Please note, these are the actual video-recorded proceedings from the live CME event and may include the use of trade names and other raw, unedited content.

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Consolidation and Maintenance Therapy

Phoenix, Arizona

Rochester, Minnesota

Jacksonville, Florida

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Disclosures

- **Consulting:** AMGEN, BMS, Celgene, Takeda, Bayer, Jansen, AbbVie, Pharmacyclics, Merck, Sanofi, Kite, and Juno.
- **SAB: Adaptive Biotechnologies**
- **Patent for FISH in MM - ~$2000/year**
- **Registered independent**
- **Believe in stem cell transplant**
- **The COI science is weak and flawed**
- **Dislike wasting your time with this slide**

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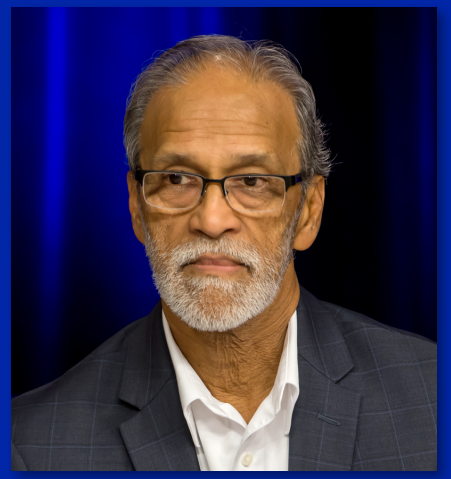
Questions regarding maintenance therapy

Dr Rupard



Dr Kumar

Dr Bessnow

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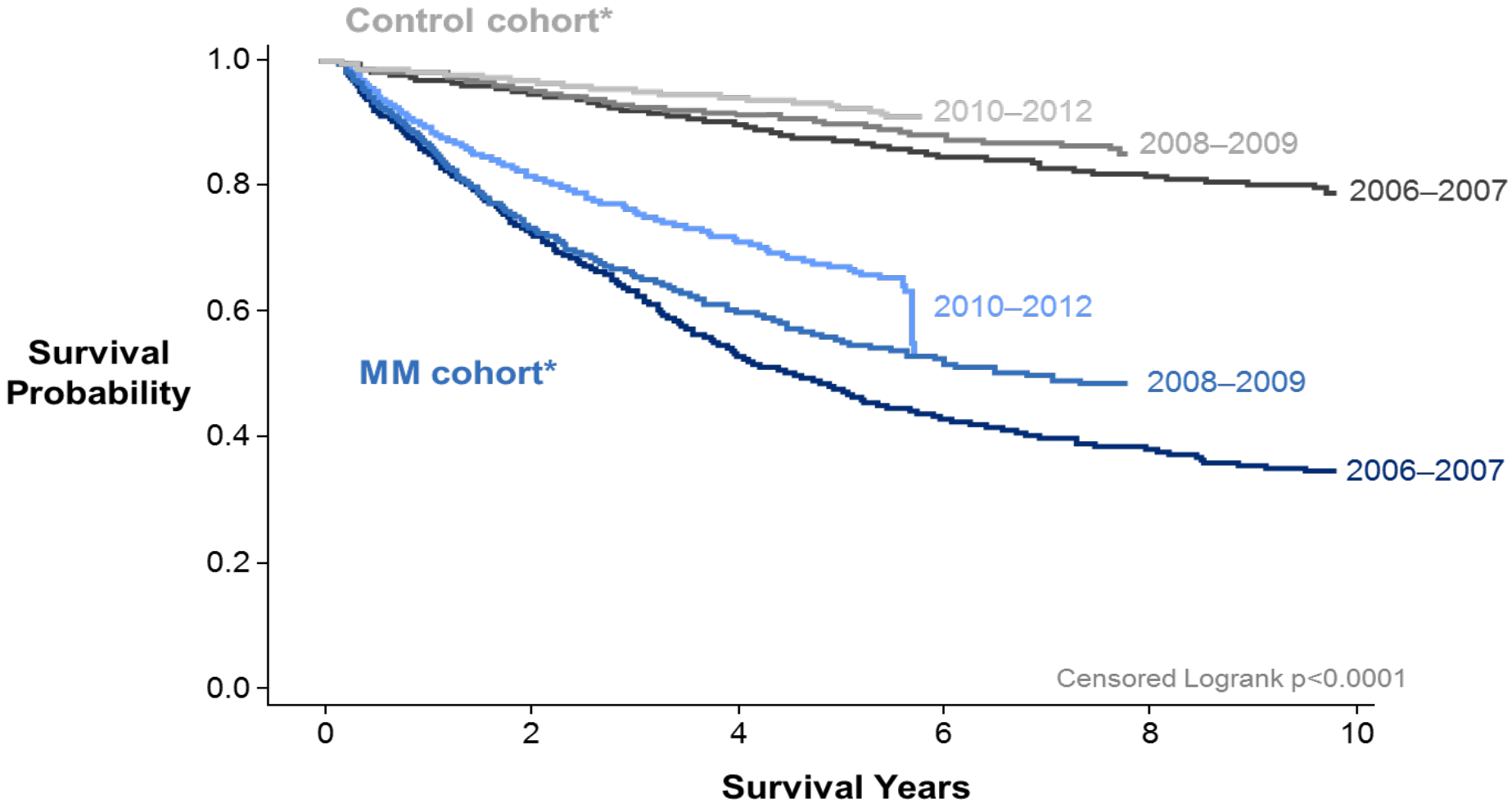
Improving Survival in MM

(n= 9,521 patients)



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Fonseca et. al., Leukemia (2017) 31, 1915–1921

