Up to 40% of patients need RT at some point.
- **Low doses work:** no clear dose-response; 10–12 Gy often controls pain, and 8 Gy in one fraction gave pain relief similar to 30 Gy in 10 fractions (74% vs 85%; [Rudzianskiene 2017](#)^[17]). For cord compression, longer fractionation gives better motor recovery.
- **Keep fields small** to protect marrow reserve and future stem cell collection; the whole fixation hardware need not be covered. Use RT with proteasome inhibitors cautiously (more cytopenias).

Surgery and procedures

- **Cord compression is an emergency:** back pain almost always comes first; MRI of the whole spine within 24 hours (CT myelography if MRI impossible), dexamethasone, then RT; fast systemic therapy may be enough with minimal deficit; surgery if the deficit progresses, the spine is unstable or retropulsed bone compresses the cord.
- **Long bones:** a lesion destroying $\geq 50\%$ of cortical thickness, or a high Mirels score, needs prophylactic fixation by an orthopaedic oncologist; radiograph the whole bone first.

- **Vertebral compression fractures:** kyphoplasty or vertebroplasty relieve pain and improve function ([CAFE^{\[18\]}](#)); assess stability (SINS) first.
- **Diagnosis:** biopsy any solitary bone lesion before fixation; complete excision of a soft-tissue plasmacytoma can be curative.

SHARE WITH PATIENTS: RADIOTHERAPY AND BONE CARE

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Radiotherapy has no role because myeloma affects the entire bone marrow?](#)

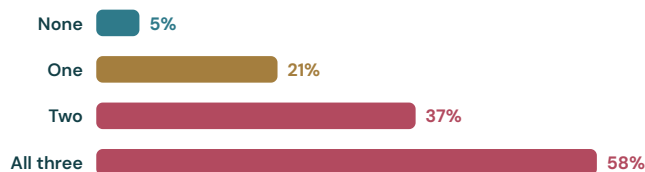
[Bone-strengthening medicines are unnecessary once cancer treatment begins?](#)

o6 Systemic therapy: indications & options

MGUS: watch, do not treat

MGUS: three risk factors decide how closely to watch

Risk of progression at 20 years by number of risk factors (%)



The three risk factors

- M protein ≥ 1.5 g/dL
- Non-IgG type (IgA, IgM)
- Abnormal free light-chain ratio

Low risk

- IgG, <1.5 g/dL, normal ratio
- Repeat tests at 6 months
- Then blood tests every 2–3 years
- Marrow and imaging often not needed

All others

- Repeat tests at 6 months
- Then yearly: SPEP, light chains, CBC, calcium, creatinine
- Usually with a specialist

Always

- Report new bone pain, fatigue, frothy urine, numbness at once
- Progression can be abrupt
- Lifetime risk ~10% (competing causes)

Prevalence: 3.2% at ≥ 50 , 5.3% at ≥ 70 , 7.5% at ≥ 85 years (Olmsted County). About 1% a year progress (non-IgM to myeloma or AL; IgM to Waldenström). A few have organ damage from the protein itself without cancer (kidney: MGRS; nerves; skin): monoclonal gammopathy of clinical significance.

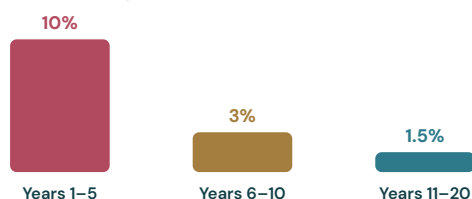
Figure 7. MGUS risk and follow-up (Rajkumar 2005; Kyle 2006 and 2018; UpToDate MGUS diagnosis and clinical course reviews).

- **Risk model:** M protein ≥ 1.5 g/dL, non-IgG type and an abnormal free light-chain ratio; 20-year progression 5%, 21%, 37% and 58% with 0, 1, 2 and 3 factors ([Rajkumar 2005](#)^[19], [Kyle 2018](#)^[20]).
- **Follow-up:** repeat tests at 6 months; low risk then every 2–3 years; others yearly with history and examination. Marrow and imaging can be skipped in low-risk MGUS without CRAB features.
- **Watch for clinical significance:** kidney damage (MGRS), neuropathy, skin disease or bleeding caused by the protein itself needs clone-directed treatment even without cancer. Bone drugs only for osteoporosis.

Smoldering myeloma

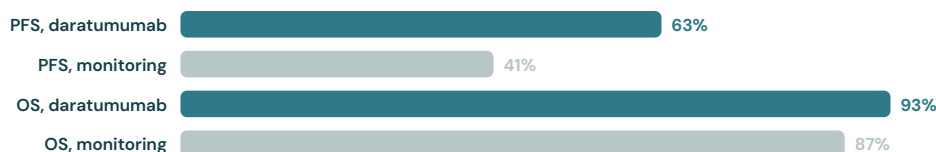
Smoldering myeloma: risk falls with time, and the 20/2/20 rule finds who to treat

Yearly risk of progression to myeloma or AL

**20/2/20 (Mayo 2018 / IMWG)**

- Marrow plasma cells >20%
- M protein >2 g/dL
- Involved/uninvolved light-chain ratio >20
- 0 = low, 1 = intermediate, 2–3 = high risk

AQUILA: daratumumab (3 years) vs active monitoring in high-risk SMM, 5-year results (%)



Low and intermediate risk: watch (tests every 3–4 months at first, MRI yearly if marrow is heavily involved). High risk: early treatment (daratumumab preferred; lenalidomide ± dexamethasone an alternative) or a trial. MRI with >1 focal lesion, ratio ≥100 or ≥60% plasma cells = myeloma, not SMM.

Figure 8. Smoldering myeloma (Kyle 2007; Lakshman 2018; AQUILA, Dimopoulos 2025; UpToDate smoldering myeloma review).

- **Risk:** 20/2/20 (marrow plasma cells >20%, M protein >2 g/dL, light-chain ratio >20); two or three factors = high risk ([Lakshman 2018](#)^[21], [IMWG 2020](#)^[22]). MRI at baseline; repeat testing 2–3 months after diagnosis, then every 3–4 months.
- **Low and intermediate risk:** observation; treatment has not been shown to improve outcomes.
- **High risk:** early, time-limited treatment rather than observation. AQUILA (390 patients): daratumumab for up to 3 years vs monitoring, 5-year PFS 63% vs 41% and OS 93% vs 87%, benefit clearest in 20/2/20 high risk ([AQUILA](#)^[23]). Alternatives: lenalidomide for 2 years ([E3A06](#)^[24]: 2-year PFS 93% vs 76%) or lenalidomide–dexamethasone ([QuiRedex](#)^[25]: OS benefit). Full myeloma regimens only in trials.

Active myeloma: first-line treatment

First-line treatment: by transplant eligibility and risk

Confirm active myeloma → FISH risk → fitness, kidneys, neuropathy, clot risk → transplant opinion (no fixed age limit)

Transplant eligible

- Induction 3–6 cycles: D–VRd or Isa–VRd (VRd if a quadruplet is not possible)
- Collect stem cells (G–CSF ± plerixafor)
- Early HCT (high-dose melphalan), or store cells for first relapse
- Maintenance: lenalidomide (± anti-CD38) ~2 years; high risk: lenalidomide + bortezomib until progression

Not transplant eligible

- D–VRd or Isa–VRd for most; DRd or VRd if frail
- VCd if lenalidomide unsafe (kidney, clots)
- 8–12 cycles, then lenalidomide-based maintenance
- Frail: dose-reduced DRd, IsaRd or Rd

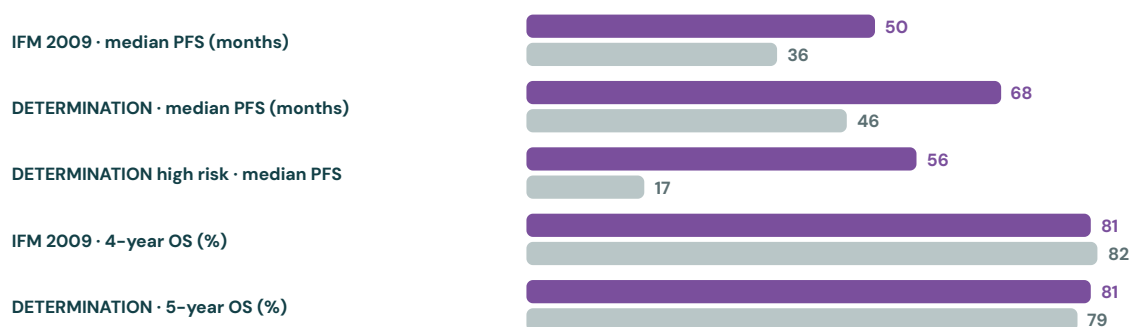
Limited resources

- Bortezomib triplet: VTd or VCd (VRd if lenalidomide affordable)
- No bortezomib: CTd or MPT
- Transplant if possible (no melphalan before collection)
- After HCT: thalidomide or lenalidomide maintenance

With every regimen: osteoclast inhibitor if bone disease or osteopenia; aspirin or anticoagulant with IMiDs; levofloxacin for the first 3 months; aciclovir with bortezomib or anti-CD38; vaccines; dental check; weekly dexamethasone; subcutaneous bortezomib.

