INTERNATIONAL MYELOMA FOUNDATION

presents

IMWG CONFERENCE SERIES

"Making Sense of Treatment"

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WEDNESDAY
JUNE 21
2017

IMWGconferenceseries.myeloma.org

Watch the **LIVESTREAM:** **3:00 AM PST/5:00 AM CT/6:00 AM ET**
(replay will also be available)

International Myeloma Working Group
A RESEARCH DIVISION OF THE IMF

Questions for Today's Conference Series

- What is ideal imaging in 2017?
- How will new agents impact frontline therapy?
- Can MRD testing in trials guide decisions?
- Are you proactive about risk assessment?
- Which new therapies will make an impact?
- How important is cost?

What is ideal imaging in 2017

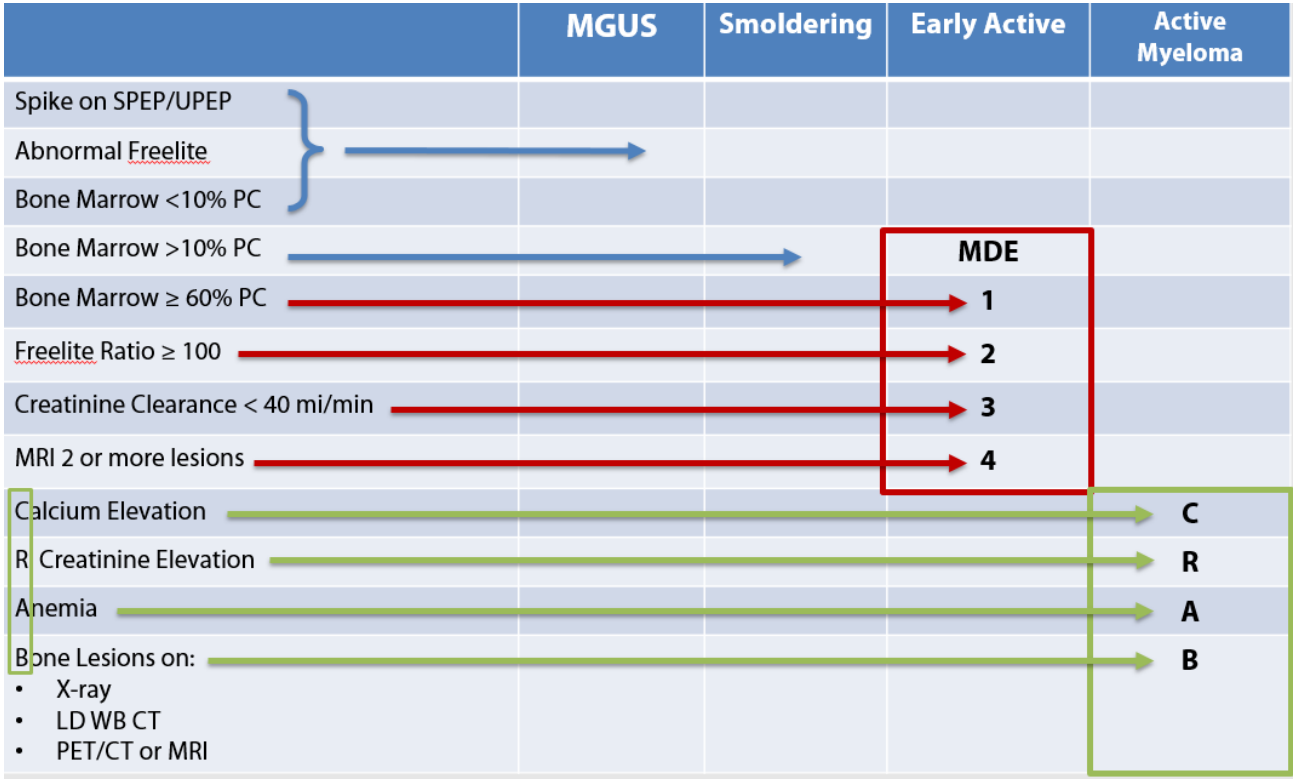
SLiM + CRAB

- S (60% Plasmacytosis)
- Li (Light chains I/U >100)
- M (MRI 1 or more focal lesion)

- C (calcium elevation)
- R (renal insufficiency)
- A (anemia)
- B (bone disease)

Rajkumar et al, IMWG updated criteria for the diagnosis of multiple myeloma Lancet Oncology, 2014; 15:e538-548

Baseline Testing Required 2017



Questions

- **Do you still use x-rays**
  which miss 20% of lesions?
- **Is your first or next step:**
  - WBLD CT?
    or
  - MRI of spine/pelvis?
    or
  - WB PET/CT?