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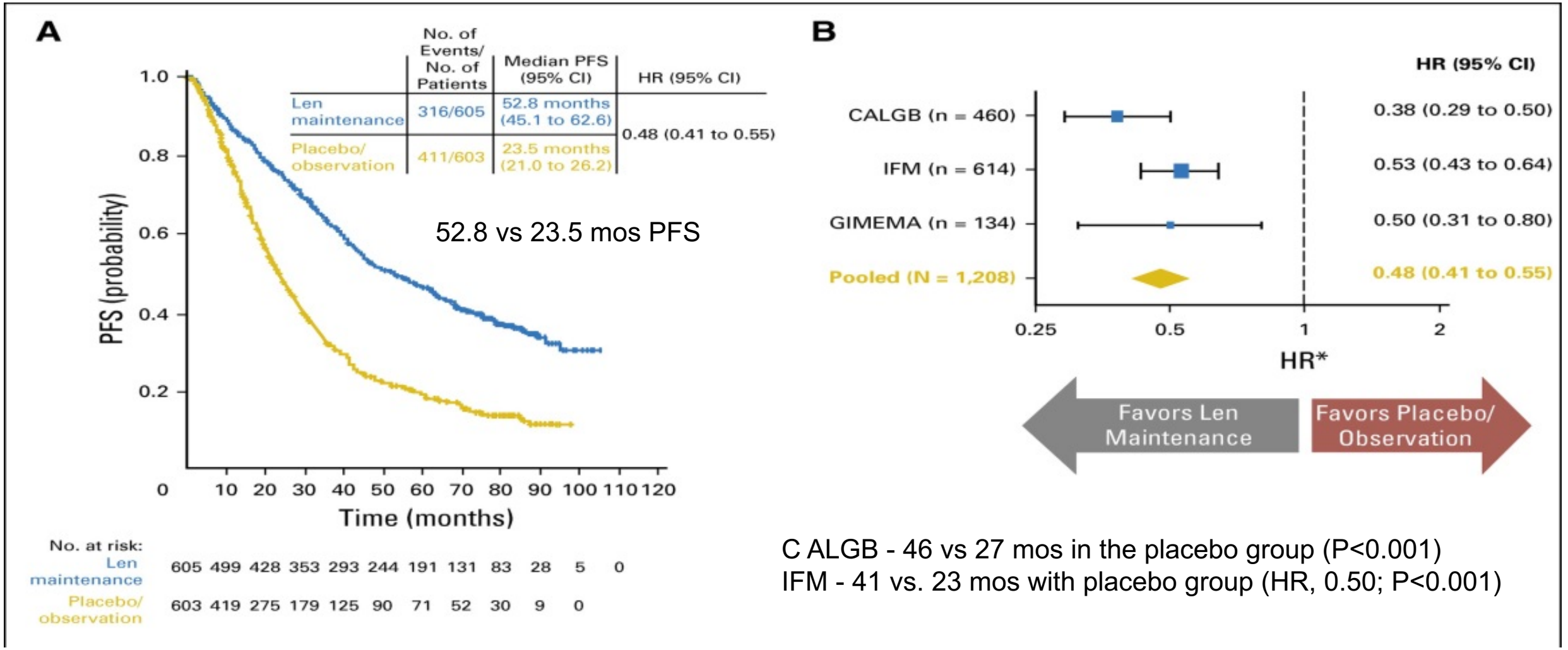
Meta-analysis for Len Maintenance



C ALGB - 46 vs 27 mos in the placebo group (P<0.001)
IFM - 41 vs. 23 mos with placebo group (HR, 0.50; P<0.001)

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McCarthy et al JCO 35:1 2017

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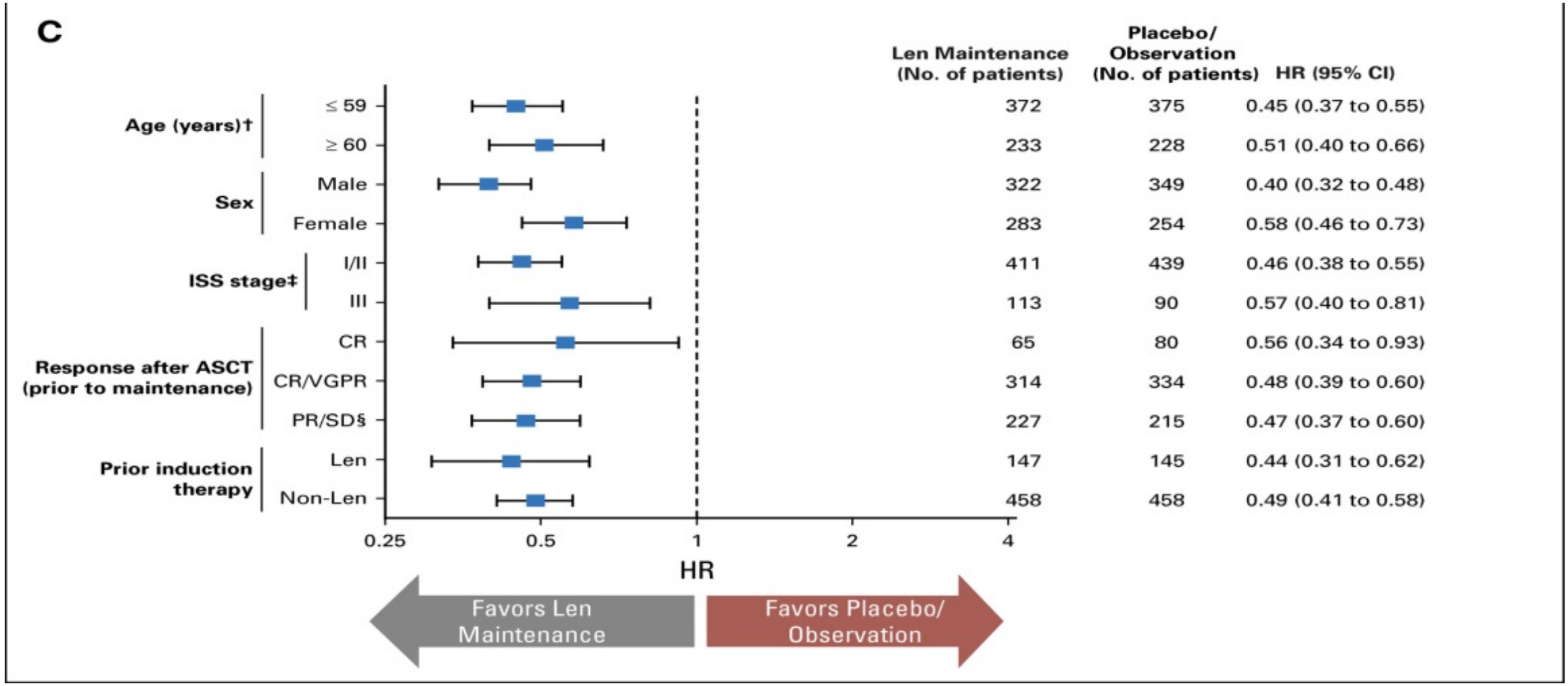
Meta-analysis for Len Maintenance