Figure 9. First-line pathways (UpToDate initial treatment, HCT, overview and resource-limited settings reviews). D = daratumumab; Isa = isatuximab; V = bortezomib; R = lenalidomide; T = thalidomide; C = cyclophosphamide; d = dexamethasone; MP = melphalan-prednisone.

- **Start promptly:** untreated symptomatic myeloma has a life expectancy under a year. Goals: reverse organ damage, deep and durable response, quality of life.
- **Quadruplets for most:** in transplant-eligible patients D–VRd beat VRd (PERSEUS, 709 patients: MRD negativity 75% vs 48%, 48-month PFS 84% vs 68%; [PERSEUS](#)^[26]); Isa–VRd deepened responses ([GMMG-HD7](#)^[27]). In transplant-ineligible or deferred patients: CEPHEUS (D–VRd, 54-month PFS 68% vs 50%; [CEPHEUS](#)^[28]) and IMROZ (Isa–VRd, 5-year PFS 63% vs 45%; [IMROZ](#)^[29]).
- **Triplets remain good options:** VRd improved OS over Rd ([S0777](#)^[30]); DRd improved OS over Rd in older patients (MAIA, 5-year OS 66% vs 53%; [MAIA](#)^[31]), suits pre-existing neuropathy and can be given dexamethasone-sparing to the frail; VCd when lenalidomide is risky (kidney injury, clots).
- **Autologous transplant:** induction 3–6 cycles, stem cell collection (G–CSF; plerixafor if poor mobilisation), then high-dose melphalan. Early HCT lengthened PFS (IFM 2009: 50 vs 36 months; DETERMINATION: 68 vs 46 months) without OS difference ([IFM 2009](#)^[32], [DETERMINATION](#)^[33]). Prefer early HCT for high risk; eligibility depends on fitness, not age; collect for two transplants if under 65.
- **Maintenance:** lenalidomide after HCT or induction delays progression ([Myeloma XI](#)^[34]). Two years appear as good as indefinite with less toxicity (ENDURANCE: 7-year OS 69% in both; [Kumar 2026](#)^[35]). Add an anti-CD38 antibody if MRD-positive; high risk: lenalidomide plus bortezomib (or carfilzomib or anti-CD38) until progression.
- **Limited resources:** VTd or VCd (VTd gave more responses than VCd before HCT; [IFM2013-04](#)^[36]), then transplant if possible and thalidomide or lenalidomide maintenance; without bortezomib, CTd or MPT (no melphalan before stem cell collection). Thalidomide maintenance prolongs remission but not survival ([Ludwig 2010](#)^[37]).
- **Practical rules:** subcutaneous, weekly bortezomib (less neuropathy); weekly rather than more frequent dexamethasone; subcutaneous daratumumab or isatuximab; dose-adjust lenalidomide for kidney function; second cancers rise with lenalidomide after HCT.

Early versus delayed autologous transplant: longer remissions, same survival

Purple = early HCT after VRd; grey = VRd continued, HCT kept for relapse.

Early HCT deepens response (more MRD negativity) and delays progression by more than a year; overall survival is unchanged because many patients receive HCT at relapse. High-risk disease: early HCT preferred. Collect cells for two transplants if under 65. Eligibility: performance and organ function, not age alone; kidney failure (even dialysis) is not an absolute bar.

Figure 10. Early vs delayed HCT (IFM 2009, Attal 2017; DETERMINATION, Richardson 2022; UpToDate HCT review).

Relapsed myeloma

Relapse: check what the disease is refractory to, then target BCMA

Refractory = progression on, or within 60 days of, a drug. Re-check FISH, kidneys, marrow reserve, infection risk, access.

First relapse

- BCMA CAR-T: cilta-cel (CARTITUDE-4: OS benefit)
- Teclistamab + daratumumab (MajesTEC-3)
- BVD: belantamab + bortezomib (DREAMM-7)
- Or a triplet with unused classes (DPd, DKd, KPd, PVD, IsaKd)
- Stored cells: second HCT is an option

Second or later

- BCMA if not yet used: CAR-T, bispecific (teclistamab, elranatamab, linvoseltamab) or belantamab
- After BCMA: talquetamab (GPC5D)
- Selinexor-based, alkylators
- Venetoclax only with t(11;14)

Safety with T-cell therapies

- CRS and neurotoxicity (ICANS): step-up dosing, monitoring
- Infections: IVIG if IgG low, PJP and antiviral prophylaxis
- Belantamab: eye examinations
- Frail or infection-prone: a triplet may be wiser

Figure 11. Relapsed myeloma (UpToDate relapsed disease and administration reviews). D = daratumumab; P = pomalidomide; K = carfilzomib; V = bortezomib; Isa = isatuximab; d = dexamethasone.

- **Assess first:** drug sensitivity (refractory = progression within 60 days of a drug), FISH, organ function, infection risk and eligibility for CAR-T or a second HCT; refer early to a centre with cellular therapy.
- **First relapse:** BCMA-directed therapy for most. Cilta-cel vs DPd/PVd in lenalidomide-refractory disease: 30-month PFS 59% vs 26%, OS 76% vs 64% ([CARTITUDE-4](#)^[4]). Teclistamab plus daratumumab vs DPd/DVd: 36-month PFS 83% vs 30%, OS 83% vs 65% ([MajesTEC-3](#)^[5]). BVD vs DVd: median PFS 37 vs 13 months, OS benefit, eye toxicity ([DREAMM-7](#)^[38]); BPd in [DREAMM-8](#)^[39].
- **Triplets of unused classes** (DPd, DKd, KPd, PVD, IsaKd, IRd) remain right for the frail, the infection-prone and those without access; a second HCT is possible with stored cells and a long first remission.
- **Later relapse:** BCMA if not yet used (ide-cel improved PFS: [KarMMA-3](#)^[40]; bispecifics: [MajesTEC-1](#)^[41]); after BCMA, talquetamab (GPC5D; [MonumenTAL-1](#)^[42]), selinexor, alkylators, venetoclax only for t(11;14); trials.

Supportive care: bone, kidney, infection, clots

Bone disease: protect the skeleton, treat the pain, fix what will break

Osteoclast inhibitor

- For lytic lesions or osteopenia/osteoporosis (many experts: all needing treatment)
- Dental examination first; calcium and vitamin D
- Creatinine clearance >30: zoledronic acid (or pamidronate); ≤30: denosumab
- Monthly for ≥2 years; never stop denosumab without one bisphosphonate dose
- Watch: jaw osteonecrosis, low calcium, kidney (bisphosphonate)

Pain, fracture, cord

- Palliative RT: 8 Gy single fraction gave pain relief similar to 30 Gy; 10–12 Gy often enough
- Keep fields small (marrow for stem cells)
- ≥50% cortical loss in a long bone → fixation; vertebral collapse → kyphoplasty
- Back pain + weakness: MRI whole spine within 24 h, dexamethasone, RT; surgery if bone in canal or worsening
- No NSAIDs (kidneys)

Myeloma lesions are purely lytic (osteoblasts are suppressed), so bone scans miss them: use low-dose CT, PET-CT or MRI. Osteoclast inhibitors prevent new events (Cochrane: 104 fewer skeletal events per 1000 treated) but do not heal old lesions. Zoledronic acid beat clodronate for survival in Myeloma IX.