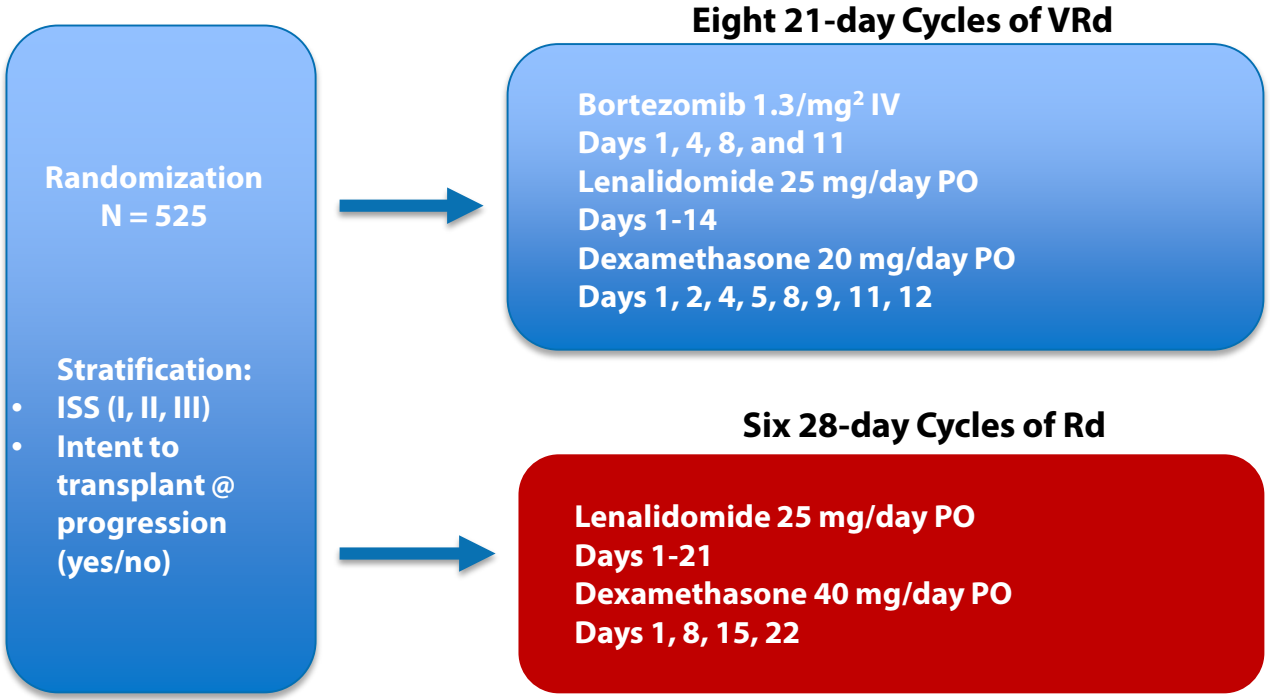
Continued…

Questions

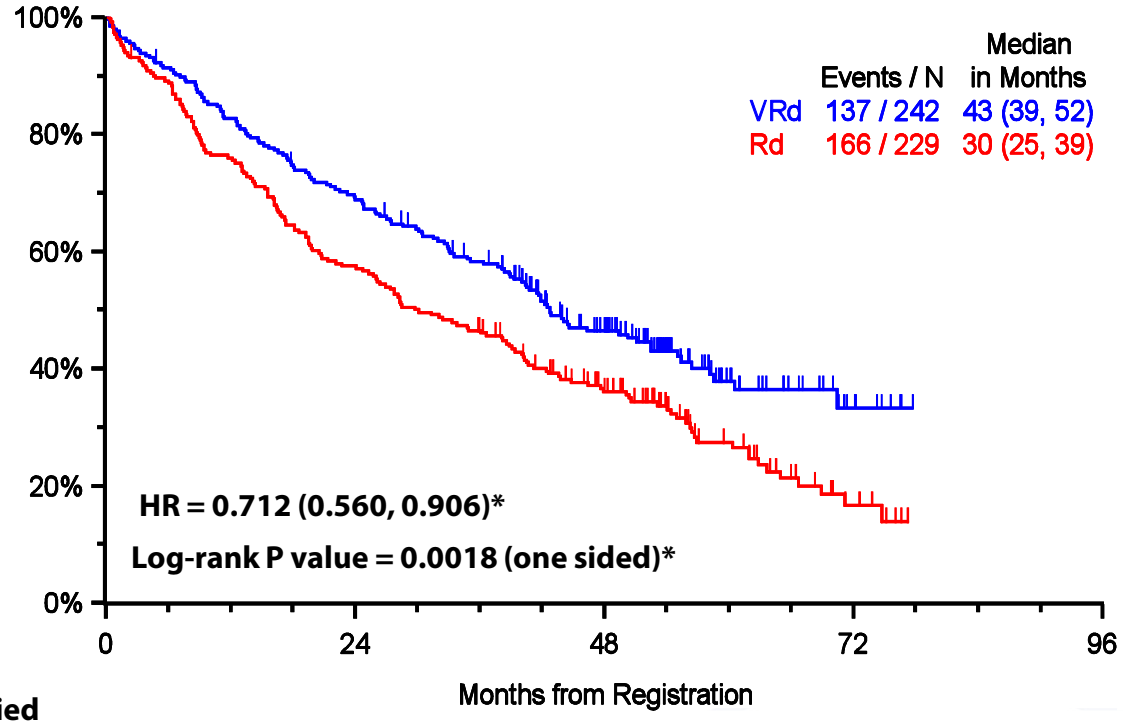
- **Do you foresee other tests to predict or confirm active disease?**

