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**DARZALEX FASPRO**  
(daratumumab and hyaluronidase)  
**for the Treatment of High-Risk  
Smoldering Multiple Myeloma**

**May 20, 2025**

Oncologic Drugs Advisory Committee

Johnson & Johnson



## Introduction

**Sen Zhuang, MD, PhD**

Vice President, Oncology Research & Development  
Johnson & Johnson

# Daratumumab is Well-Established Standard of Care Treatment for Multiple Myeloma (MM)

- Initial approval in 2015
  - > 500,000 patients treated worldwide
- 10 FDA approved indications, the most of any MM therapy
  - From frontline through relapsed refractory MM
  - Approved as monotherapy and in combinations
- Recommended in MM guidelines, including NCCN

# Daratumumab Consistently Demonstrates Positive Benefit-Risk in Multiple Myeloma

- Consistent and compelling PFS benefit across approved indications
  - HR ranging from 0.37 to 0.63
- Improvements in OS demonstrated
  - HR ranging from 0.56 to 0.82
- Well-established favorable safety profile, including in combinations

# AQUILA Study Designed to Address Limitations of Prior Studies in SMM

- Study design based on
  - Learnings from prior studies in SMM
  - Collaboration with myeloma experts
  - Agreement from global health authorities
- Enrollment criteria, endpoints, and use of advanced imaging addressed many of the limitations from prior studies
- AQUILA provides a robust assessment of a finite daratumumab treatment in high-risk SMM

# AQUILA Supports Daratumumab Positive Benefit-Risk<sup>CO-6</sup> for Patients with High-Risk SMM

## Unmet Need

- Half of patients with high-risk SMM likely develop active MM within 2-3 years
- Patients need safe/effective treatment that delays progression to MM
- Current standard of care is observation

## Efficacy

- Statistically significant improvement in time to progression to active myeloma or death (PFS)
- Evidence of positive OS trend
- Supported by all secondary endpoints
- Comparable HRQoL over time

## Safety

- Well-established safety profile
- Clinicians familiar in monitoring and managing AEs
- Most AEs reported align with labeling and were low grade

**36-month daratumumab monotherapy significantly delays progression to active MM that requires continuous combination therapy with associated toxicities**

# Proposed Indication

**DARZALEX FASPRO<sup>1</sup> as monotherapy for the treatment of adult patients with high risk smoldering multiple myeloma**

# Agenda

<b>Introduction</b>	<b>Sen Zhuang, MD, PhD</b> Vice President, Oncology Research & Development Johnson & Johnson
<b>Unmet Medical Need</b>	<b>Sagar Lonial, MD</b> Chair and Professor, Dept of Hematology and Medical Oncology Emory University School of Medicine
<b>Efficacy</b>	<b>Robin Carson, MD</b> Vice President, Oncology Research & Development Clinical Leader, Daratumumab Johnson & Johnson
<b>Safety</b>	<b>Robyn Dennis, MD</b> Senior Medical Director, Oncology Research & Development Johnson & Johnson
<b>Clinical Perspective</b>	<b>Vincent Rajkumar, MD</b> Edward W. and Betty Knight Scripps Professor of Medicine Mayo Clinic