Figure 12. Bone disease (Myeloma IX, Morgan 2010; Raje 2018; Rudzianskiene 2017; UpToDate osteoclast inhibitor, fracture, cord compression and overview reviews).

- **Osteoclast inhibitors:** for lytic lesions or osteopenia (many guidelines: all patients needing treatment). Zoledronic acid improved OS over clodronate (Myeloma IX: median 52 vs 46 months; [Myeloma IX](#)^[43]); denosumab matched zoledronic acid with less kidney toxicity but more hypocalcaemia ([Raje 2018](#)^[44]). Creatinine clearance >30: zoledronic acid; ≤30: denosumab. Monthly for at least 2 years; dental clearance first; calcium and vitamin D; never stop denosumab without a bisphosphonate dose.
- **Hypercalcaemia:** fluids, glucocorticoids, zoledronic acid (preferred over pamidronate; denosumab if refractory or kidney failure); check ionised calcium if high calcium without symptoms (a protein can bind calcium). **Hyperviscosity** (rare in myeloma): plasma exchange if symptomatic.

Kidney injury in myeloma: treat the clone fast, then the kidney

Why the kidney fails

- Light-chain cast nephropathy (myeloma kidney): commonest
- Hypercalcaemia, dehydration
- NSAIDs, contrast, bisphosphonates
- Nephrotic albuminuria → AL or deposition disease: kidney biopsy

First 48 hours

- Start bortezomib + dexamethasone ± anti-CD38 at once
- Fluids to ~3 L urine a day (unless overloaded)
- Stop NSAIDs, ACE inhibitors, ARBs, diuretics
- Correct calcium; dialysis for usual reasons

Then

- Aim: rapid fall in involved light chains
- Plasma exchange or high cut-off dialysis: debated
- Denosumab if bone drug needed and CrCl ≤30
- Adjust lenalidomide; avoid nephrotoxins for life

Creatinine is raised in about half at diagnosis (>2 mg/dL in ~20%). With very high involved light chains and no other cause, cast nephropathy can be presumed; otherwise biopsy the kidney. Proteinuria on dipstick is usually albumin (AL, deposition disease), not light chains.

Figure 13. Kidney disease (MYRE, Bridoux 2017; UpToDate kidney disease etiology/evaluation and treatment reviews). ARB: angiotensin receptor blocker.

- **Cast nephropathy:** start bortezomib, dexamethasone ± anti-CD38 at once; fluids for about 3 L of urine a day; stop NSAIDs, ACE inhibitors, ARBs and diuretics; correct calcium; dialysis for the usual indications, not to remove light chains. Plasma exchange or high cut-off dialysis is debated ([MYRE](#)^[45]).

Preventing the complications that kill: infection and clots**Infection**

- Levofloxacin for the first 3 months (TEAMM: fewer fevers or deaths, 19% vs 27%)
- Aciclovir/valaciclovir with bortezomib, anti-CD38, carfilzomib
- Pneumococcal, influenza and recombinant zoster vaccines, ideally before treatment
- PJP prophylaxis with prolonged T-cell suppression (CAR-T, bispecifics)
- HBV screen before anti-CD38; IVIG for recurrent infection with low IgG

Clots (with IMiDs)

- IMiDs: thalidomide, lenalidomide, pomalidomide
- Score the risk: SAVED ≥ 2 or IMPEDE VTE ≥ 8 = high
- Standard risk: aspirin (with gastric protection)
- High risk: LMWH, a DOAC or warfarin
- Maintenance on a single IMiD: aspirin
- After a clot on an IMiD: anticoagulate until 1–3 months after the IMiD stops

SAVED: surgery in 90 days (+2), Asian population (-3), previous VTE (+3), age ≥ 80 (+1), high-dose dexamethasone (+1 or +2). It was derived in US registries: how the "Asian" point applies to Indian patients is untested.

Figure 14. Supportive care (TEAMM, Drayson 2019; SAVED, Li 2019; IMPEDE VTE, Sanfilippo 2019; UpToDate infections and VTE reviews).

- **Infection** is a leading cause of death, highest in the first 3 months. Levofloxacin for the first 12 weeks reduced fever or death (19% vs 27%; [TEAMM^{\[46\]}](#)); aciclovir or valaciclovir with proteasome inhibitors and anti-CD38 antibodies; pneumococcal, influenza and recombinant zoster vaccines; PJP prophylaxis and IVIG with T-cell-engaging therapies.
- **Thrombosis** with IMiDs: SAVED ≥ 2 ([SAVED^{\[47\]}](#)) or IMPEDE VTE ≥ 8 ([IMPEDE VTE^{\[48\]}](#)) = high risk → LMWH, a DOAC or warfarin; otherwise aspirin. Single-agent IMiD maintenance: aspirin.

India now (October 2026)

- Indian data are web-verified: a North Indian series of 696 patients (median age 66, 5-year OS 83%; Yanamandra 2021), an Eastern Indian FISH series (median age 57; Jha 2023) and a 2016 expert panel noting that most patients pay themselves, few undergo transplant because of cost and stigma, and generic bortezomib and lenalidomide have widened access.
- Availability and cost in India of daratumumab and isatuximab, carfilzomib, pomalidomide, belantamab, BCMA CAR-T cells, teclistamab and talquetamab, denosumab, free light chain assays, FISH/NGS and PET-CT, and access to autologous transplant, to be confirmed by the treating team.

SHARE WITH PATIENTS: TREATMENT, RELAPSE AND KIDNEYS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Multiple myeloma can't be treated effectively?

Every patient with myeloma needs chemotherapy immediately?

Every myeloma patient needs a bone marrow transplant?

If myeloma has damaged the kidneys, recovery is impossible?

If myeloma returns after treatment, no further options remain?

Quick reference (also as a printable PDF on the Printable Teaching Resources page)

Table A. Diagnosis and staging tests and what they change

Test	When	What it changes	Pitfalls
SPEP + serum immunofixation	Every suspected plasma cell disorder	Size and type of M protein; MGUS vs SMM threshold (3 g/dL)	SPEP misses small or light-chain-only proteins
Serum free light chains (κ, λ, ratio)	Screening, light-chain myeloma, follow-up	Ratio ≥100 (involved ≥100 mg/L) = myeloma; MGUS risk	Ratio rises in kidney disease; use one manufacturer for follow-up
24-h urine electrophoresis + immunofixation	Protein found or ratio abnormal; baseline	Bence Jones protein; nephrotic albuminuria (AL, deposition disease)	Urine dipstick does not detect light chains
CBC, calcium, creatinine, albumin, LDH, B2M	Every case	CRAB; R-ISS; high-risk (B2M ≥5.5 with normal creatinine)	Check ionised calcium if high calcium without symptoms
Marrow aspirate + biopsy (CD138 or flow); FISH ± NGS	All except low-risk MGUS	≥10% clonal cells; 20/2/20; IMS/IMWG risk	Focal disease: a low count does not exclude myeloma
Whole-body low-dose CT (or PET-CT, MRI)	Every non-IgM protein except low-risk MGUS	Lytic lesions = myeloma; PET for extramedullary disease	Bone scans miss lytic lesions; X-rays are insensitive
Whole-body or spine-pelvis MRI	Suspected SMM or solitary plasmacytoma	>1 focal lesion = myeloma; rules out more lesions	Equivocal lesions: repeat in 3–6 months
Kidney biopsy	Albuminuria, or kidney injury without very high light chains	Cast nephropathy vs AL, deposition disease, MGRS	Correct bleeding risk first
HBV, HCV, HIV; echocardiogram, pulmonary function	Before anti-CD38, HCT or CAR-T	Antiviral prophylaxis; transplant fitness	Daratumumab interferes with blood-bank cross-matching