How will new agents impact frontline therapy?

SWOG S0777 Study Design: VRd versus Rd

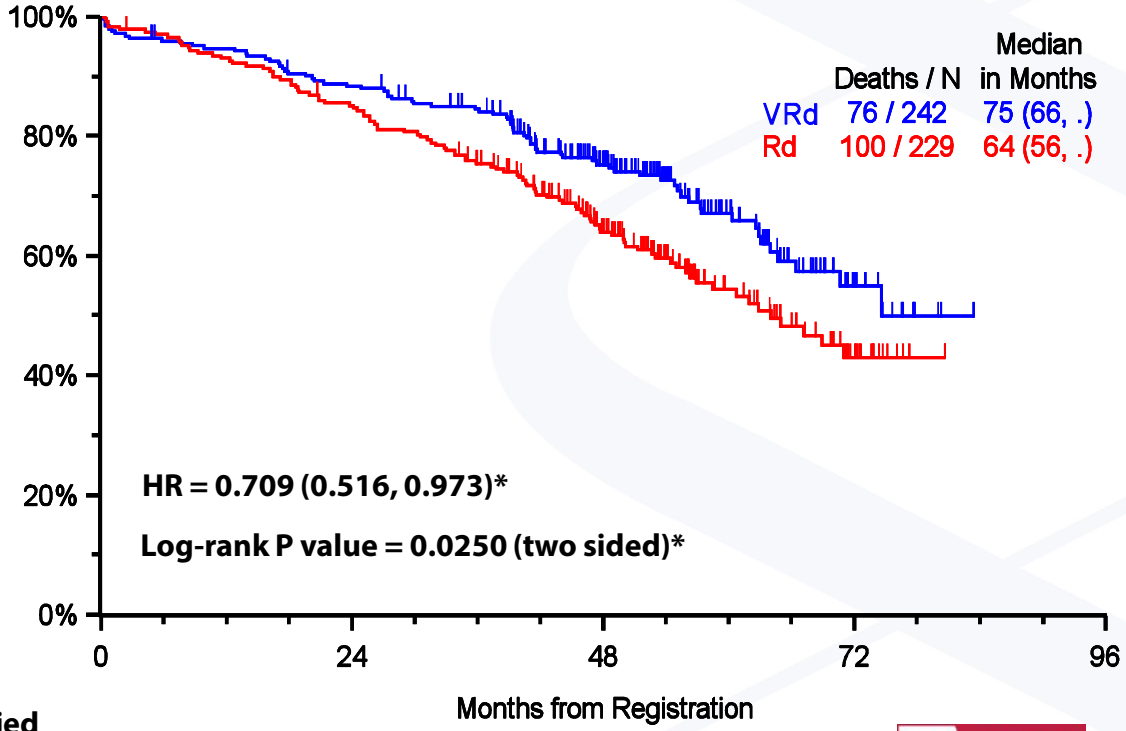


Progression-Free Survival By Assigned Treatment Arm



*Stratified

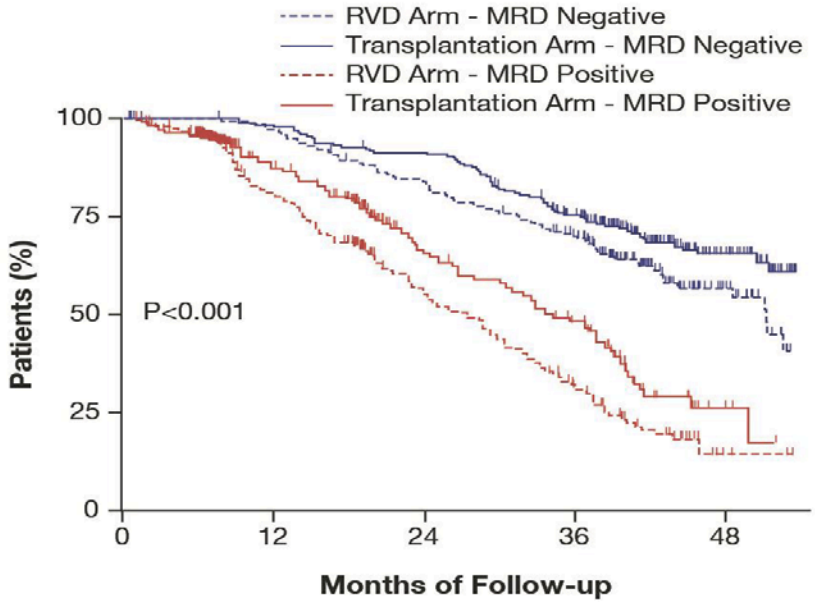
Overall Survival By Assigned Treatment Arm



*Stratified

IFM 2009: Impact of MRD Negative

PFS



No. at Risk					
RVD Arm – MRD Negative	0	136	145	115	28
Transplantation Arm – MRD Negative	0	171	202	155	45
RVD Arm – MRD Positive	350	158	83	42	4
Transplantation Arm – MRD Positive	350	137	62	41	5

Frontline: ASCO 2017

New Combos

- Durvalumab + Rd (Lonial et al: Abstract #TPS 8055)
- Elotuzumab + VRd (Laubach et al: Abstract #8002)
- KRd versus KCd: ≥VGPR 74% versus 61% (Gay et al: Abstract #8003)
- Dara + KRd (Jakubowiak et al: Abstract #8000)

Questions

What is the future of frontline therapy?

- **When** ≥ triple therapy feasible
  - ➢ VRd or VTD + Dara or ? + ?
- **Then**
  - ➢ Upfront ASCT whenever possible?

    or
  - ➢ New novel combo without ASCT?

Can MRD testing in trials guide decisions?

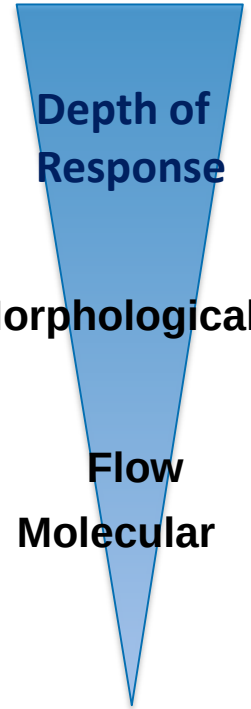
Value of Lenalidomide Maintenance Post-ASCT