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McCarthy et al JCO 35:1 2017

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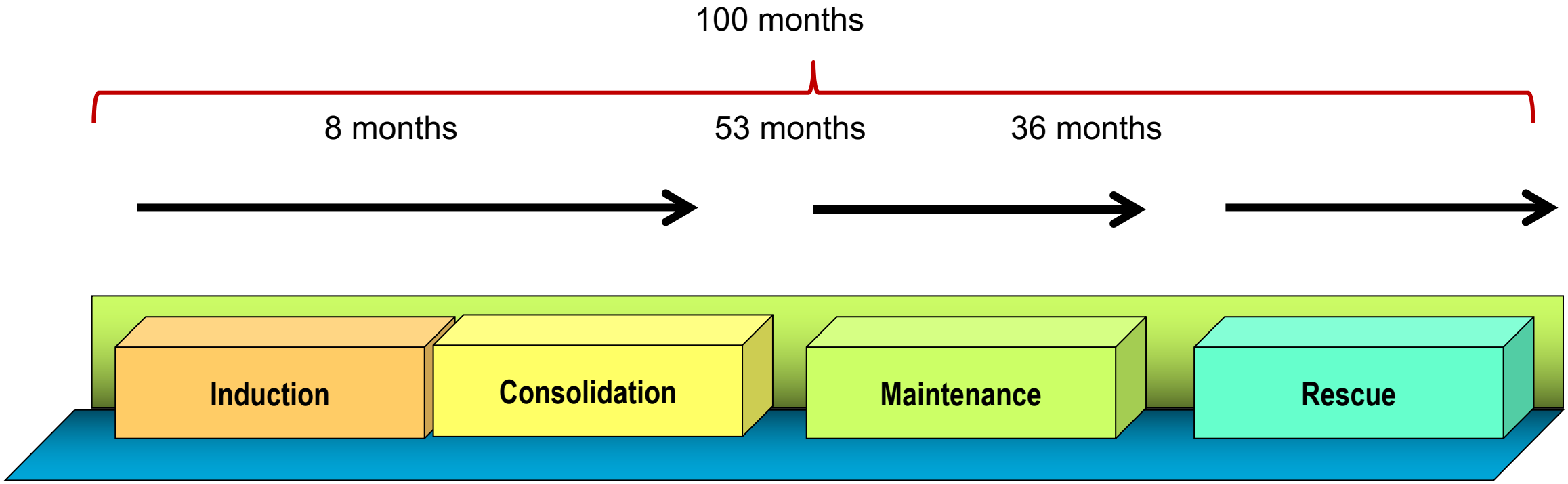
Multiple Myeloma Treatment Lines 2018



