Multiple Myeloma: Maintenance Therapy to Prolong Survival and Improve Life after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

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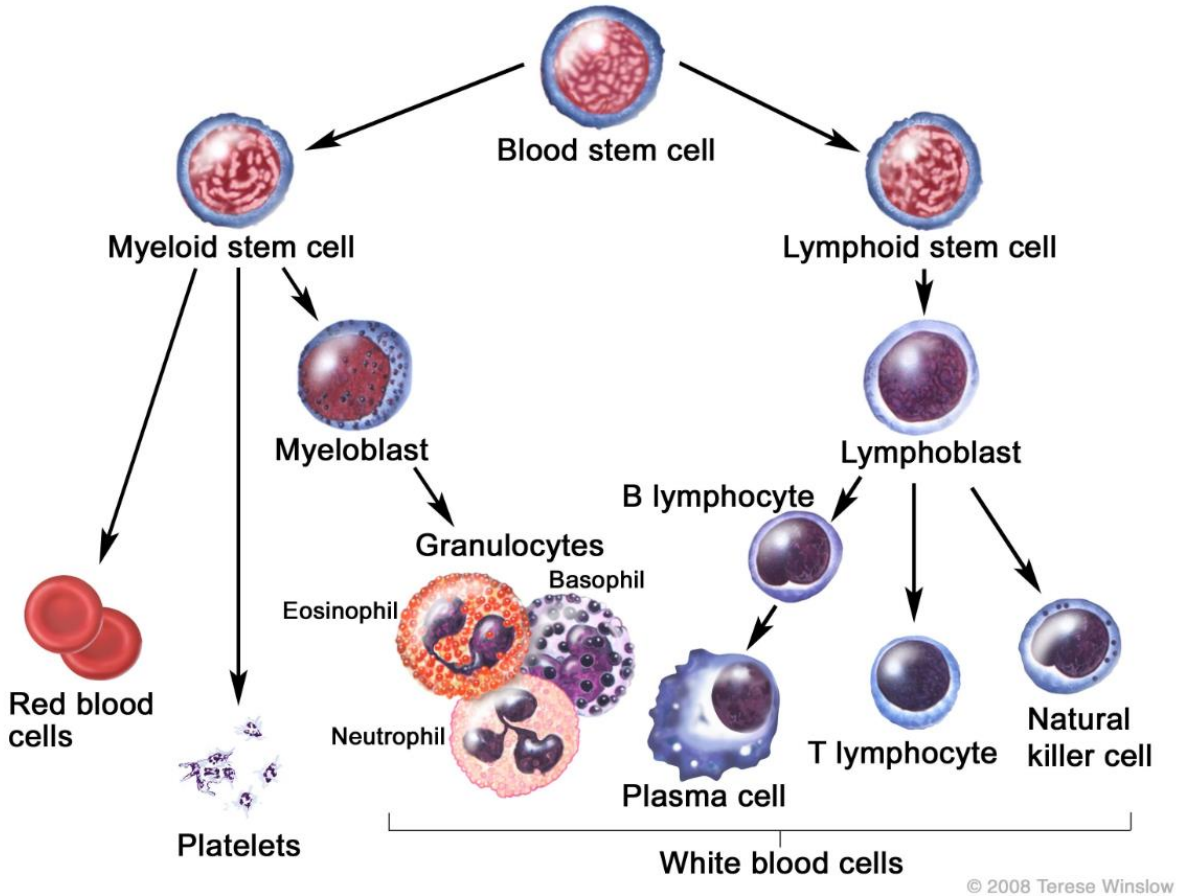
Learning Objectives

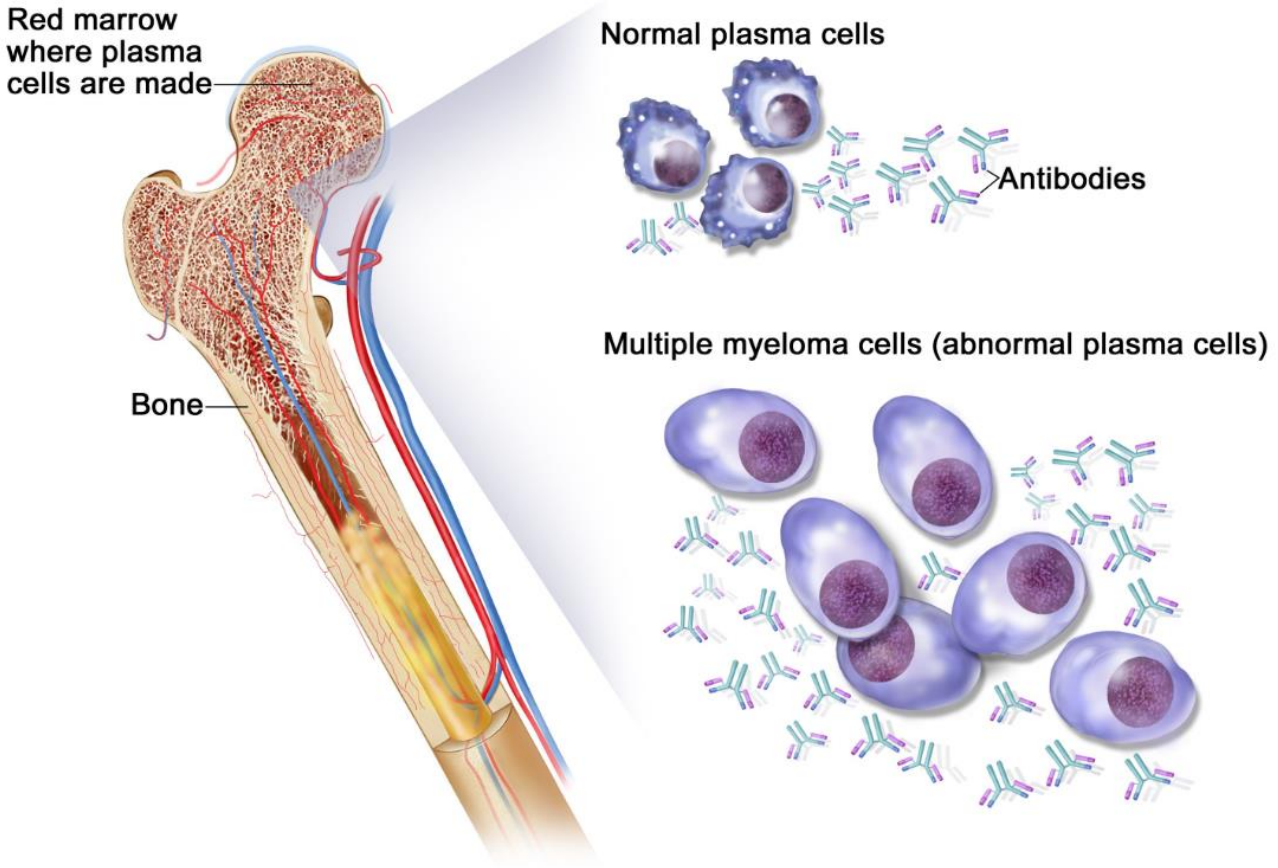
- Learn how Multiple Myeloma is diagnosed and staged
- Identify the treatment schema for newly diagnosed Multiple Myeloma patients.
- Identify what is maintenance treatment in Multiple Myeloma.
- Learn about the different treatment strategies used for maintenance in patients with Multiple Myeloma and why they are used.