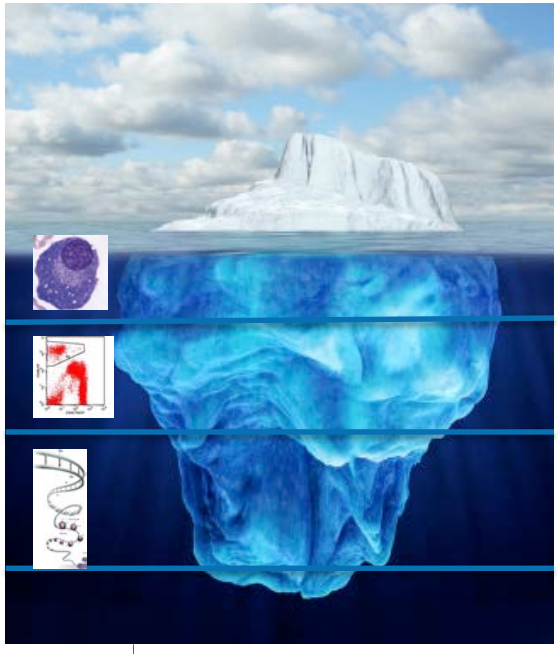
Meta-analysis of overall survival*

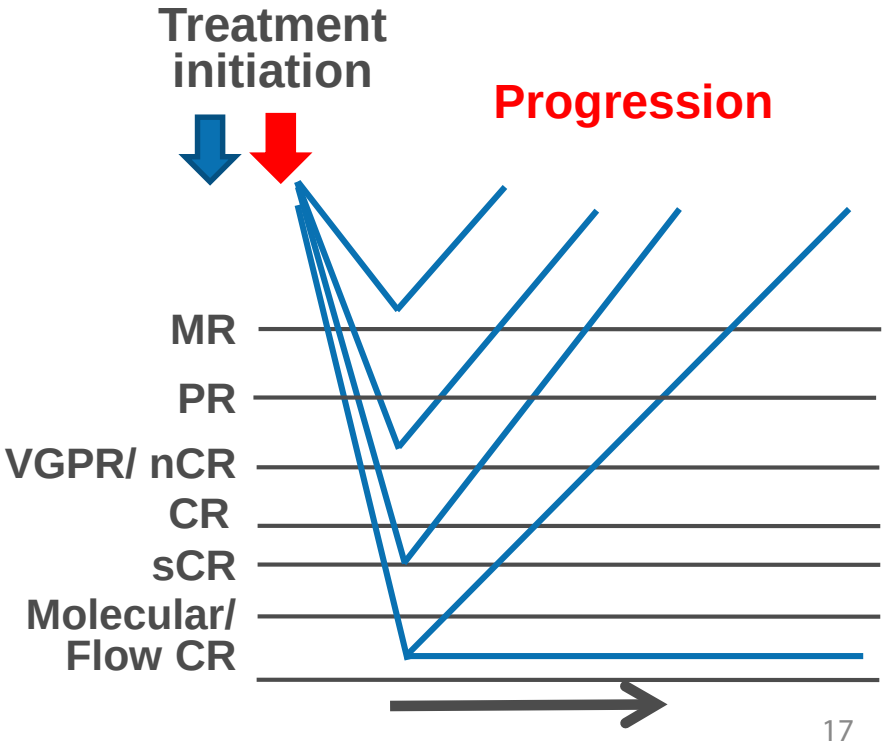
- 3 randomized trials: 1,209 patients
- Median follow up 6.6 years
- Median overall survival: 86 months v. not reached: P = 0.001
- At 5 years 66% v. 71%