Table B. Treatment by setting

Setting	Standard choice	Key evidence	Notes
MGUS, low risk	Observe; tests at 6 months, then every 2–3 years	Rajkumar 2005 ^[19]	Bone drug only for osteoporosis
MGUS, other	Observe; yearly tests	Kyle 2018 ^[20]	Report new symptoms at once
SMM, low or intermediate risk	Observe closely	Lakshman 2018 ^[21]	MRI to exclude focal lesions
SMM, high risk (20/2/20)	Daratumumab for up to 3 years (or lenalidomide ± dexamethasone); trial	AQUILA ^[23]	OS 93% vs 87% at 5 years
Solitary plasmacytoma of bone	RT 35–50 Gy; observe	ILROG 2018 ^[15]	RT even after complete excision
Extramedullary plasmacytoma	Incomplete excision: RT 40–50 Gy; complete: observe	Ozsahin 2006 ^[16]	Doses <40 Gy did worse
Myeloma, transplant eligible	D–VRd or Isa–VRd × 3–6 → collect → HCT → maintenance	PERSEUS ^[26] , GMMG–HD7 ^[27]	High risk: early HCT; two-drug maintenance

Setting	Standard choice	Key evidence	Notes
Myeloma, not transplant eligible	D–VRd or Isa–VRd; DRd or VRd if frail; then maintenance	CEPHEUS ^[28] , IMROZ ^[29] , MAIA ^[31]	Frail: dose-reduced, dexamethasone-sparing
Limited resources	VTd or VCd (VRd if possible); CTd or MPT without bortezomib	IFM2013–O4 ^[36]	Thalidomide maintenance after HCT
Maintenance, standard risk	Lenalidomide ~2 years (± anti-CD38)	ENDURANCE ^[35]	Indefinite: same OS, more toxicity
First relapse	BCMA-directed (cilta-cel, teclistamab + daratumumab, BVd) or a triplet of unused classes	CARTITUDE-4 ^[4] , MajesTEC-3 ^[5]	Triplet if infection-prone or no access
Later relapse	BCMA if unused; talquetamab; selinexor; venetoclax for t(11;14)	MonumenTAL-1 ^[42]	Trials encouraged

Table C. Treatment options: evidence and best fit

Option	Best for	Evidence	Watch for
D–VRd (daratumumab + VRd)	Fit patients, standard or high risk, ± HCT	PERSEUS ^[26] : 48-month PFS 84% vs 68%; CEPHEUS ^[28] : 54-month 68% vs 50%	Cytopenias, infections; plerixafor more often
Isa–VRd	As D–VRd	IMROZ ^[29] : 5-year PFS 63% vs 45%; GMMG–HD7 ^[27]	Infusion reactions, infections
VRd	When a quadruplet is not possible	S0777 ^[30] : median OS NR vs 69 months vs Rd	Neuropathy (use subcutaneous, weekly)
DRd	Older, frail, pre-existing neuropathy	MAIA ^[31] : 5-year OS 66% vs 53%	Neutropenia, pneumonia
VCd / VTd	Kidney injury, clot risk, limited resources	IFM2013–O4 ^[36] : VTd more responses	Thalidomide: neuropathy, clots, constipation
Autologous HCT	Fit patients (age is not a bar)	DETERMINATION ^[33] : PFS 68 vs 46 months; OS same	Mucositis, infection; second myeloid cancers
Lenalidomide maintenance	After HCT or induction	Myeloma XI ^[34]	Second cancers, cytopenias, diarrhoea
Cilta-cel (BCMA CAR–T)	Lenalidomide-refractory, 1–3 prior lines	CARTITUDE-4 ^[4] : 30-month OS 76% vs 64%	CRS, ICANS, delayed neurotoxicity, cytopenias
Teclistamab + daratumumab	1–3 prior lines, not anti-CD38-refractory	MajesTEC-3 ^[5] : 36-month OS 83% vs 65%	CRS, infections (IVIg, prophylaxis)
Belantamab + bortezomib (BVd)	Relapse (outside the US mainly)	DREAMM-7 ^[38] : median PFS 37 vs 13 months	Corneal toxicity: eye checks
Talquetamab (GPC5D)	After BCMA therapy	MonumenTAL-1 ^[42]	Taste, skin and nail changes; weight loss

Table D. Managing problems during treatment

Problem	Prevent	Recognise	Act
Bacterial infection	Levofloxacin first 3 months; vaccines	Fever, cough, burning urine	Same-day assessment; IVIG if IgG low and recurrent

Problem	Prevent	Recognise	Act
Herpes zoster	Aciclovir/valaciclovir with PIs and anti-CD38	Painful band-like rash	Treatment-dose antiviral
Venous thrombosis	Aspirin or anticoagulant with IMiDs (SAVED, IMPEDE VTE)	Leg swelling, breathlessness	Anticoagulate; continue until 1–3 months after IMiD
Peripheral neuropathy	Subcutaneous, weekly bortezomib; avoid in pre-existing neuropathy	Numbness, burning, unsteadiness	Reduce or hold bortezomib/thalidomide
Kidney injury	Fluids; no NSAIDs or contrast if avoidable	Less urine, rising creatinine	Urgent anti-myeloma therapy; correct calcium
Hypercalcaemia	Effective therapy; avoid dehydration	Thirst, vomiting, confusion, constipation	Fluids, steroids, zoledronic acid (denosumab if refractory)
Jaw osteonecrosis	Dental clearance before; avoid extractions	Exposed bone, jaw pain	Stop the bone drug; dental/oral surgery care
Cord compression	Imaging for new back pain	Back pain, leg weakness, bladder change	MRI within 24 h, dexamethasone, RT; surgery if retropulsed bone
CRS / ICANS (CAR-T, bispecifics)	Step-up dosing; trained centre	Fever, low BP, low oxygen; confusion, writing change	Tocilizumab, steroids per grade
Cardiac events (carfilzomib)	Blood pressure control	Breathlessness, chest pain	Hold drug; cardiology

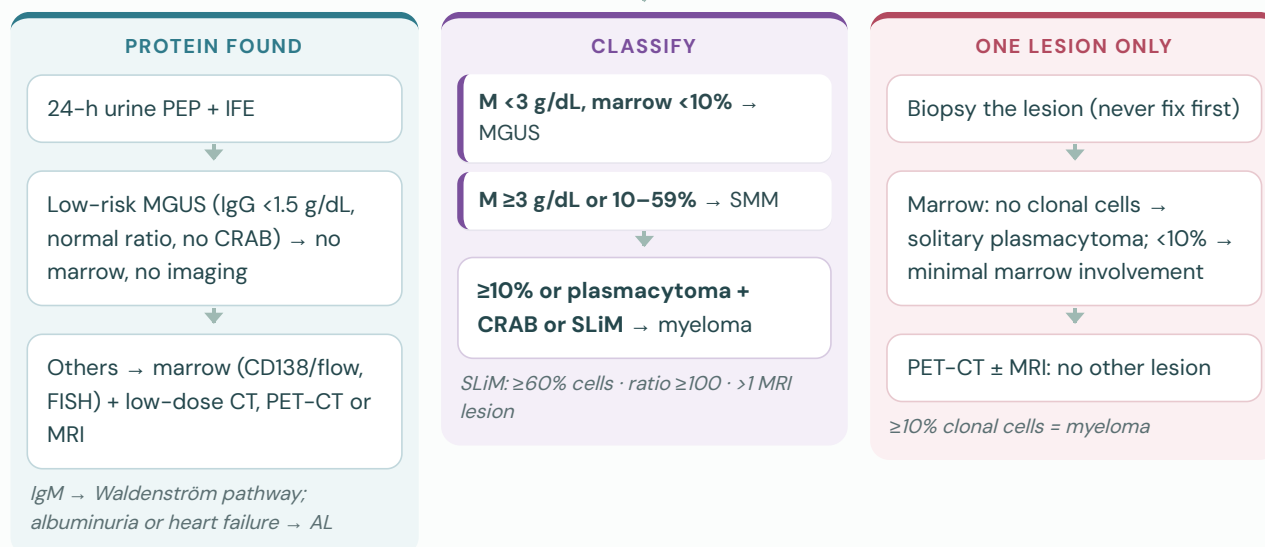
07 Management algorithms

Five decision paths pull together sections 02–06.