What is Multiple Myeloma?

- Multiple Myeloma (MM) is a blood cancer of a type of blood cell called a plasma cell.
- Plasma cells normally make antibodies to help fight infections.
- MM happens when plasma cells divide out of control making abnormal proteins called M-protein.
- MM is more common in African Americans and male patients.
- The median age at diagnosis is 69 years.

What is Multiple Myeloma?

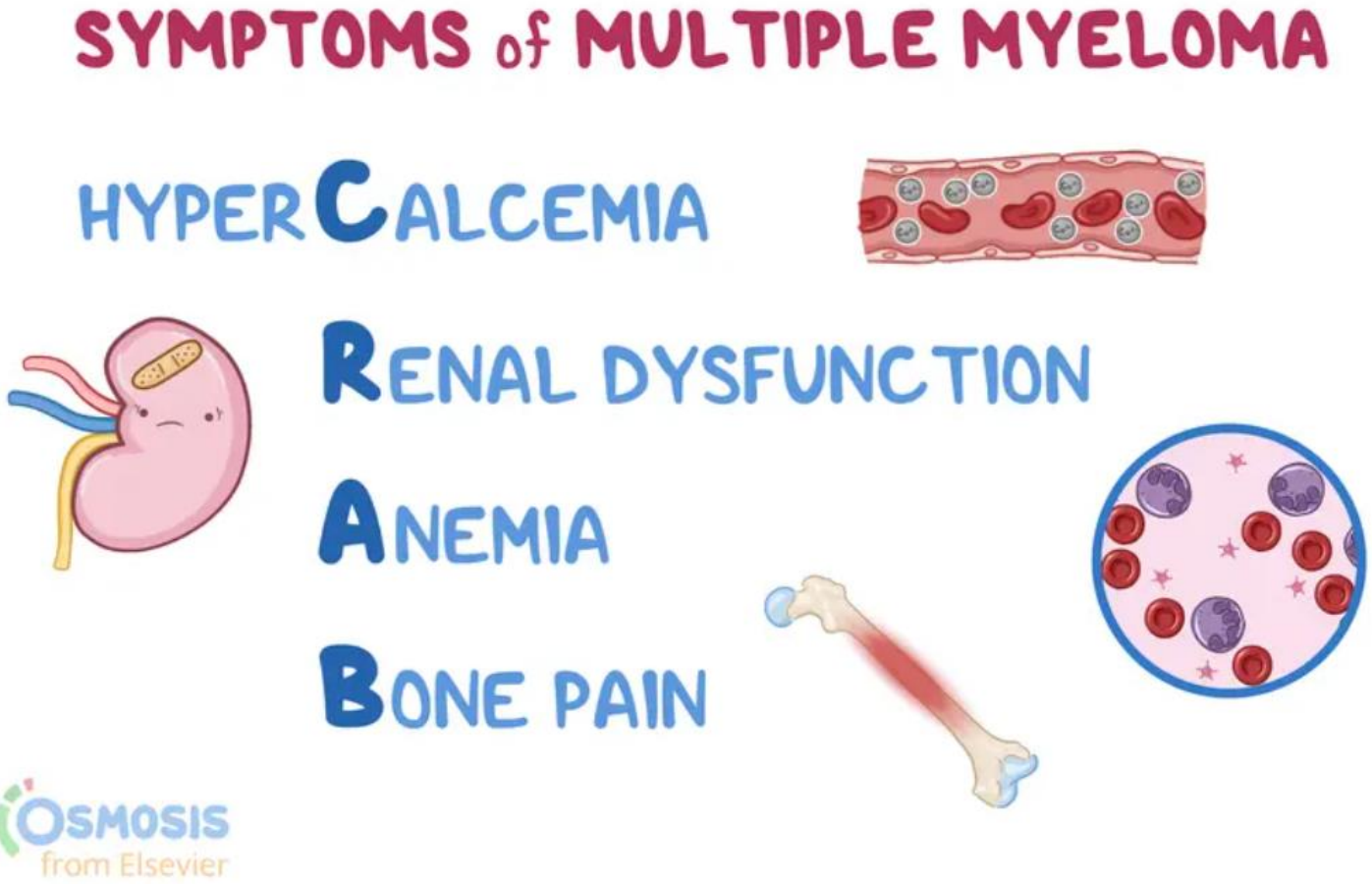




NCI 2024

How is Multiple Myeloma Diagnosed and Staged?

- Multiple Myeloma (MM) is diagnosed with blood work, body imaging (CT scan or PET CT), and a bone marrow biopsy.
- There are 3 different stages of MM based on how much disease is present and certain mutations in the myeloma cells.



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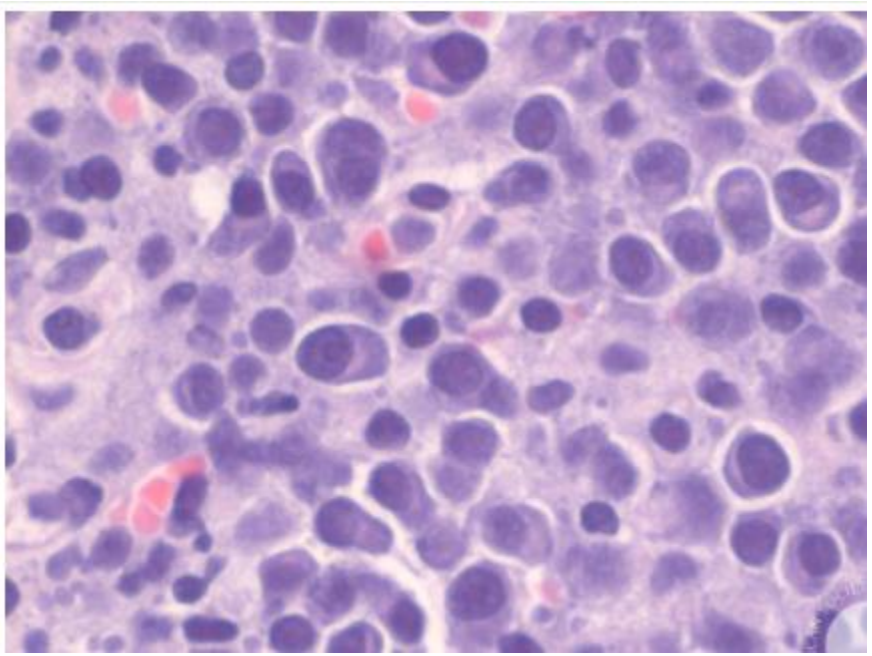
How is Multiple Myeloma Diagnosed and Staged?