VRD
KRD

SCT

Lenalidomide
Ixazomib

Dara-Pd
K-Pd
Ixa-Rd
Elo-Rd

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Fonseca, unpublished

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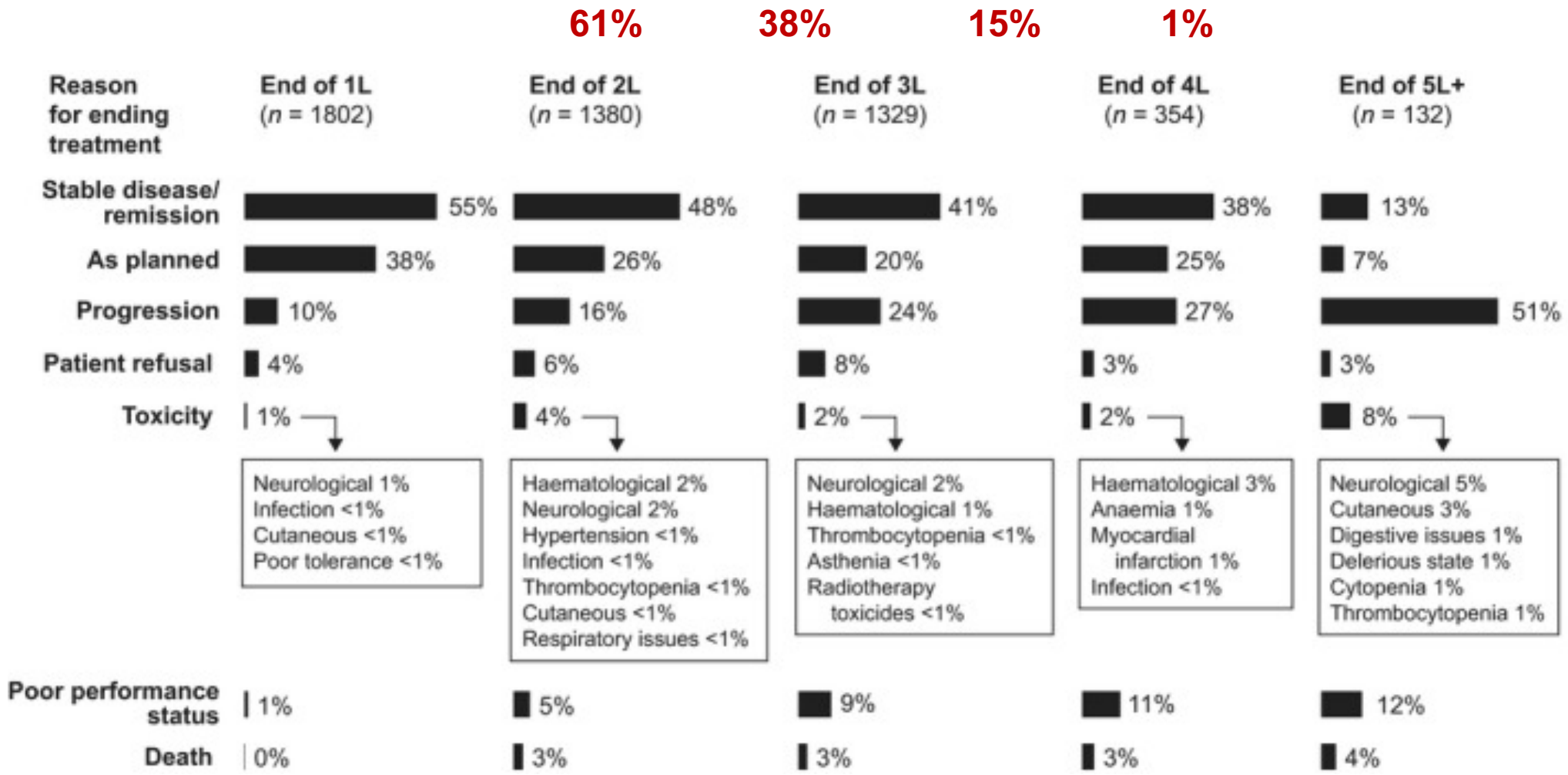
High rate of attrition



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Br J Haematol. 2016 Oct;175(2):252-264

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What approach to maintenance therapy should be used for a pt with persistent cytopenias after SCT?

- Neutropenia – PI
- Thrombocytopenia – IMID

How do you manage an IMID rash?

- Hang in there
- Topical or oral steroids

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Are there patients for whom you would opt for something other than single-agent lenalidomide?

- High risk patients
  - PI plus IMID
  - High risk of relapse
  - Data for similar outcomes is limited but suggestive
  - Oral ixazomib combination
  - TOURMALINE like with low dex
- Maybe t(11;14) in the future?

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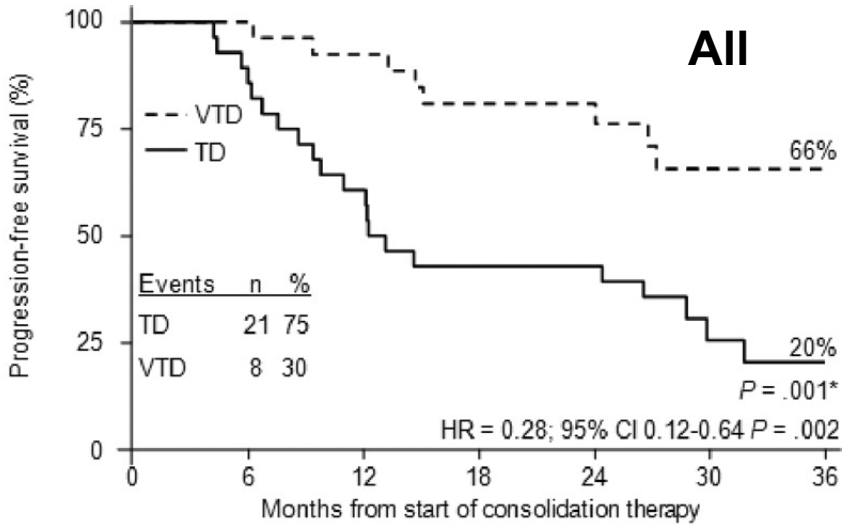
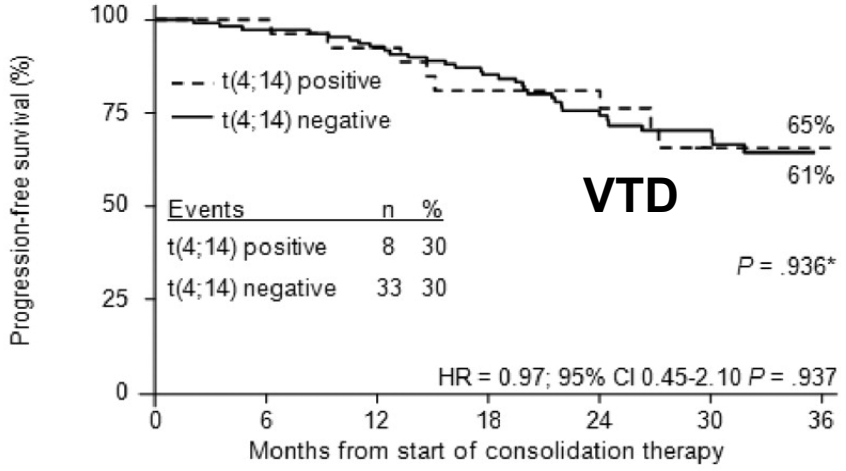
Landmark Start of Consolidation