ALGORITHM 1

Suspected plasma cell disorder: to a named diagnosis

Back pain with anaemia, raised protein or ESR, unexplained kidney injury, high calcium, lytic lesion, recurrent infections → CBC, calcium, creatinine, SPEP + immunofixation, serum free light chains, immunoglobulins

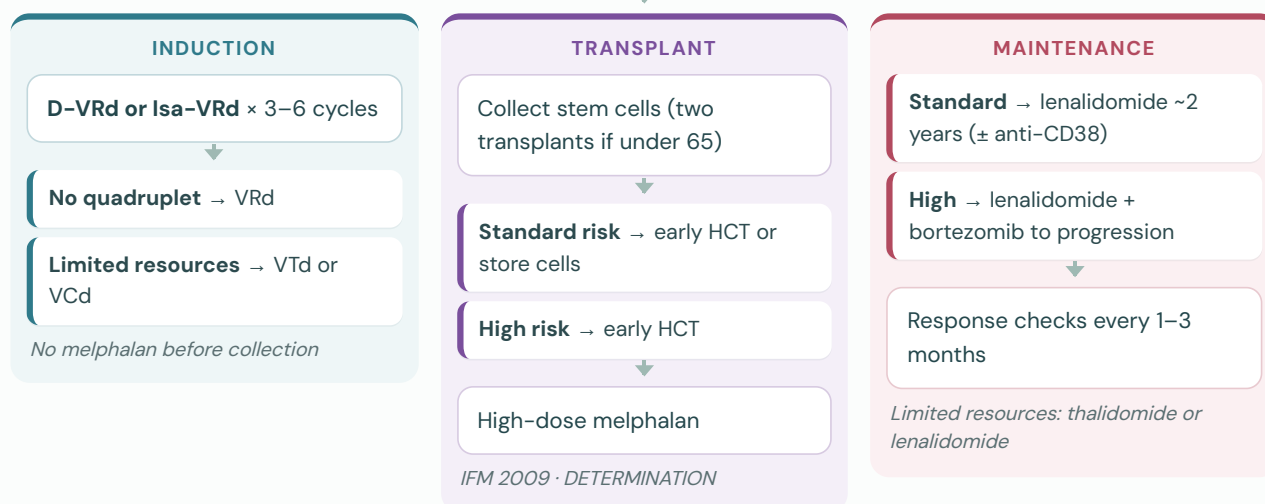


All: protect the kidneys (no NSAIDs, no dehydration) while tests run · MRI the whole spine within 24 h for back pain with weakness.

ALGORITHM 2

Newly diagnosed myeloma, transplant eligible

Active myeloma, fit for HCT → FISH risk, kidneys, neuropathy, clot and infection risk; bone drug, dental check, prophylaxis

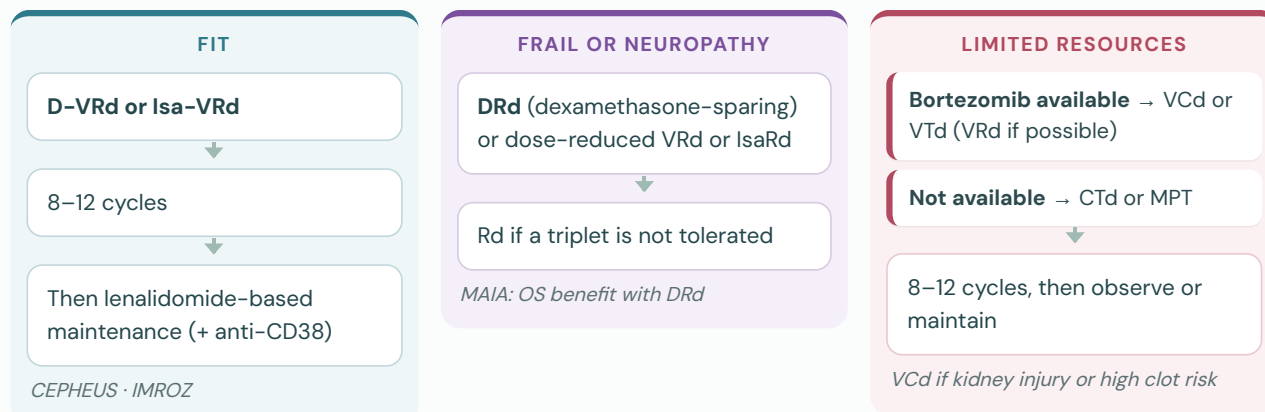


All: weekly dexamethasone · subcutaneous bortezomib · aspirin or anticoagulant with IMiDs · levofloxacin first 3 months · aciclovir · vaccines.

ALGORITHM 3

Newly diagnosed myeloma, not transplant eligible

Active myeloma, not fit for HCT (or HCT deferred) → frailty assessment, kidneys, neuropathy, resources

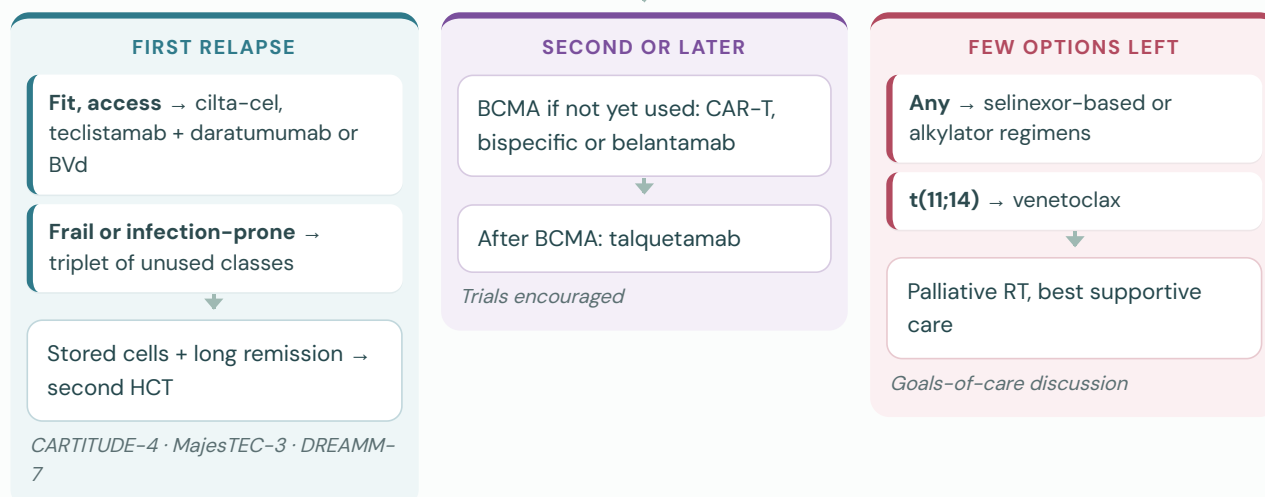


All: treat now (untreated symptomatic myeloma kills within a year) · bone drug by creatinine clearance · clot and infection prevention.

ALGORITHM 4

Relapsed myeloma

Biochemical or clinical relapse confirmed → refractory to which classes? FISH again, organ function, infection risk, CAR-T or second HCT eligibility



All: CRS and ICANS training for T-cell therapies · IVIG if IgG low · PJP and antiviral prophylaxis · eye checks with belantamab.

ALGORITHM 5

Precursors and solitary plasmacytoma

No myeloma-defining event → what is it, and how risky?