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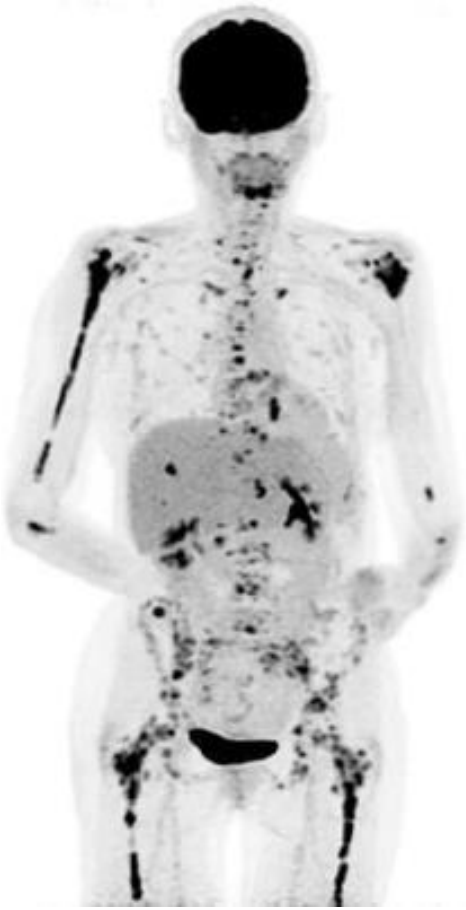


The Revised International Staging System (R-ISS)

- Stage 1
  - Normal albumin (>3.5 g/dL)
  - Beta 2-microglobulin less than 3.5 mg/L
- Stage 2
  - Not Stage 1 or 3
- Stage 3
  - Beta 2-microglobulin greater than 5.5 mg/L
  - Very low albumin

Revised International Staging System (R-ISS)

Stage	Criteria
I	Sβ2M < 3.5 mg/l Serum albumin ≥ 3.5 g/dl Standard-risk chromosomal abnormalities (CA) by iFISH Normal LDH
II	Not R-ISS stage I or III
III	Sβ2M ≥ 5.5 mg/L and either High-risk CA by FISH OR High LDH

International Myeloma Foundation

*Certain qualifiers such as lactate dehydrogenase (LDH) and chromosome changes are also used to identify Stage 1, 2 and 3

How is Multiple Myeloma treated?

Induction

- 3-4 drug regimen for tumor debulking
- Immunomodulatory drugs (IMiDs), proteosome inhibitors (PIs) and monoclonal antibodies

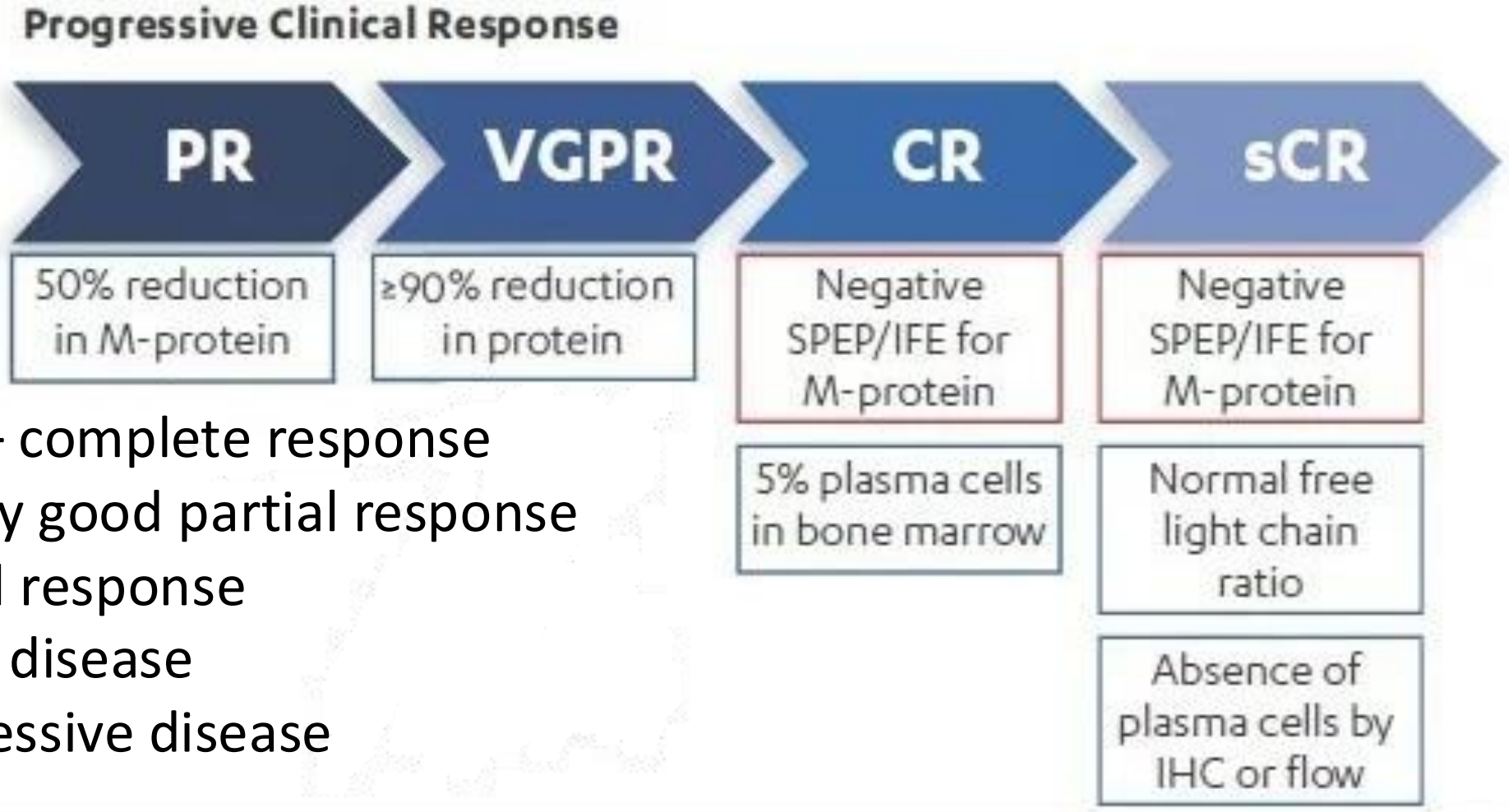
Consolidation

- High-dose chemotherapy and autologous stem cell transplant for eligible patients vs more chemotherapy