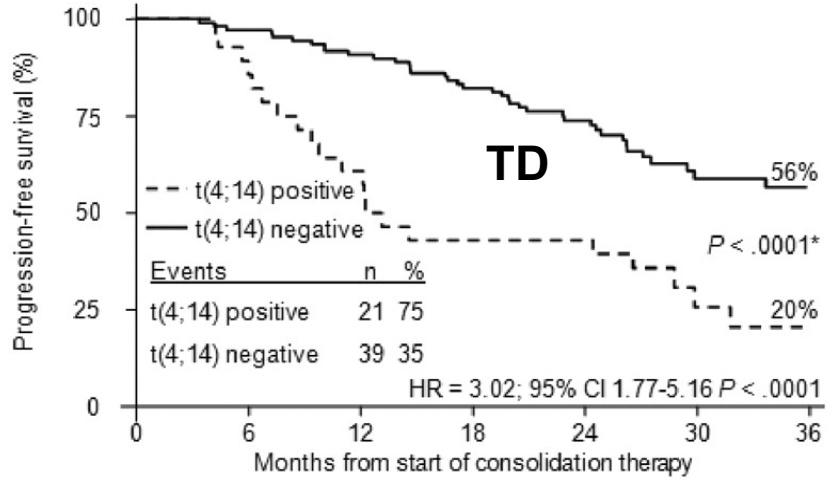


t(4;14) & no - 17p13



Number at risk

t(4;14) negative	110	106	100	87	58	38	18
t(4;14) positive	27	27	24	20	17	9	6



Number at risk

t(4;14) negative	110	106	98	84	59	30	14
t(4;14) positive	28	24	17	12	12	5	2

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Cavo M et al. Blood 2012;120:9-19

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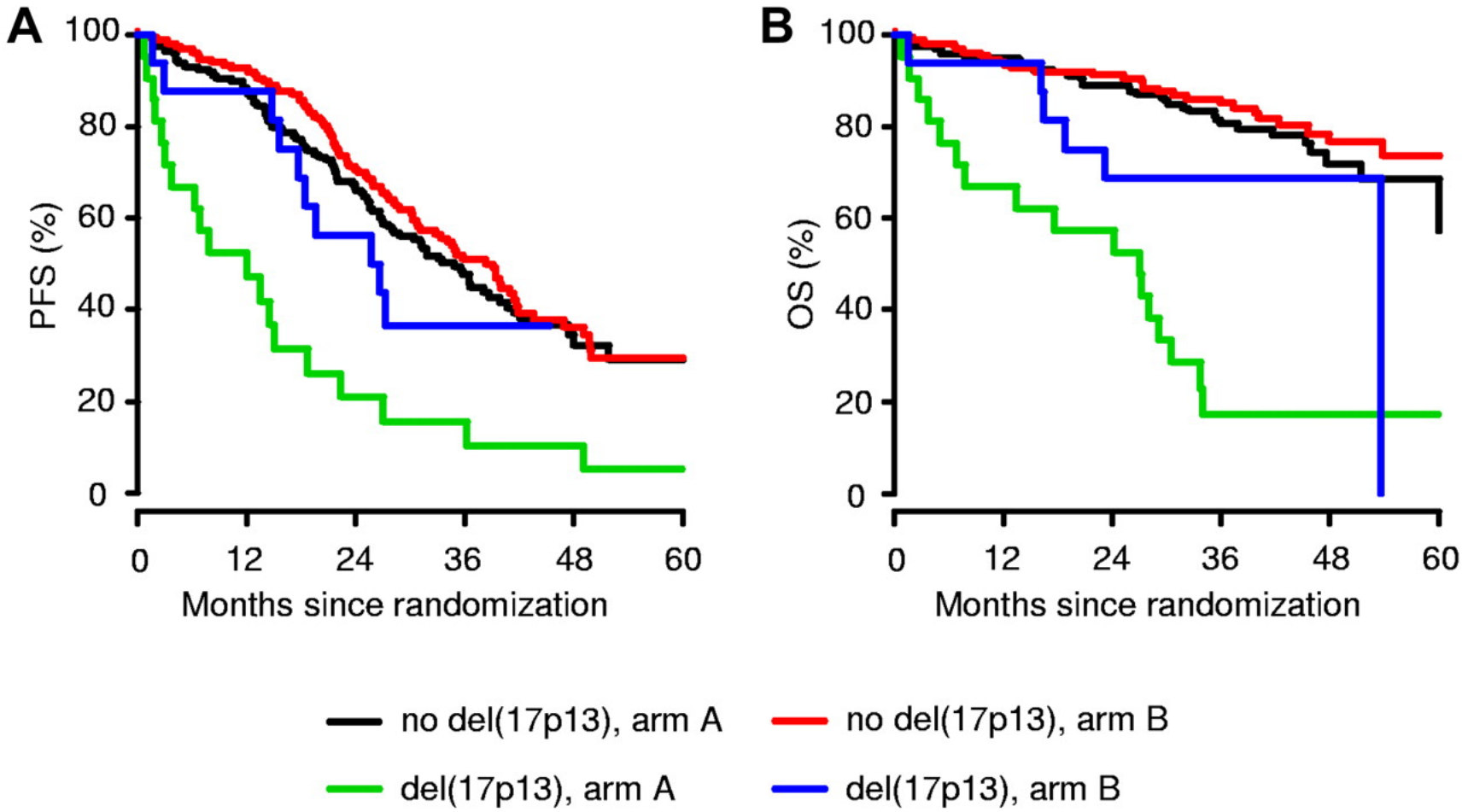
Effects of Bortezomib on Del(17p13) MM