MGUS

Low risk → tests at 6 months, then every 2–3 years

Others → yearly

Organ damage from the protein
→ MGRS or other MGCS work-up

No treatment for MGUS itself

SMOLDERING

MRI; repeat tests in 2–3 months

Low/intermediate → observe every 3–4 months

High (20/2/20) → daratumumab or lenalidomide ± dex, or trial

AQUILA: PFS and OS benefit

SOLITARY PLASMACYTOMA

Bone → RT 35–50 Gy

Soft tissue → RT 40–50 Gy if not fully excised

Then observe: M protein, light chains, imaging

Minimal marrow involvement: closer watch

All: educate about red-flag symptoms · bone drug only for osteoporosis · progression can be abrupt.

o8 Survivorship, follow-up & late effects

IMWG response: from a 50% fall to no detectable disease

PR	≥50% fall in serum M protein (urine ≥90% or <200 mg/24 h)
VGPR	≥90% fall, or seen on immunofixation only
CR	Negative immunofixation, no plasmacytoma, marrow <5%
sCR	CR + normal light-chain ratio + no clonal cells on biopsy
MRD-	No clone at 1 in 100,000 cells (NGF or NGS); sustained if repeated 1 year apart

Measure before each cycle at first: SPEP + serum free light chains (urine every ~6 months). No measurable protein: follow light chains, marrow or PET-CT. Progression = 25% rise from the lowest value (serum ≥0.5 g/dL absolute), new lesions or CRAB. MRD testing is mostly for trials; daratumumab can show up as an IgG κ band.

Figure 15. Response categories (IMWG 2016, Kumar 2016; UpToDate response review).

Living with myeloma: a rhythm of tests for life

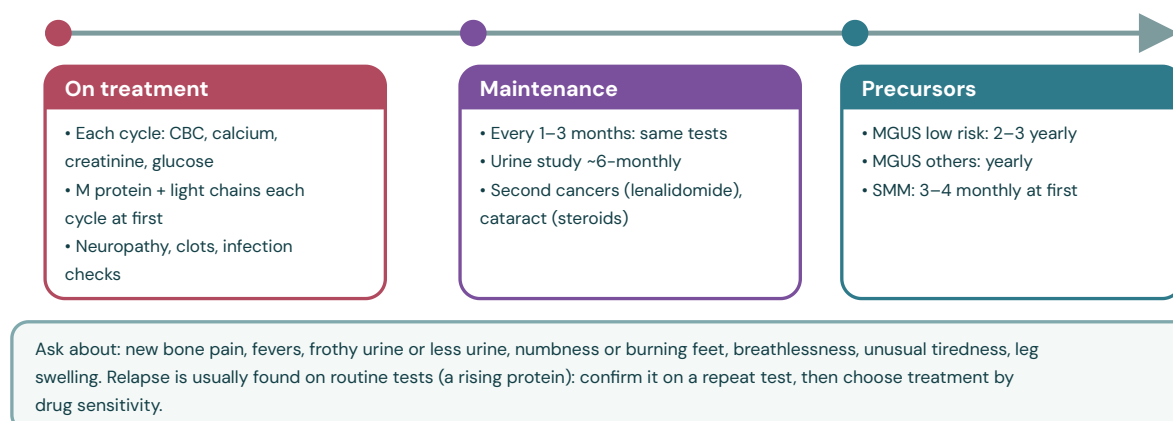


Figure 16. Follow-up rhythm (UpToDate response, MGUS and smoldering myeloma reviews). Individualise.

- **Response (IMWG):** partial (≥50% fall), very good partial (≥90%), complete (negative immunofixation, marrow <5%), stringent complete and MRD-negative (1 in 100,000 cells) ([Kumar 2016](#)^[49]). MRD-guided decisions remain investigational outside trials.
- **Monitoring:** before each cycle at first (CBC, calcium, creatinine, glucose, M protein and light chains); urine every ~6 months; marrow only to confirm CR or when unsure; imaging for symptoms, plasmacytomas or non-secretory disease.
- **Late effects:** neuropathy (bortezomib, thalidomide), second cancers (lenalidomide after HCT), cataract and diabetes (steroids), jaw osteonecrosis (bone drugs), myeloid neoplasms after HCT, vertebral collapse and height loss, chronic kidney disease.
- **Living with myeloma:** a chronic, relapsing illness managed in lines of treatment. Encourage walking and safe exercise (avoid heavy lifting and twisting with spinal disease), hydration, vaccines, dental care, fall prevention, and honest discussion of goals at each relapse.

SHARE WITH PATIENTS: LIFE WITH MYELOMA

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A normal blood count means myeloma has completely disappeared?

Myeloma patients should avoid all exercise because their bones are weak?

People with multiple myeloma can't live meaningful, productive lives?

09 Landmark trials

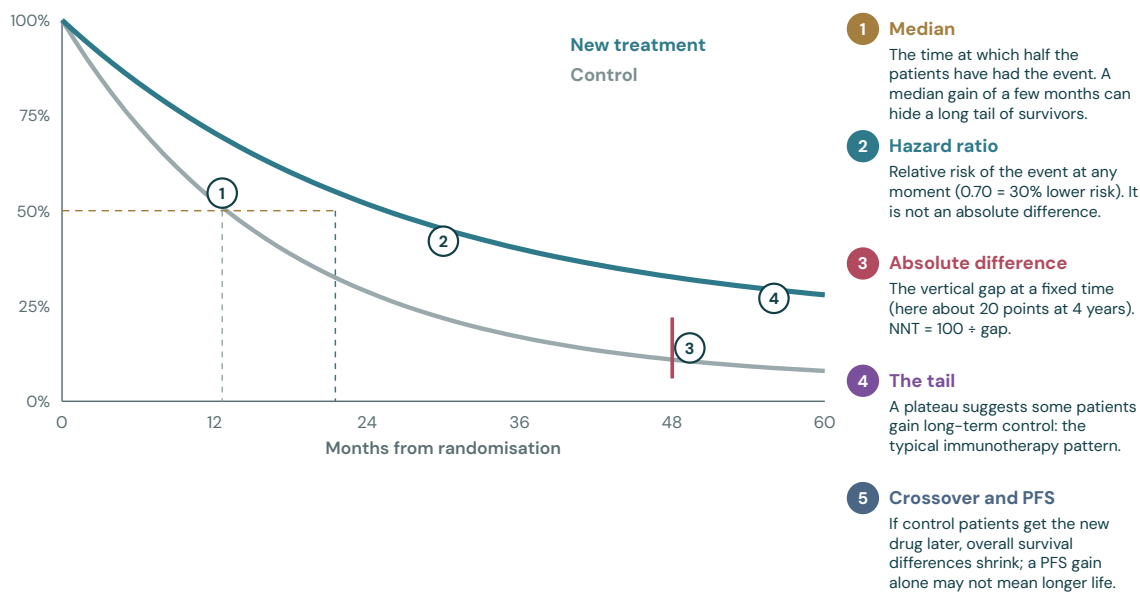


Figure 17. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

The trials behind today's choices

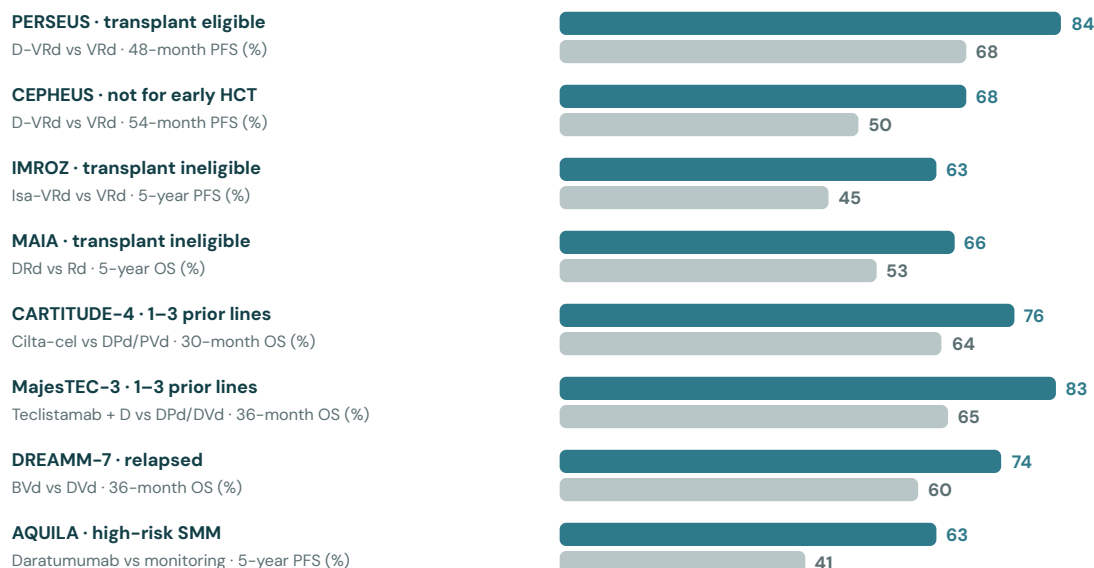


Figure 18. Landmark results as reported in the UpToDate initial treatment, relapsed disease and smoldering myeloma reviews.