Maintenance

- Minimum 2 years of 1-2 drugs to prevent myeloma from returning

Response Criteria in Multiple Myeloma – International Myeloma Working Group (IMWG)



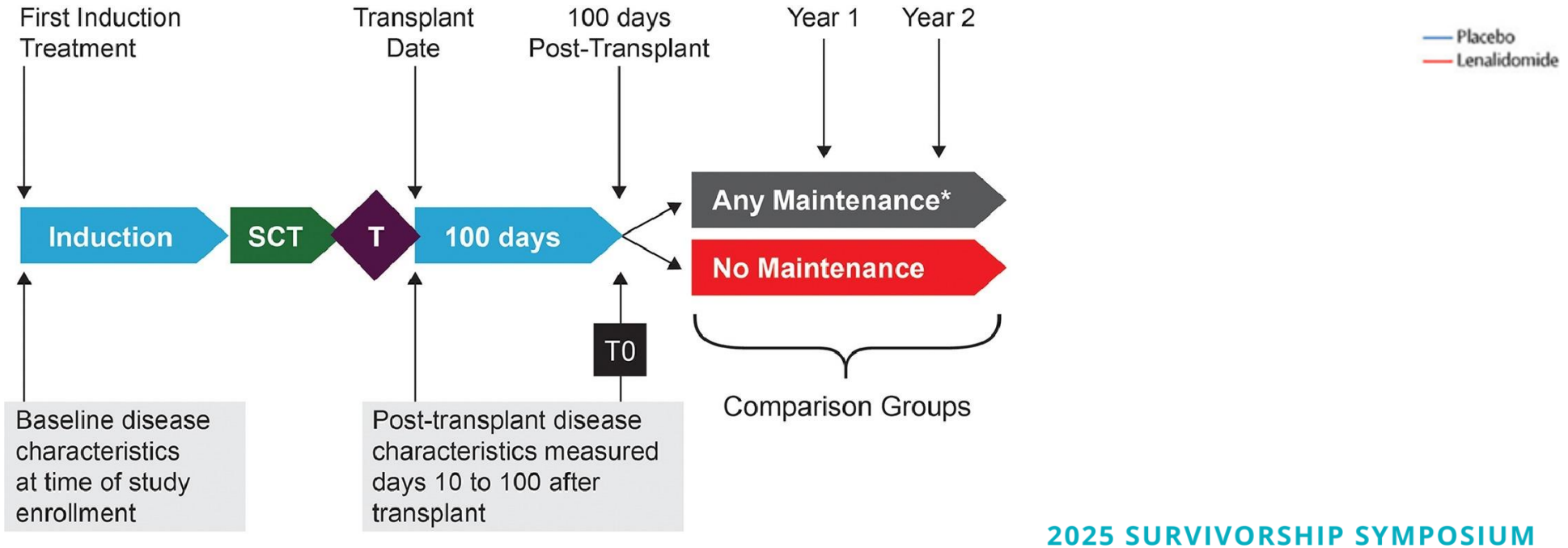
- sCR or CR – complete response
- VGPR – very good partial response
- PR – partial response
- SD – stable disease
- PD – progressive disease

Maintenance Therapy in Multiple Myeloma

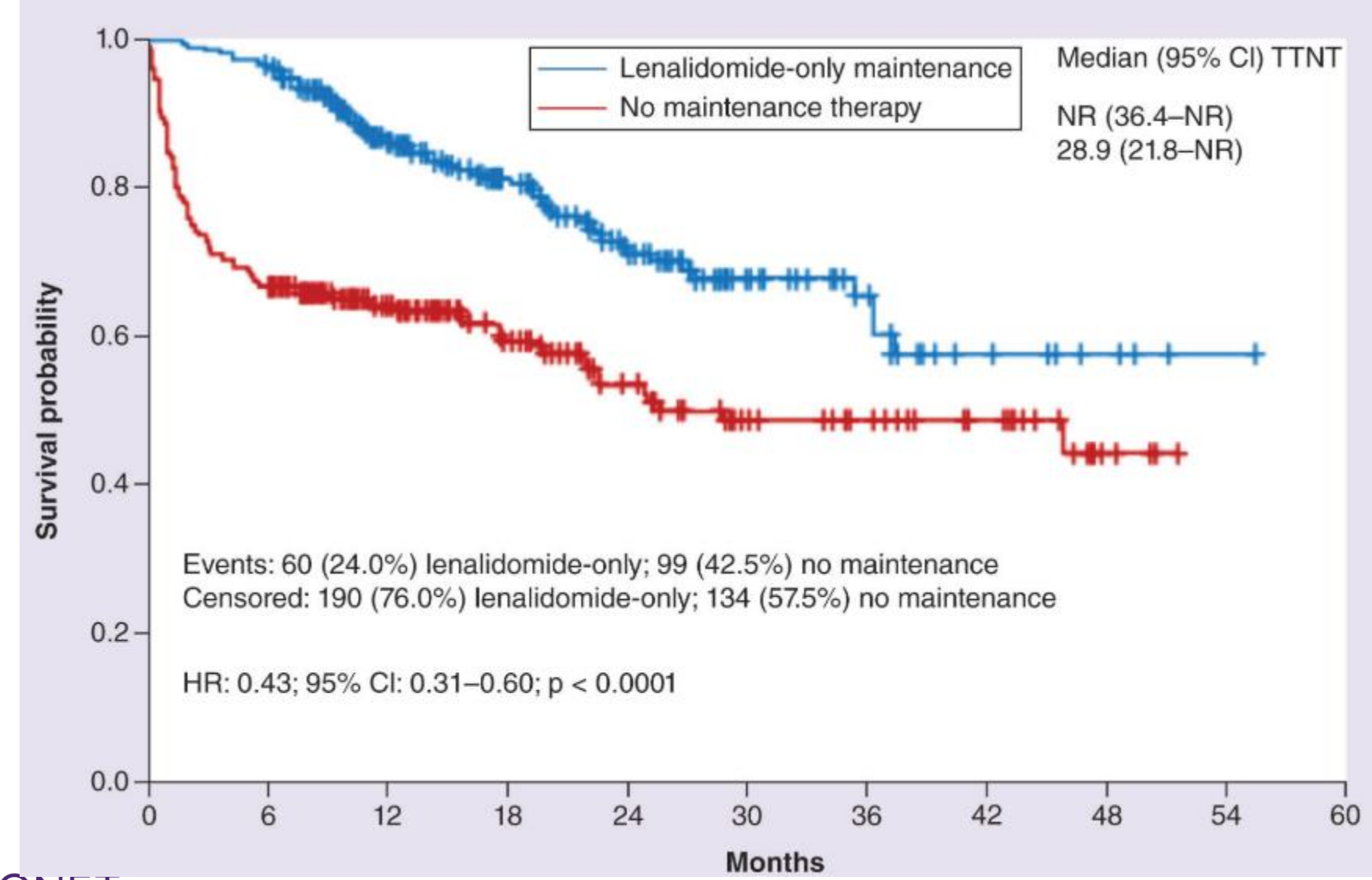
- What is maintenance therapy?
  - Chemotherapy given (usually after autologous transplant) for several years in patients with MM
- What are the goals of maintenance?
  - Prevent disease progression and death
- What drugs are used?
  - The preferred drug is lenalidomide (Revlimid)
  - Other recommended drugs are bortezomib, ixazomib, daratumumab and carfilzomib
- What does the data show?