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Neben K et al. Blood 2012;119:940-948

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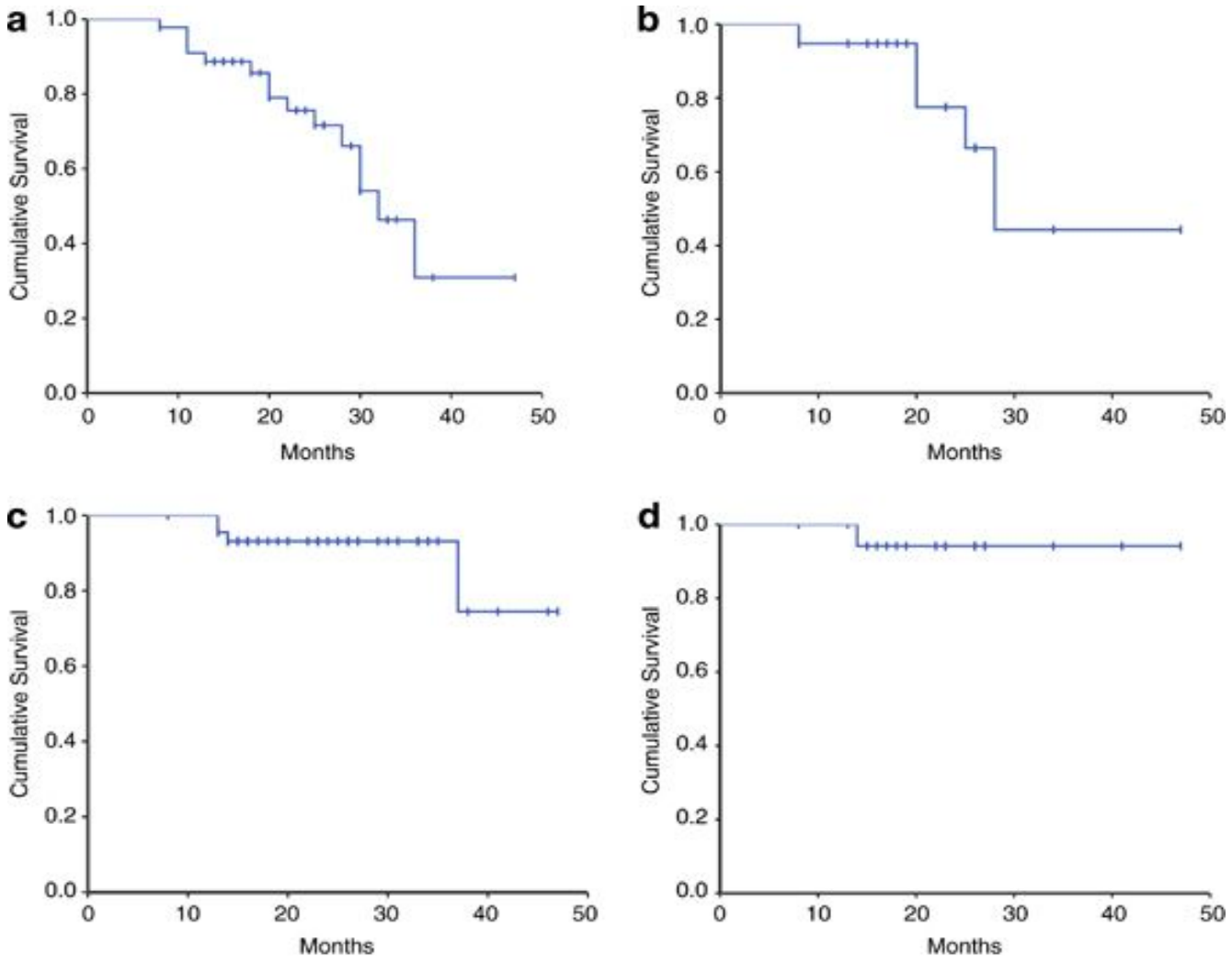
Maintenance with bortezomib after SCT



Nooka et al Leukemia volume 28, pages 690–693 (2014)
Leukemia. 2018 Mar;32(3):712-718
Biol Blood Marrow Transplant. 2017 Feb;23(2):262-268.