- **PERSEUS**^[26] and **CEPHEUS**^[28]: daratumumab added to VRd → deeper MRD negativity, longer PFS → quadruplet induction for most.
- **IMROZ**^[29]: Isa-VRd vs VRd in transplant-ineligible patients → 5-year PFS 63% vs 45%.
- **MAIA**^[31]: DRd vs Rd in older patients → OS benefit → DRd for the frail and those with neuropathy.
- **IFM 2009**^[32] and **DETERMINATION**^[33]: early HCT → longer PFS, same OS → timing can be individualised.

- [CARTITUDE-4](#)^[4] and [MajesTEC-3](#)^[5]: BCMA CAR-T and teclistamab plus daratumumab improve OS at first relapse.
- [AQUILA](#)^[23]: daratumumab in high-risk smoldering myeloma → fewer progressions and better OS → early treatment for high-risk SMM.
- [TEAMM](#)^[46] and [Myeloma IX](#)^[43]: simple supportive care (antibiotic prophylaxis, zoledronic acid) saves lives.

10 Practice pearls & pitfalls

- Back pain + anaemia + high ESR or total protein in an adult: SPEP with immunofixation and serum free light chains before more painkillers.
- Unexplained kidney injury with bland urine: check free light chains the same day; cast nephropathy is a race against time.
- A normal SPEP, a negative dipstick or a normal X-ray does not exclude myeloma.
- Image with low-dose whole-body CT, PET-CT or MRI; bone scans miss lytic lesions.
- Never fix a solitary bone lesion without a biopsy; never call a plasmacytoma "solitary" without marrow and whole-body imaging.
- Most MGUS never progresses: risk-stratify, reassure, and explain red-flag symptoms.
- High-risk smoldering myeloma: offer early treatment; low risk: watch.
- Avoid NSAIDs, dehydration and contrast in myeloma; dose-adjust lenalidomide and bisphosphonates for kidney function.
- Every patient on an IMiD needs clot prevention; every patient starting treatment needs levofloxacin, aciclovir (with PIs and anti-CD38) and vaccines.
- Back pain with leg weakness or bladder change: whole-spine MRI within 24 hours and dexamethasone.
- At relapse, ask "refractory to what?" before choosing; BCMA-directed therapy improves survival.

11 Case vignettes: lines of management

Nine cases from the clinic.

CASE 1 Myeloma · back pain · transplant eligible

Six months of "lumbar spondylosis"

58 years, man

ISS II

Standard risk

A 58-year-old farmer from a village near Nellore has had low back pain for 6 months, treated with diclofenac and physiotherapy. He has lost 4 kg and feels tired. Haemoglobin 8.9 g/dL, ESR 110 mm/h, total protein 9.8 g/dL with albumin 3.1 g/dL, creatinine 1.4 mg/dL, calcium 10.6 mg/dL.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

SUSPECT

Anaemia, high ESR and a wide globulin gap with back pain: myeloma until proved otherwise. Stop NSAIDs (kidneys).

2

DIAGNOSE

SPEP: 4.8 g/dL spike, IgG κ on immunofixation; κ/λ ratio 38. Marrow: 42% clonal plasma cells. Low-dose whole-body CT: lytic lesions in L2, pelvis and skull; L2 wedge collapse without canal compromise.

3

STAGE

Beta-2 microglobulin 4.1 mg/L, LDH normal; FISH: hyperdiploid, no del(17p), no high-risk translocation, no 1q gain: standard risk; R-ISS II.

4

TREAT

Quadruplet (D-VRd) if available, otherwise VRd or VTd, for 3–6 cycles; stem cell collection; early or deferred HCT discussed; lenalidomide maintenance for about 2 years. Zoledronic acid after dental check; aspirin; levofloxacin and aciclovir; vaccines; kyphoplasty if L2 pain persists.

TEACHING POINTS

- Back pain with anaemia and high ESR: test for a monoclonal protein.
- Use CT, PET-CT or MRI, not X-rays.
- Transplant eligibility is about fitness, not age.

See: Sections 02, 03 and 06, Algorithm 2.

CASE 2 Light-chain myeloma · kidney injury

Vomiting, confusion and a creatinine of 6

66 years, woman

Light chain κ

Cast nephropathy

A 66-year-old has 2 weeks of vomiting, thirst and confusion after taking painkillers for rib pain. Creatinine 6.2 mg/dL (normal 3 months ago), calcium 13.1 mg/dL, haemoglobin 9.4 g/dL. Urine dipstick: trace protein only. SPEP: no spike.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

SUSPECT

Acute kidney injury with high calcium, anaemia and bland urine: light-chain cast nephropathy. A negative SPEP and dipstick do not exclude it.

2

DIAGNOSE

Serum free κ 4800 mg/L, λ 9 mg/L (ratio >500); urine immunofixation: free κ . Marrow 55% κ -restricted plasma cells. Very high light chains and no other cause: biopsy can be deferred.

3

TREAT TODAY

Isotonic fluids, then fluids for ~3 L urine a day; glucocorticoids; zoledronic acid is avoided (clearance <30) → denosumab or calcitonin bridge; stop NSAIDs; start bortezomib + dexamethasone ± daratumumab at once. Dialysis only for usual indications.

4

THEN

Goal: rapid fall in free κ . Plasma exchange or high cut-off dialysis debated. Many recover kidney function; dose-adjust lenalidomide later; transplant still possible with good recovery.

TEACHING POINTS

- Unexplained AKI: free light chains on day 1.
- Treat the clone fast: kidney recovery depends on it.
- Denosumab rather than a bisphosphonate when clearance ≤ 30 .

See: Sections 02, 03 and 06 (kidney), Algorithm 1.

CASE 3 MGUS · low risk**An incidental band on a health check**

61 years, man

IgG κ 0.7 g/dL

Normal ratio

A 61-year-old bank manager had SPEP at a corporate health check because total protein was 8.4 g/dL. A 0.7 g/dL IgG κ band was found. He is well; CBC, calcium and creatinine are normal.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

CLASSIFY

IgG, <1.5 g/dL, normal free light-chain ratio, no CRAB features: low-risk MGUS (20-year progression about 5%).

2

AVOID HARM

No marrow biopsy and no imaging needed; no treatment; no bone drug unless osteoporosis.

3

FOLLOW

Repeat SPEP, light chains, CBC, calcium and creatinine at 6 months; if stable, every 2–3 years.

4

EDUCATE

Report new bone pain, fatigue, frothy or reduced urine, numbness or infections promptly; progression can be abrupt.

TEACHING POINTS

- Most MGUS never progresses.
- Three risk factors guide follow-up intensity.
- Over-investigation and over-labelling harm patients.

See: Section 06 (MGUS), Algorithm 5.

CASE 4 Smoldering myeloma · high risk**A large protein, no symptoms**

54 years, woman

20/2/20: 3 factors

MRI clear

A 54-year-old teacher is found to have an IgA λ protein of 3.4 g/dL during evaluation of a raised ESR. She is well. Haemoglobin, calcium and creatinine are normal.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 WORK UP

Marrow: 30% clonal plasma cells (no $\geq 60\%$); light-chain ratio 26 (not ≥ 100); whole-body MRI: no focal lesions; low-dose CT: no lytic lesions. Smoldering myeloma.

2 STRATIFY

Plasma cells $> 20\%$, M protein > 2 g/dL, ratio > 20 : all three 20/2/20 factors = high risk.

3 DECIDE

Discuss early treatment: daratumumab for up to 3 years (AQUILA: better PFS and OS) or lenalidomide-based therapy if that is what is available; a trial if one exists. Full myeloma regimens are not used.

4 FOLLOW

If she declines: tests every 3–4 months and yearly MRI, with clear red-flag advice.