Lenalidomide Maintenance – Pivotal Trials

- CALGB 100104/IFM 2005-02 – Randomized Phase III trials
  - Newly diagnosed patients after induction
  - Received auto transplant after Melphalan conditioning
  - Randomized to maintenance with lenalidomide or placebo
  - **Patients on lenalidomide maintenance lived longer (better PFS/OS)**



Lenalidomide Maintenance – Pivotal Trials

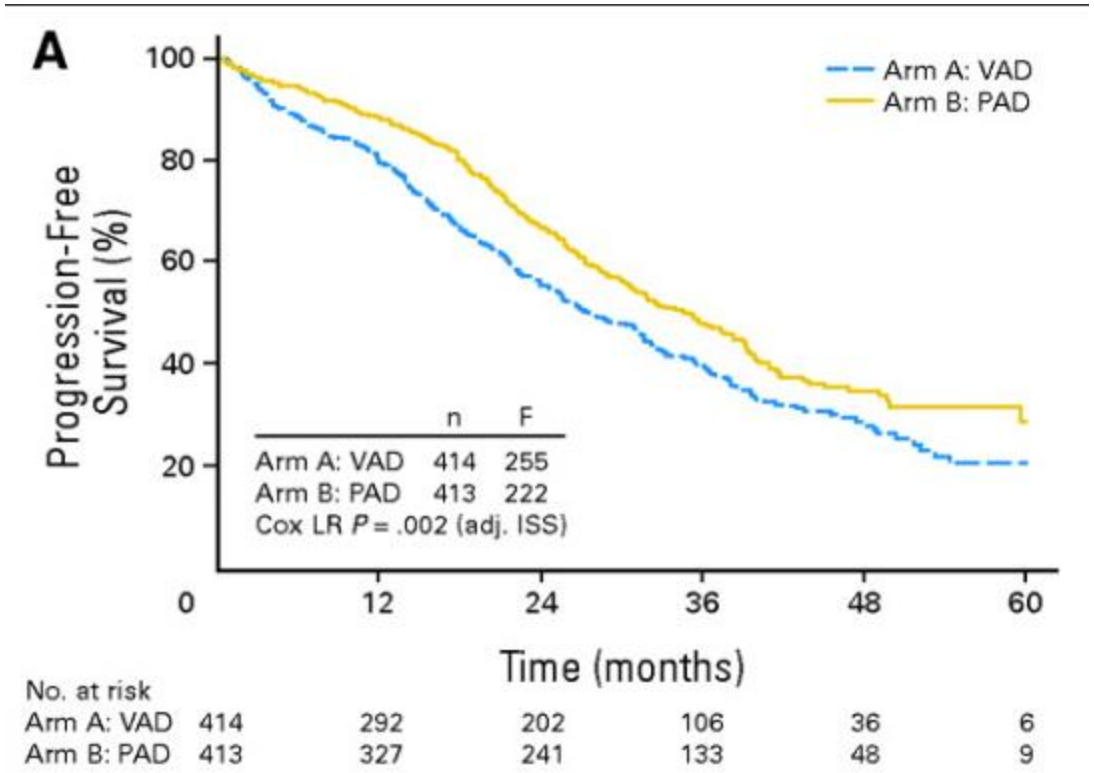


Bortezomib Maintenance – Pivotal Trials

- UPFRONT trial – bortezomib in transplant ineligible patients
- Nordic Myeloma Group Phase III trial
- Bortezomib improved PFS without affecting quality of life
- HOVON-65/GMMG-HD4 – Randomized Phase III trial of bortezomib induction and maintenance
- Compared bortezomib maintenance to thalidomide maintenance
- **Patients on bortezomib did better than those on thalidomide**