  6 years 58% v. 65%
  7 years 50% v. 62%
- Benefit for ≤ PR as well as VGPR/CR patients

*ASCO Attal et al 2016

Depth of Response and PFS

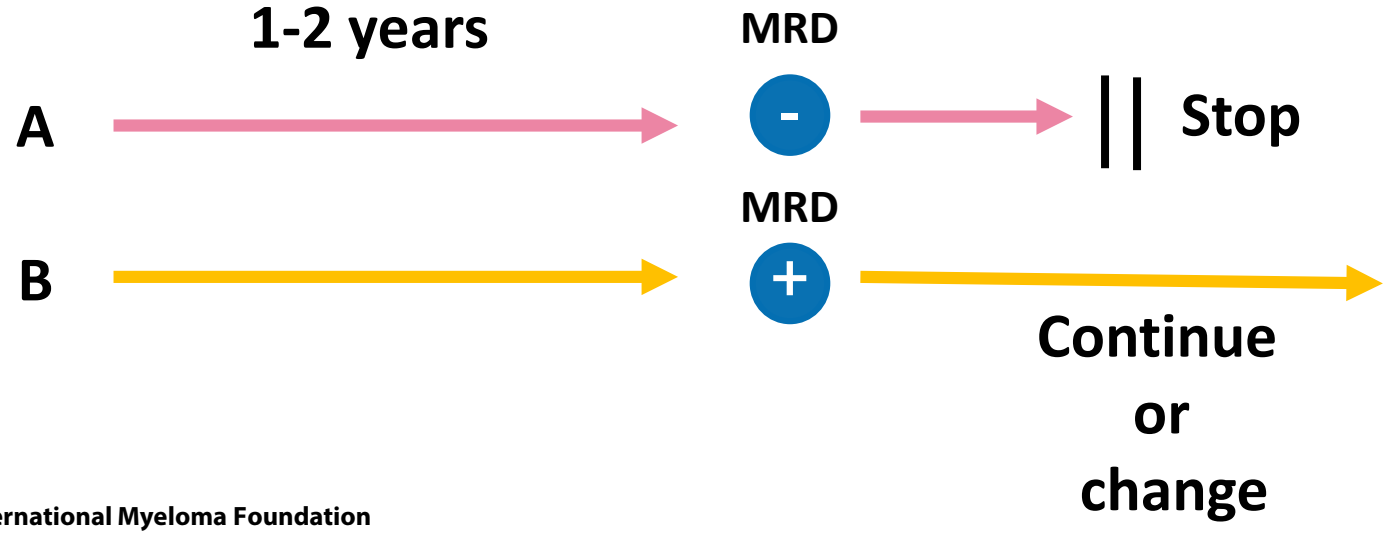






Questions

Can MRD testing solve our maintenance problems?



Are you proactive about risk assessment?