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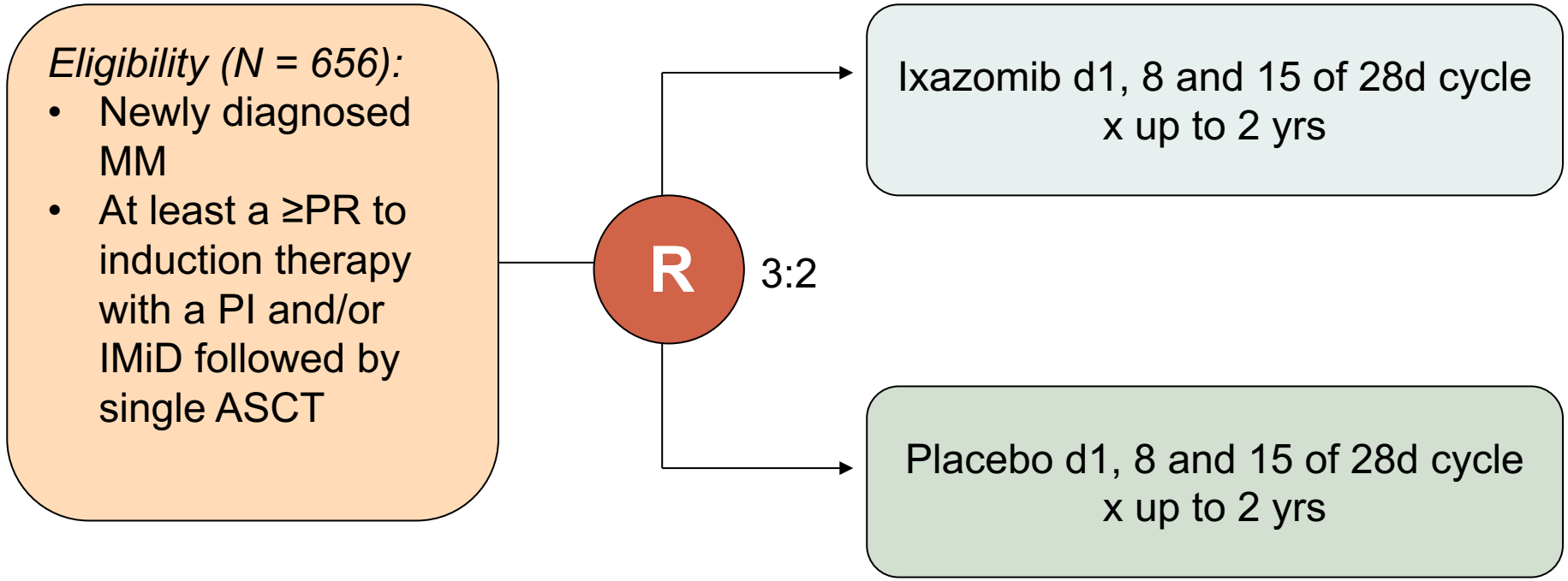
TOURMALINE-MM3 Phase III Study Design

Trial Identifier: NCT02181413 (Active, not recruiting)



Primary Endpoint: PFS per independent review committee

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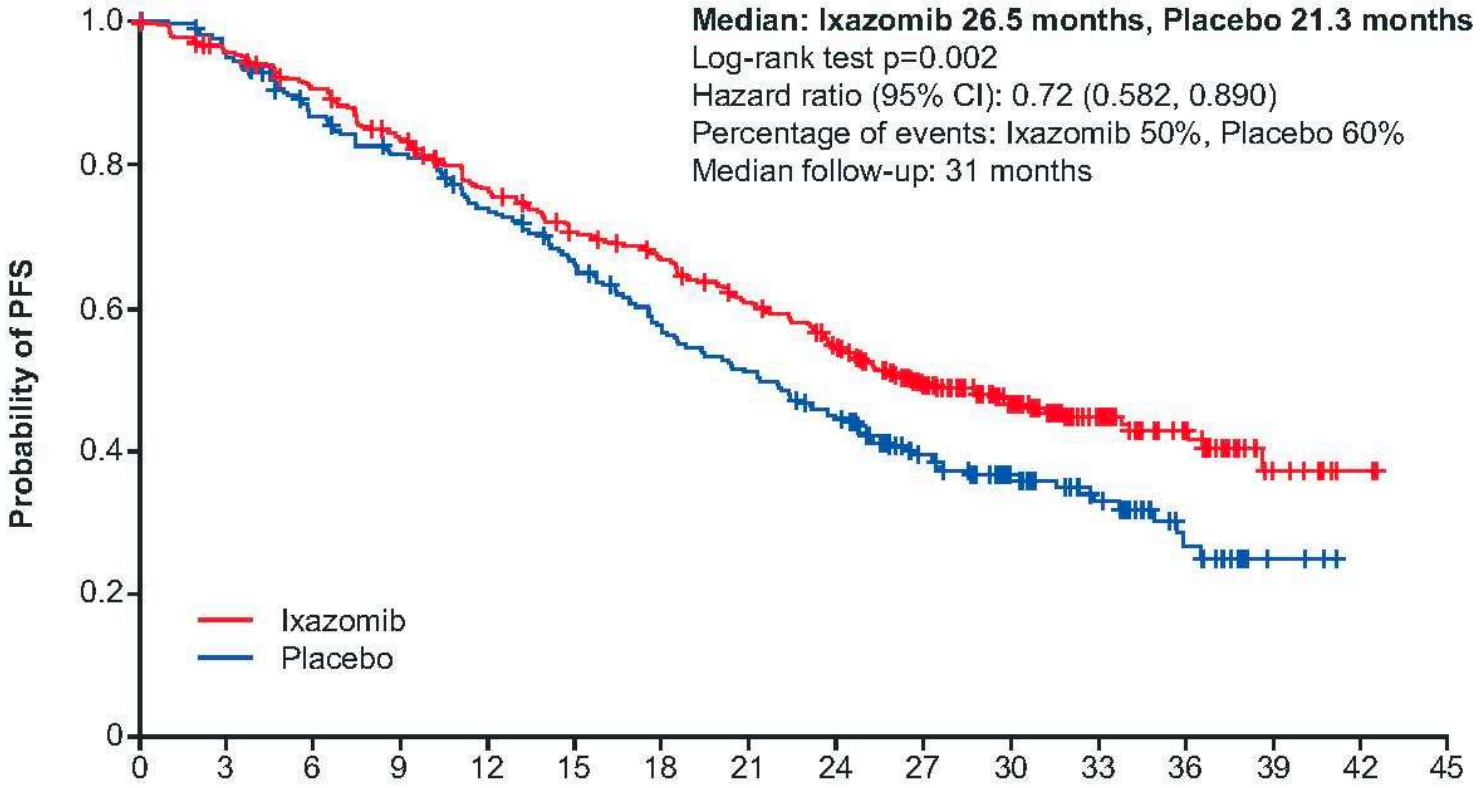
TOURMALINE-MM3 Study Primary Endpoint: PFS



Number of patients at risk

Ixazomib	395	363	340	311	279	255	238	213	187	135	93	56	35	9	3	0
Placebo	261	238	210	195	174	153	130	117	100	69	46	32	15	3	0	0