Bortezomib Maintenance – Pivotal Trials

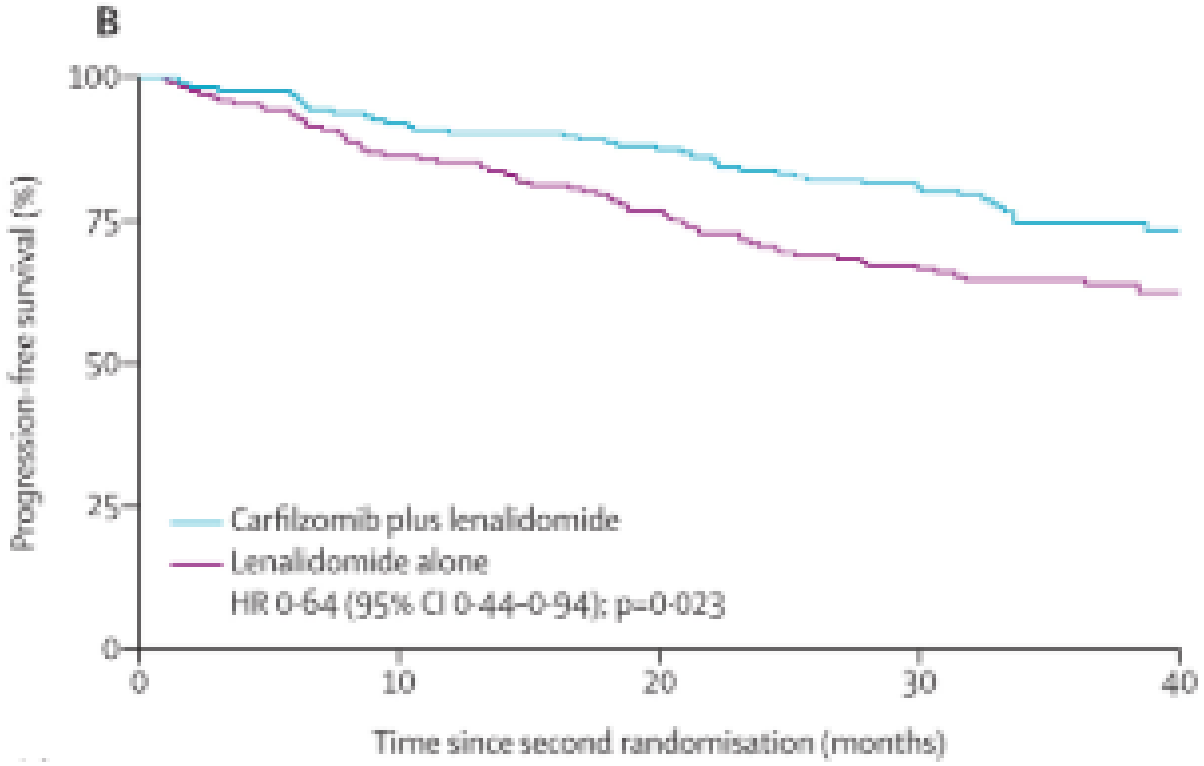
- HOVON-65/GMMG-HD4



Carfilzomib/Lenalidomide Maintenance – Pivotal Trial

- FORTE trial – Phase 2 trial in transplant eligible newly diagnosed MM patients
  - Induction with carfilzomib-lenalidomide-dexamethasone **(KRd)** vs carfilzomib-cyclophosphamide-dexamethasone (KCd)
  - Followed by auto transplant
  - Chemo consolidation and maintenance with either carfilzomib/ lenalidomide or lenalidomide alone

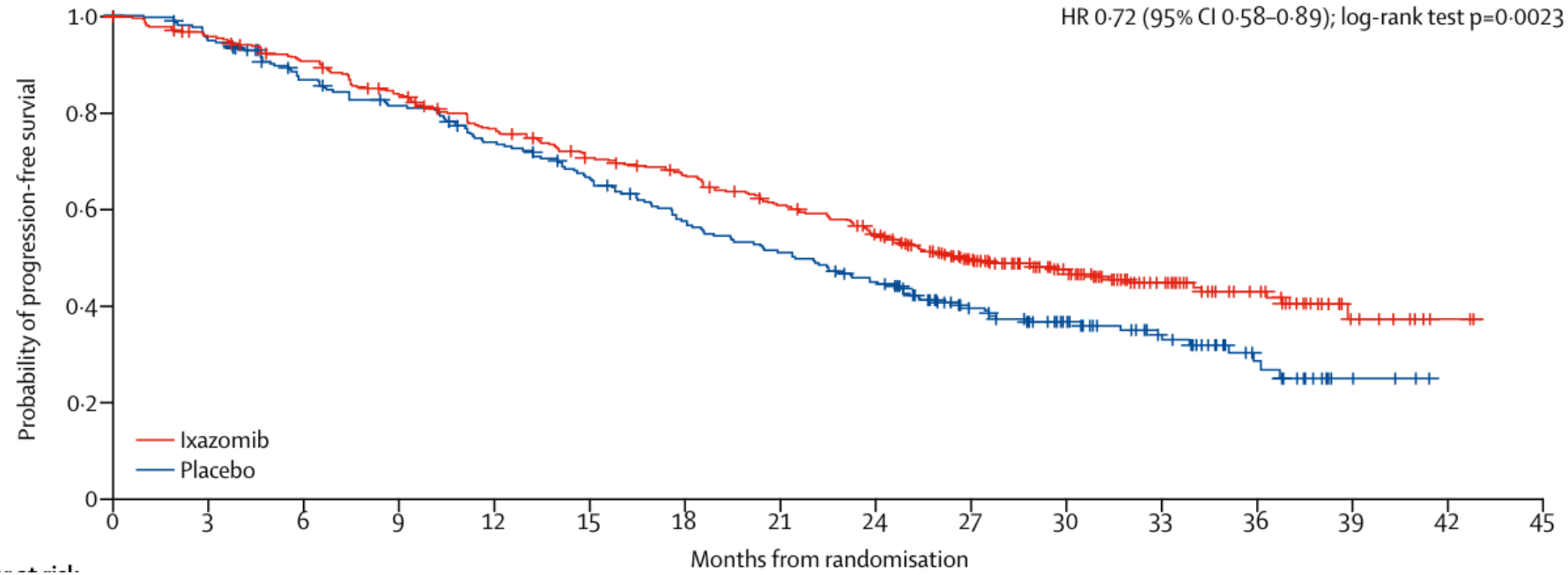
Carfilzomib/Lenalidomide Maintenance – Pivotal Trial



- **KRd followed by auto transplant followed by carfilzomib/lenalidomide maintenance improved PFS**
- Carfilzomib maintenance had higher adverse events than lenalidomide alone
- Useful in high-risk cytogenetic groups

Ixazomib Maintenance – Pivotal Trial

- TOURMALINE-MM3 trial – Phase III randomized trial of oral ixazomib maintenance after autologous stem cell transplant
- **Ixazomib maintenance improved progression-free survival (PFS). No change in OS**



Daratumumab Maintenance – GRIFFIN Trial

- Dara-RVD in newly diagnosed MM induction, transplant and consolidation with Dara/Len vs Len maintenance alone.
- **Patients on Dara/Len did better**