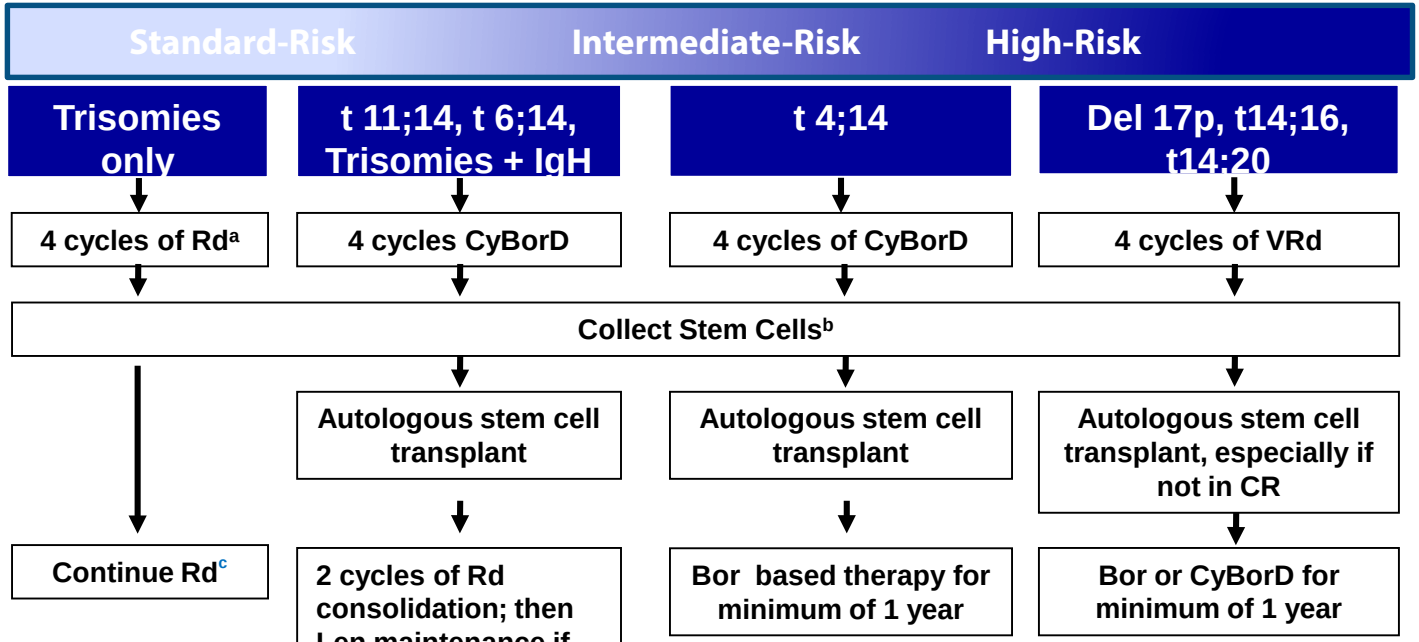
mSMART 2.0: Classification of Active MM

High-Risk 20%	Intermediate-Risk 20%	Standard-Risk 60%
▪ FISH ▪ Del 17p ▪ t(14;16) ▪ t(14;20) ▪ GEP ▪ High risk signature	▪ **FISH** ▪ **t(4;14)*** ▪ **Cytogenetic Deletion 13 or hypodiploidy** ▪ **PCLI ≥3%**	All others including: ▪ Hyperdiploid ▪ t(11;14) ▪ t(6;14)
3 years	4-5 years	8-10 years

Mikhael et al Management of Newly Diagnosed Symptomatic Multiple Myeloma: Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013 Mayo Clin Proc April 2013;88:360-376

mSMART – Off-Study

Transplant Eligible



[a] *Bortezomib containing regimens preferred in renal failure or if rapid response needed*
[b] *If age >65 or > 4 cycles of Rd Consider G-CSF plus cytoxan or plerixafor*
[c] *Continuing Rd for patients responding to Rd and with low toxicities; Dex is usually discontinued after first year*
** Consider risks and benefits; If used, consider limited duration 12-24 months*

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v12 //last reviewed March 2014