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Abstract 301 To be presented Sunday at 7:30 Dimopoulos et al

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TOURMALINE-MM3 Study: Adverse Events

Grade ≥3 Adverse Event	Ixazomib (n = 395)	Placebo (n = 261)
Any event	42%	26%
Infections	15%	8%
Pneumonia	6%	4%
Neutropenia	5%	3%
Thrombocytopenia	5%	<1%

- Peripheral neuropathy (ixazomib vs placebo): 19% vs 15% (Grade 3: <1% vs 0)
- Second primary malignancies: 3% in both arms
- Discontinuation due to AEs (ixazomib vs placebo): 7% vs 5%
- Serious AEs (ixazomib vs placebo): 27% vs 20%
- Deaths (ixazomib vs placebo): 1 patient vs none

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For how long to give and is it ever reasonable to give a break?

- We simply do not know
- FIRST and MM-015 studies show value of longevity of treatment
- Balance tolerance access and toxicity
- But perhaps in selected cases you can use
  - MRD testing?

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How do we interpret MRD?

SAMPLE-LEVEL MRD RESULT

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Residual Sequences Detected

ESTIMATED MRD VALUE:

42 residual clonal cells per million nucleated cells (Range: 21 - 66)

Sequence determining MRD result: IGH Sequence A

No Residual Sequences Detected

ESTIMATED MRD VALUE:

0 residual clonal cells (Range: 0 - 1)

Sequence determining MRD result: IGH Sequence C

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No Residual Sequence(s) Detected

0 residual clonal cells

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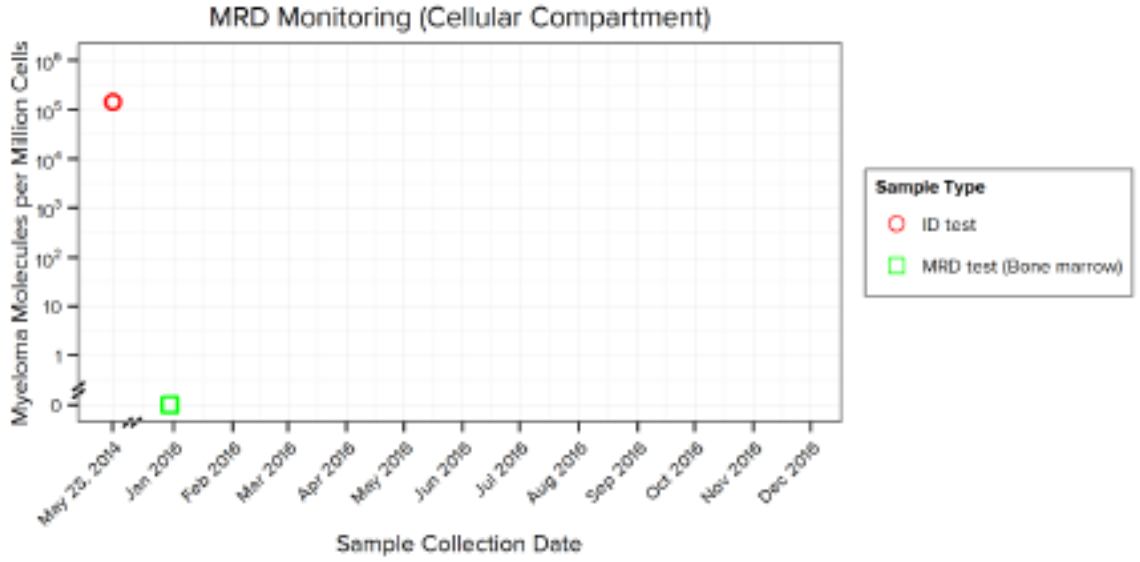
High risk clinical validation del(17p13) patient

Test Results

Minimal Residual Disease (MRD) Status	Estimated Myeloma Molecules per Million Cells
NEGATIVE	0.0

Interpretation

The sample is NEGATIVE for the presence of myeloma gene rearrangements. Myeloma gene rearrangements were previously identified in an ID sample (December 24, 2015, Accession No. 205825). The previously identified myeloma gene rearrangements are NOT present in the current MRD sample, which is consistent with the sample being NEGATIVE for myeloma cells. The results of this test should be interpreted in the complete clinical context, including the patient's clinical presentation and current treatment regimen.



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Rafael Fonseca, unpublished

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MRD is not everything, it's the only thing!

ORDERING PHYSICIAN
Rafael Fonseca

INSTITUTION
Mayo Clinic Arizona Division of Hematology and Medical Oncology

ASSAY DESCRIPTION

The Adaptive clonoSEQ® Assay is an NGS-based immunosequencing platform for the detection, quantification and analysis of measurable residual disease (MRD) in B-cell malignancies. The assay uses multiplex PCR, high throughput sequencing and a proprietary algorithm for the purpose of evaluating lymphoid clonal distribution and expansions in genomic DNA (gDNA).

The clonoSEQ Tracking (MRD) Test assesses and quantifies the presence of previously identified index and/or dominant DNA sequences (typically associated with malignancy) and can identify newly emerging dominant sequences.

TRACKING RESULT

No Residual Sequence(s) Detected

0 residual clonal cells

RESULTS SUMMARY

- Genomic DNA was extracted from a fresh bone marrow sample.
- The index sequence identified in the diagnostic sample from this patient was not detected in the current sample.
  The sensitivity of this assay is directly related to the total number of cells (or cellular equivalents of genomic DNA) analyzed. There were 1,602,132 total nucleated cells evaluated from this sample.
- **The test result should only be used taking into account all available clinical information and should not be used as the sole determinant to guide patient care and management.**

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R Fonseca, personal information April 2018