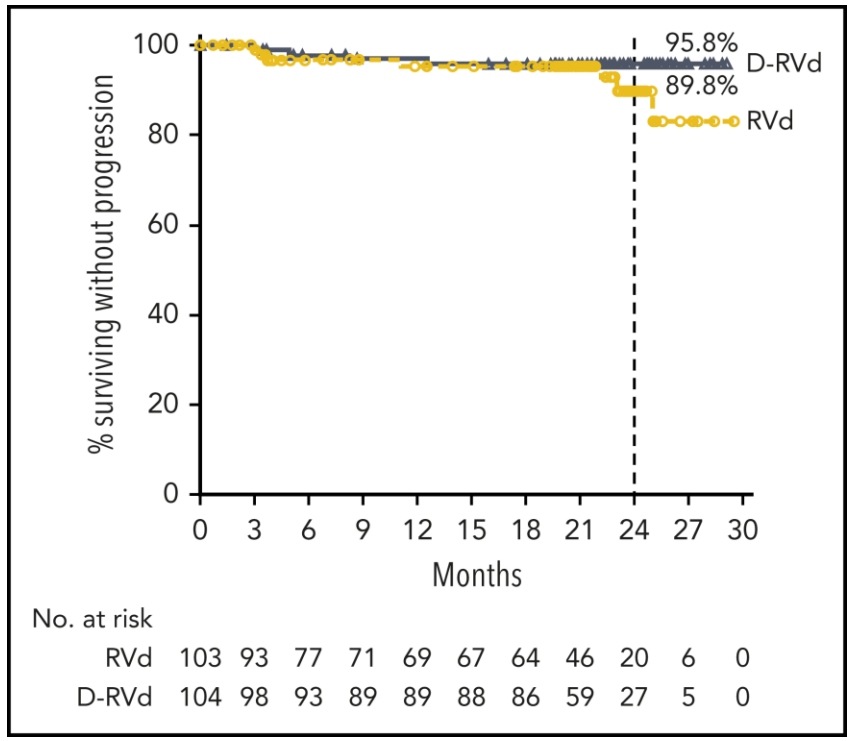
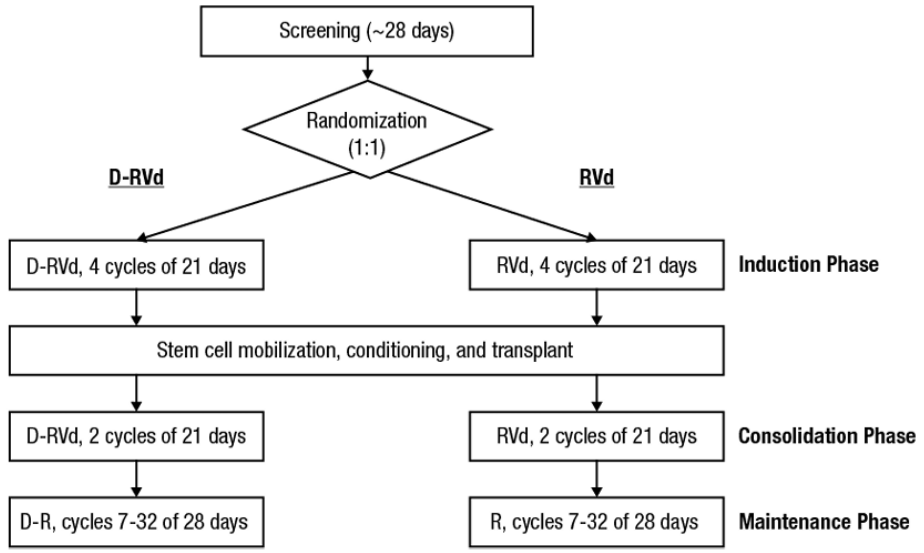


Figure S1. Trial design.



D-RVd, daratumumab/lenalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; D-R, daratumumab/lenalidomide; R, lenalidomide.

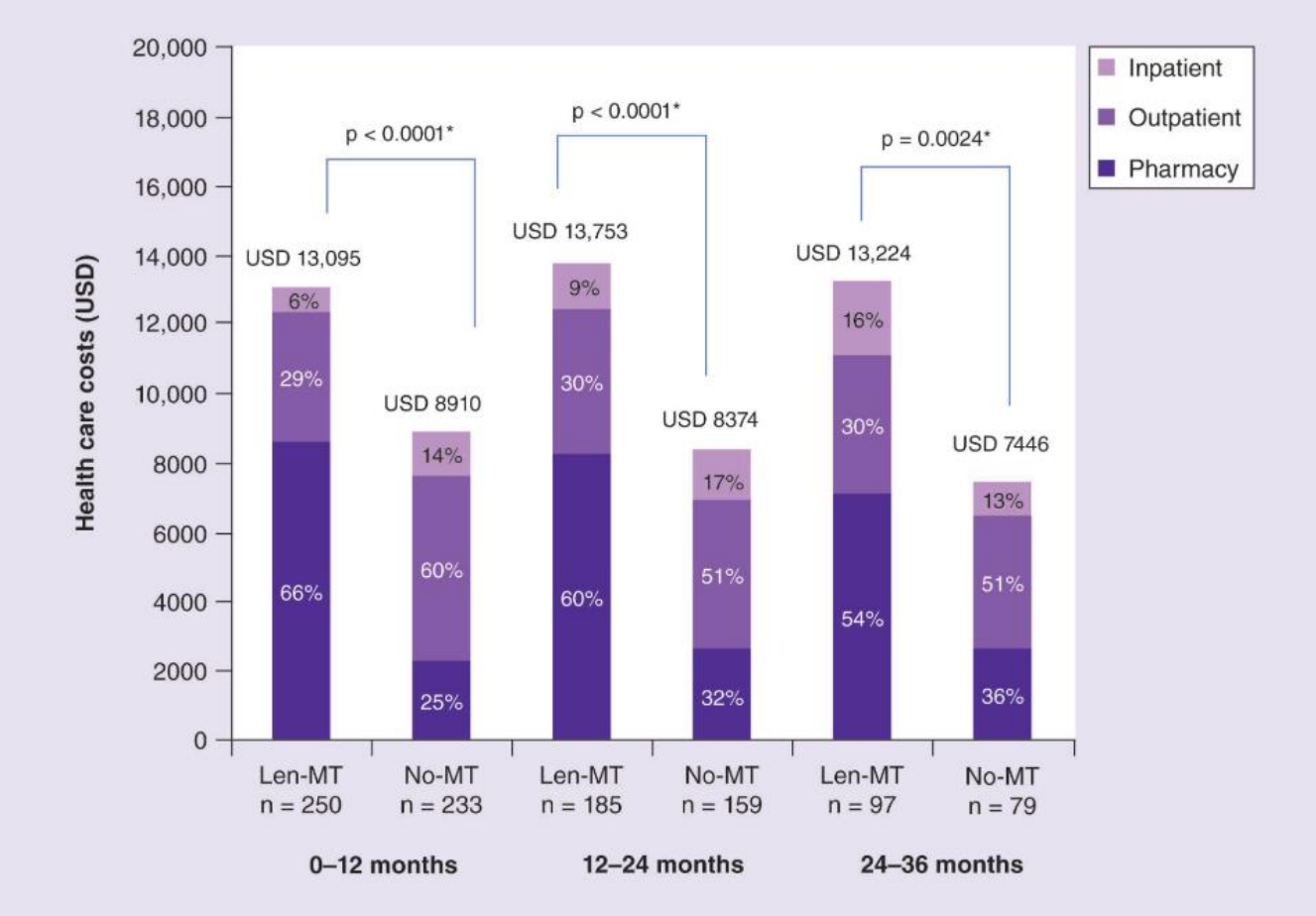
Summary of Maintenance in Multiple Myeloma