Question

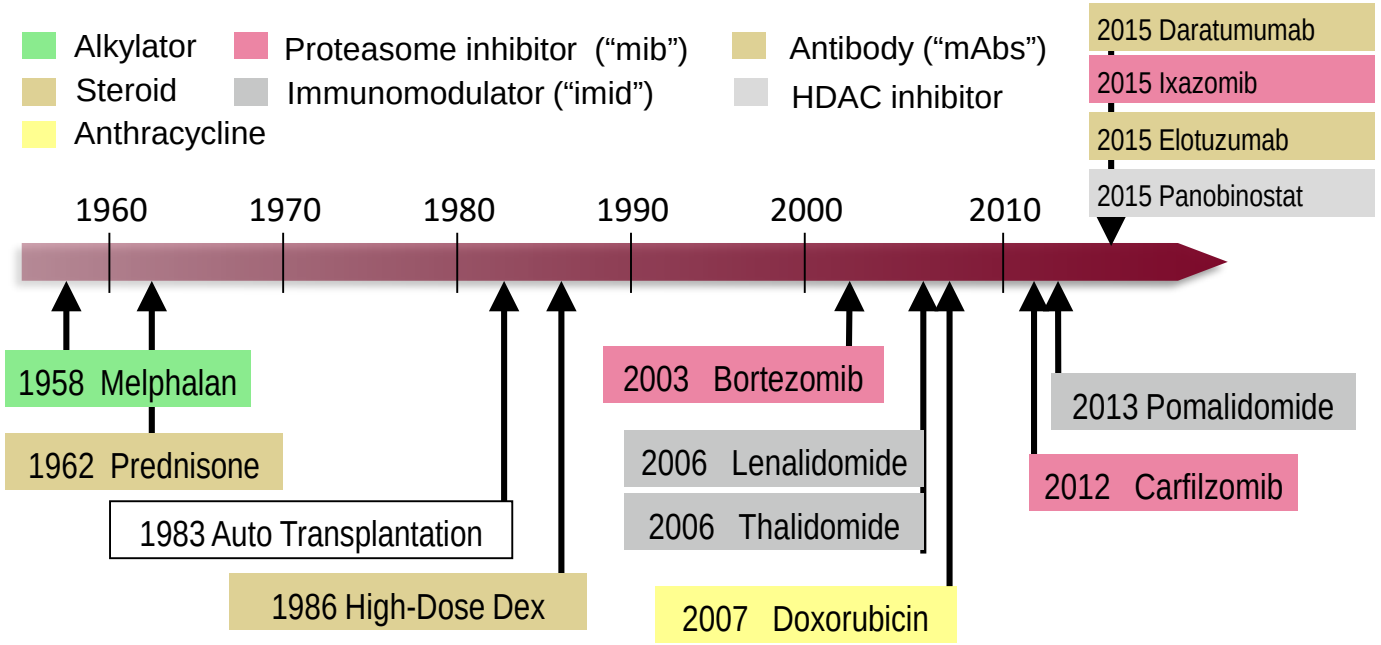
Are you proactive about risk status

or

Wait for relapse?

Which new therapies will make an impact?

Approved Treatment Options 2017



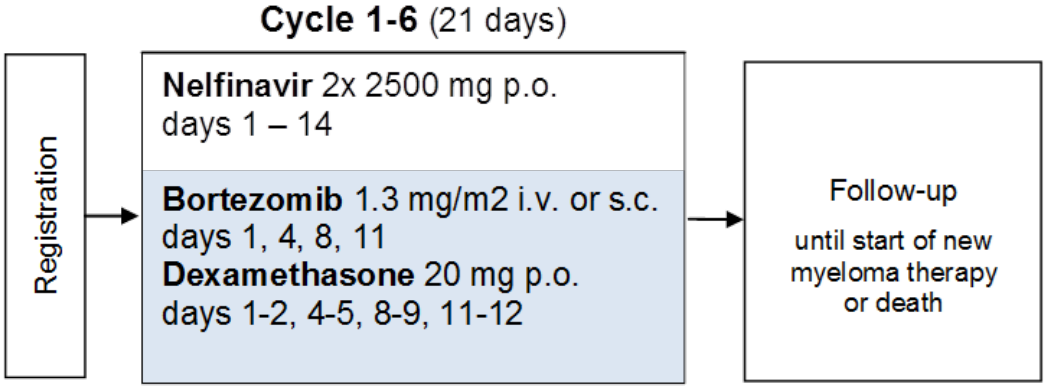
Auto = Autologous; Dex= Dexamethasone

Relapse Therapy: ASCO 2017

- **Dara updates**
  - CASTOR: Dara Vd (Lentzsch et al: Abstract #8036)
    MRD at 10^{-5}: 10% v 2%
  - Pollux: Dara Rd (Bahlis et al: Abstract #8025)
    MRD at 10^{-5}: 25% v 6%
- **Isatuximab** + Pom/Dex (Mikhael et al: Abstract #8007)
  +/- Pom/Dex (Richardson et al: Abstract #8057)
- **Checkpoint** Atezo + Len/Dara (Cho et al: Abstract #8053)
  Durvalumab + Dara (Richardson et al: Abstract #8054)
  Nivolumab + Pom/Dex ± Elo (Lonial et al: Abstract #8052)
  [CheckMate 602]