TEACHING POINTS

- SMM is a spectrum: 20/2/20 separates watch from treat.
- SLiM features make it myeloma, not SMM.
- Early treatment of high-risk SMM improves survival.

See: Section O6 (smoldering), Algorithm 5.

CASE 5 Solitary plasmacytoma of bone

Mid-back pain and a collapsed vertebra

47 years, man

T9 lesion

Marrow clean

A 47-year-old electrician has 2 months of mid-back pain. MRI: a destructive T9 lesion with mild epidural extension, no cord signal change, no weakness.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 DIAGNOSE

CT-guided biopsy: sheets of λ -restricted plasma cells (CD138+). Marrow aspirate and biopsy: no clonal plasma cells. PET-CT and whole-spine MRI: no other lesion. Small IgG λ band; no CRAB.

2 STABILISE

SINS score and spinal surgery opinion: stable; dexamethasone not needed (no deficit).

3 TREAT

Involved-site RT 40–45 Gy over about 4 weeks covering T8–T10 with margin; no chemotherapy, no bisphosphonate.

4 FOLLOW

M protein and light chains every 3–6 months, imaging if symptoms; persistence of the M protein at 1 year increases myeloma risk; half or more eventually develop myeloma.

TEACHING POINTS

- Biopsy before fixation or RT.
- Solitary needs marrow and whole-body imaging to prove it.
- RT 35–50 Gy cures some; follow for life.

See: Sections O3, O5 and O6, Algorithm 5.

CASE 6 Solitary extramedullary plasmacytoma**Nose bleeds and a blocked nostril**

52 years, man

Nasal cavity

Incompletely excised

A 52-year-old shopkeeper has had right nasal obstruction and recurrent epistaxis for 4 months. An ENT surgeon removed a "polyp" piecemeal; histology shows plasma cells.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**CONFIRM**

Immunohistochemistry: CD138+, κ-restricted plasma cells; exclude MALT lymphoma with plasmacytic differentiation (CD20, light chains, flow).

2**STAGE**

PET-CT: residual nasal disease only; marrow <5% polyclonal plasma cells; no M protein; normal CBC, calcium, creatinine.

3**TREAT**

Involved-site RT 40–50 Gy (incompletely excised); no chemotherapy.

4**FOLLOW**

Local recurrence <7%; about 10–15% develop myeloma; median survival over 10 years. ENT review and blood tests every 3–6 months at first.

TEACHING POINTS

- Nasal "polyp" with plasma cells: full staging before calling it solitary.
- Incomplete excision → RT 40–50 Gy.
- SEP behaves better than SPB.

See: Sections 02, 05 and 06, Algorithm 5.

CASE 7 Myeloma · frail older adult**Fatigue, falls and an IgA protein**

78 years, woman

Frail

Neuropathy (diabetes)

A 78-year-old widow with diabetic neuropathy, two recent falls and haemoglobin 8.6 g/dL has IgA κ myeloma (2.9 g/dL) with lytic lesions and 35% marrow plasma cells. Creatinine clearance 45 mL/min. She lives with her son.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**ASSESS**

Frailty assessment (age, function, comorbidity): frail. Not a transplant candidate. FISH: t(11;14), standard risk.

2**TREAT**

DRd with early stopping of dexamethasone (avoids bortezomib neuropathy; MAIA OS benefit), doses adjusted for kidney function; if daratumumab is unaffordable: dose-reduced Rd or VCD with subcutaneous weekly bortezomib if neuropathy allows.

3**PREVENT**

Aspirin with lenalidomide (SAVED low); levofloxacin for 3 months; aciclovir with daratumumab; vaccines; zoledronic acid with dental check; fall prevention, vitamin D and calcium.

4**PLAN**

Lenalidomide maintenance as tolerated; t(11;14) noted for venetoclax at relapse.

TEACHING POINTS

- Frailty, not age, decides intensity.
- DRd suits neuropathy and older patients.
- Supportive care prevents early deaths.

See: Sections O4 and O6, Algorithm 3.

CASE 8 Myeloma · first relapse**Rising protein on maintenance**

55 years, man

Lenalidomide-refractory

Post-HCT

A 55-year-old engineer received VRd, autologous HCT and lenalidomide maintenance. At 30 months his IgG rises from 0.2 to 1.4 g/dL over two visits, with new rib pain.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**CONFIRM**

Progression ($\geq 25\%$ rise, ≥ 0.5 g/dL absolute, new rib lesion on PET-CT): clinical relapse on lenalidomide = lenalidomide-refractory. Repeat FISH: new 1q gain.

2**OPTIONS**

BCMA-directed: cilta-cel (CARTITUDE-4) at a CAR-T centre, teclistamab plus daratumumab (MajesTEC-3), or BVd (DREAMM-7). Alternatives if not accessible: DPd, DKd or KPd.

3**SAFETY**

CRS/ICANS monitoring with T-cell therapies; IVIG for low IgG; PJP and antiviral prophylaxis; eye checks with belantamab.

4**ALSO**

Palliative RT 8 Gy single fraction to the painful rib; continue zoledronic acid.

TEACHING POINTS

- Ask "refractory to what?" at every relapse.
- BCMA-directed therapy improves survival from first relapse.
- Refer early for cellular therapy.

See: Section O6 (relapse), Algorithm 4.

CASE 9 Emergency · cord compression**Back pain, then weak legs**

69 years, man

Known myeloma

T6 compression

A 69-year-old on VRd for myeloma reports worsening thoracic back pain for a week and, since yesterday, difficulty climbing stairs and passing urine.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**RECOGNISE**

Back pain then weakness and urinary retention: epidural spinal cord compression until proved otherwise.

2

IMAGE

MRI of the whole spine with contrast within 24 hours (transfer if needed): T6 plasmacytoma compressing the cord; no retropulsed bone.

3

TREAT

Dexamethasone at once; urgent RT with fractionation (better motor recovery); spinal surgery if the spine is unstable, bone is in the canal or weakness progresses; systemic therapy continued or intensified.

4

SUPPORT

Bladder catheter, bowel care, pressure care, clot prevention, physiotherapy and rehabilitation.

TEACHING POINTS

- Motor outcome depends on how fast you act.
- Image the whole spine, not one level.
- Most myeloma compressions respond to RT plus dexamethasone.

See: Sections O5 and O6, Algorithm 1.

12 References & guidelines

- NCCN Guidelines: Multiple Myeloma, and Systemic Light Chain Amyloidosis/Waldenström for the differentials (current versions); International Myeloma Working Group and IMS/IMWG consensus papers listed below; ILROG radiotherapy guidelines; WHO Classification 5th edition and the International Consensus Classification (2022).
- Cross-checked in October 2026 against 28 UpToDate topic reviews: multiple myeloma: clinical features, laboratory manifestations and diagnosis; pathobiology; staging and prognostic studies; overview of management; initial treatment; use of hematopoietic cell transplantation; determining eligibility for autologous HCT; treatment of relapsed disease; evaluating response to treatment; administration considerations for common therapies; treatment protocols; management in resource-limited settings; the use of osteoclast inhibitors; prevention of venous thromboembolism; infections in patients with multiple myeloma; kidney disease in myeloma and other monoclonal gammopathies (etiology and evaluation; treatment and prognosis); monoclonal gammopathy of renal significance; clinical presentation and evaluation, and management, of pathologic fractures; neoplastic epidural spinal cord compression; radiation therapy for painful bone metastases; laboratory methods for analyzing monoclonal proteins; diagnosis of MGUS; clinical course and management of MGUS; smoldering multiple myeloma; solitary plasmacytoma of bone; solitary extramedullary plasmacytoma. All trial citations below come from the reference lists of these reviews; the three Indian papers were found and verified by web search on 17 October 2026.
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Educational summary for health professionals, written in our own words from current guidelines and primary trials. No drug doses are given. Hodgkin, aggressive B-cell, indolent B-cell, T-cell and cutaneous lymphomas are parts 1–5; Waldenström macroglobulinaemia is covered in the indolent B-cell module; AL amyloidosis, POEMS syndrome and plasma cell leukaemia are mentioned here only as differentials. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.