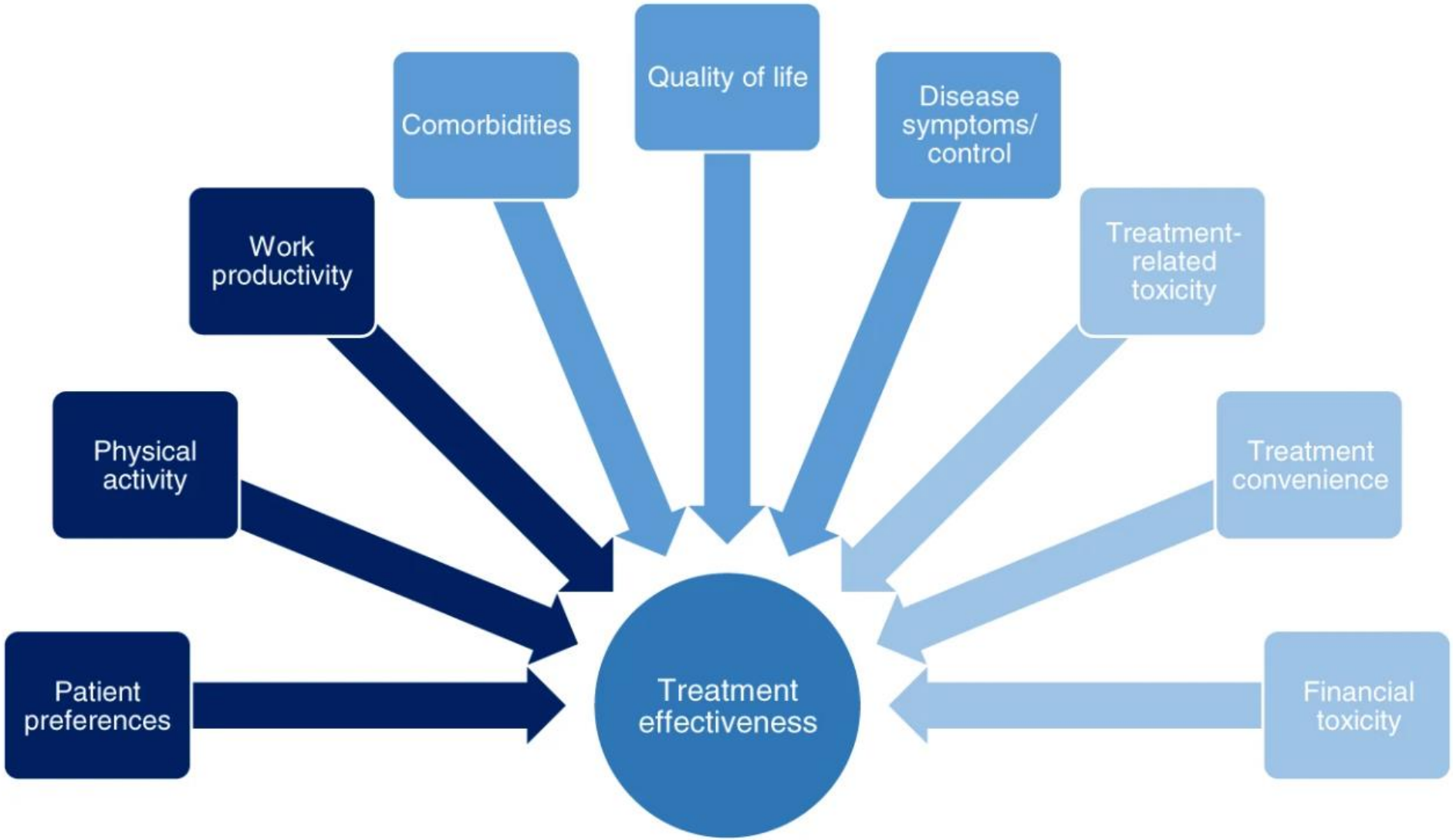
- Lenalidomide is the only drug FDA-approved for maintenance.
- The use of drug combinations might be beneficial in patients with certain chromosome changes that predict for high-risk of relapse.
- There is no consensus on when to stop maintenance, but many studies suggest no added benefit after 3-4 years.
- Using special techniques like next-generation sequencing might predict when it is safe to stop maintenance.

Summary of Maintenance in Multiple Myeloma

- Maintenance therapy is associated with higher costs upfront.
- Despite higher upfront cost, the goal of maintenance is to prevent costs down the line by preventing relapse and treatment for relapse myeloma.
- Side effects of maintenance treatment are usually very manageable.
- Daratumumab seems to be the most promising drug in terms of efficacy and side effect profile.

Real World Cost Analysis of Lenalidomide Maintenance





There are multiple factors of importance to MM patients regarding their treatment that impact on the effectiveness of that treatment in the real-world setting.

CONCLUSIONS

- Maintenance therapy is standard of care in newly diagnosed multiple myeloma patients. It improves outcomes, including overall survival, time to next treatment, and patient quality of life.
- Lenalidomide remains the preferred agent of choice with multiple other options available under specific circumstances.

MAINTENANCE THERAPY
Preferred Regimens • Lenalidomide[h] (category 1)
Other Recommended Regimens • Carfilzomib/lenalidomide[i,h] • Daratumumab/lenalidomide[i,h]
Useful In Certain Circumstances • Bortezomib ± lenalidomide[i,h] • Ixazomib (category 2B)

Questions?

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Let Us Know How We Can Help You

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