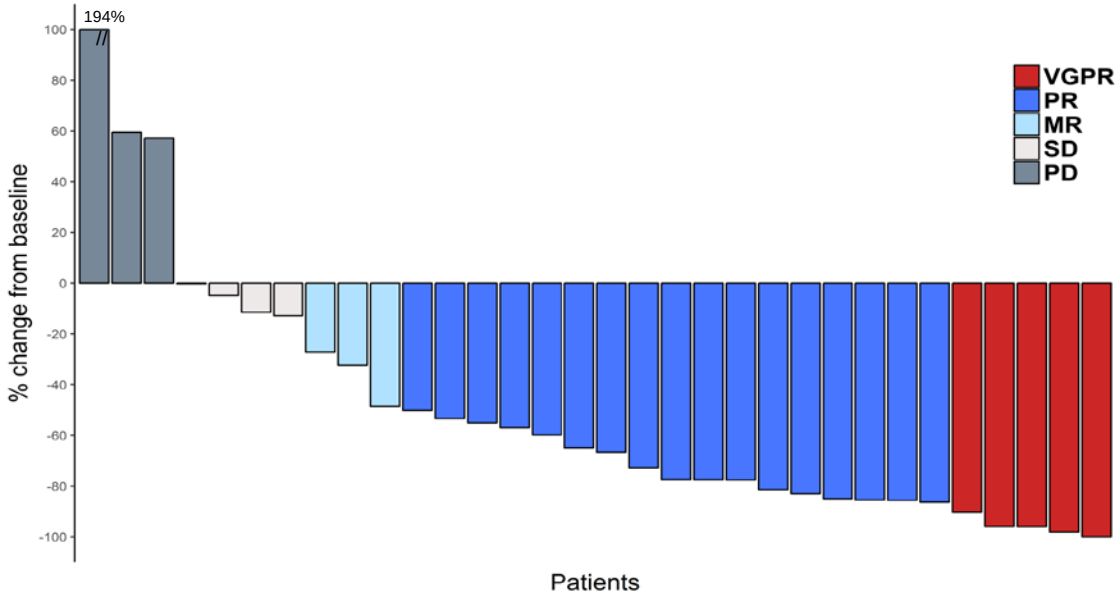
Trial Design for Nelfinavir Study

- Prospective, single-arm, multi-center, open-label phase II



- Simon's two stage design, n=34
  ≤ 15% response rate uninteresting, ≥ 30% response rate promising
  power=80%, alpha=5%
- Completion after cycle 6 (18 weeks maximum trial therapy)
- Academic trial without industry (finance/drug) support

Best responses



Maximum relative change in serum M-protein or serum free light chain concentration in individual evaluable patients.

Question

Which new therapies have an impact in the frontline setting?

How Good are the “New” Novel Therapies?

- **CAR-T**
  - Efficacy
  - Toxicities: “cytokine storm”; immune deficiency…
  - Cure potential ??
- **Checkpoint inhibitors**
  - Efficacy in combo
  - Immune toxicities
  - Early use a concern?
- **Other agents**
  - Selinexor
  - Nelfinavir
  - New IMiD beyond Pom

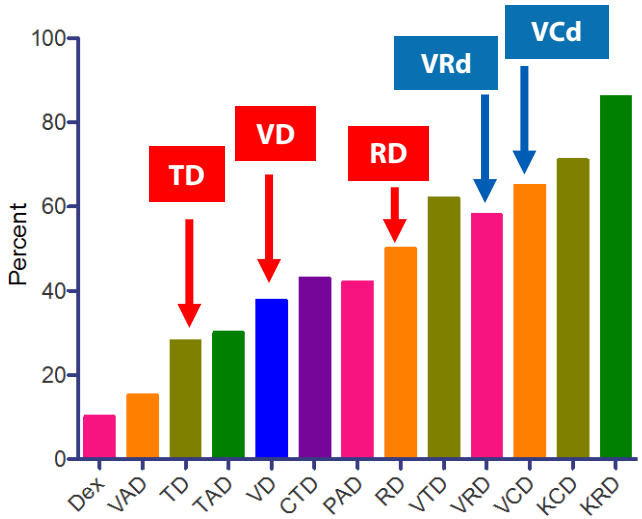
Question

How important is cost?

Increasing depth of response in myeloma with newer drugs

At least VGPR after 4 cycles induction in newly diagnosed MM

RD or CyBorD
$100,000 per year



VRD or KRD
$250,000 per year

KRD - Dytfield Haematologica 99(9) e162-4 201
KCD – Bringhen Blood 124(1) 63-69 2014
VCD – Khan Br J Haematol 156(3) 326-333 201
VRD – Roussel J Clin Oncol 32(25) 2712-2717 2014
TD & VTD – Cavo Blood 2012
RD – Rajkumar Lancet Oncol 11(1) 29-37

K – Carfilzomib
C – Cyclophosphamide
V – Bortezomib
R – Lenalidomide
A – Doxorubicin
D – Dexamethasone

Question

How much does cost truly impact access; choices; outcomes?

- **A few patients?**
- **Many patients?**
- **All patients?**

Thank you for your support!

Bristol-Myers Squibb

Takeda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