# Additional Experts

**Peter Voorhees, MD**

**Professor of Medicine,**  
Atrium Heath Levine Cancer  
Institute, Wake Forest University School of Medicine

Johnson & Johnson

**Katharine Gries, PharmD, PhD**

**Senior Director, Patient Reported Outcomes**

**Ivo Nnane, PhD**

**Distinguished Scientist II, Clinical Pharmacology**

**Ke Zhang, PhD**

**Senior Director, Biostatistics**



# Background and Unmet Need

## Sagar Lonial, MD

Chair and Professor

Department of Hematology and Medical Oncology

Anne and Bernard Gray Family Chair in Cancer

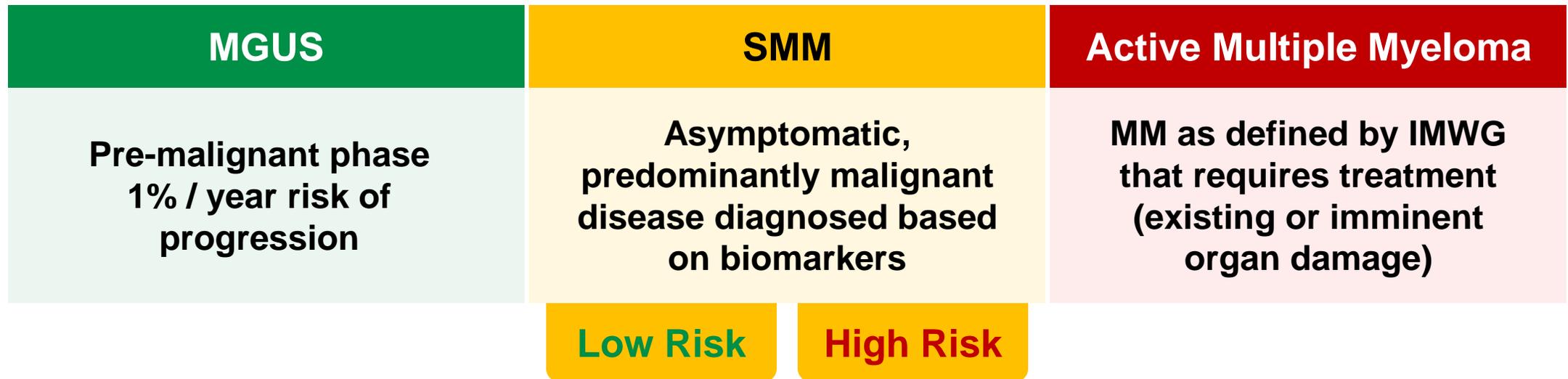
Chief Medical Officer

Winship Cancer Institute

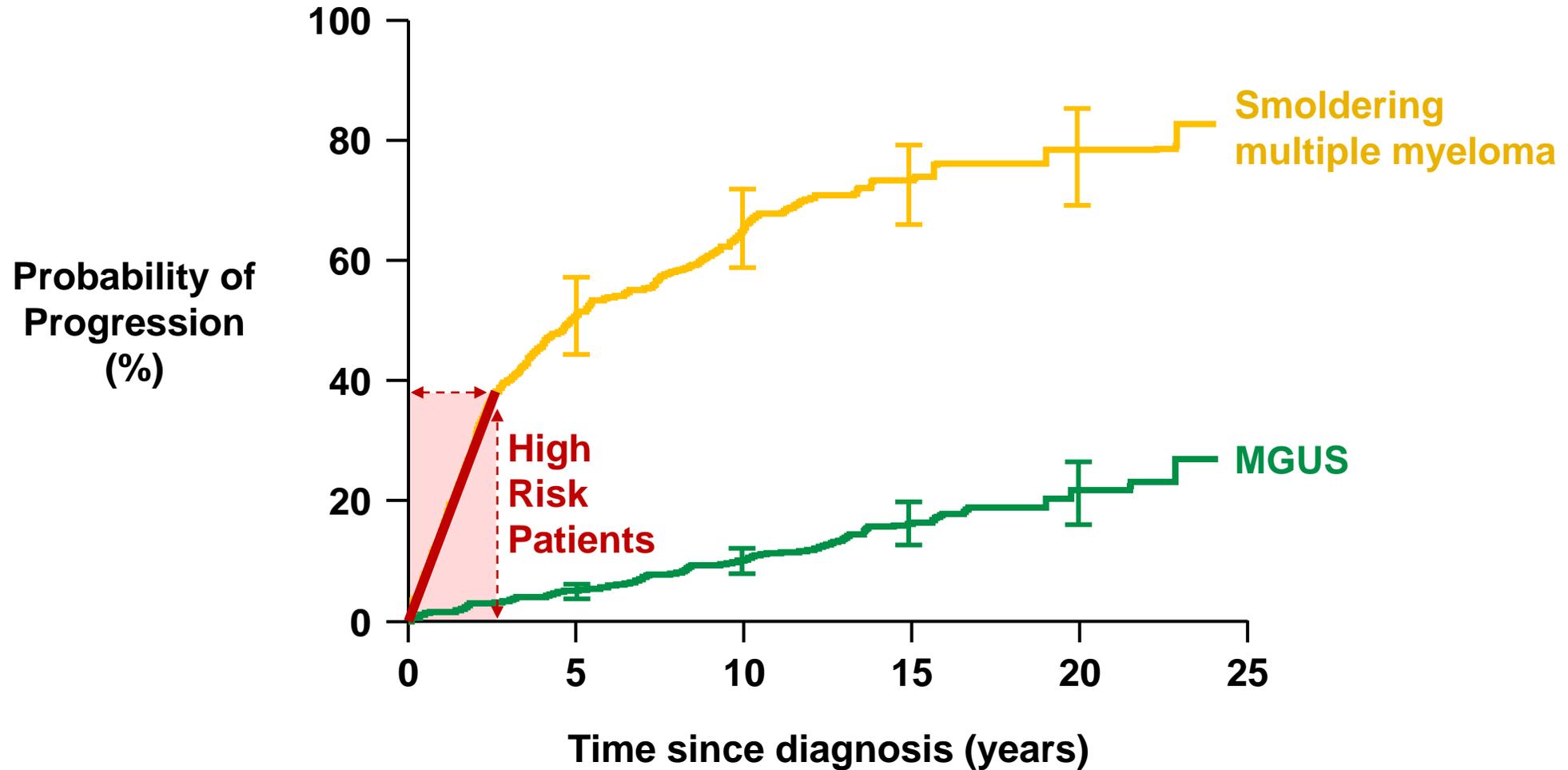
Emory University School of Medicine

# SMM as Part of Multiple Myeloma Disease Continuum

Increasing Tumor Burden 



# Natural History of Patients with SMM to MM



# Clinical Relevance of Definition of Myeloma Based on IMWG Criteria (Requiring Intensive Therapy)

SLiM / CRAB Criteria Signalling Progression to Myeloma	Clinical Relevance
≥ 60% BMPCs	<b>Cytopenias, infections, bleeding</b>
FLC ratio ≥ 100	<b>Renal failure</b>
> 1 focal lesions on MRI	<b>Bone disease and fracture</b>
Serum calcium > 1 mg/dL higher than ULN	<b>Fracture and renal failure</b>
Creatinine clearance < 40 mL/min or serum creatinine > 2 mg/dL	<b>Renal failure</b>
Hemoglobin > 2.0 g/dL below the limit of normal or < 10.0 g/dL (anemia)	<b>Fatigue, cytopenias, infections, bleeding</b>
≥ 1 osteolytic lesions on skeletal radiography, CT, or PET-CT	<b>Fracture</b>

# Key Thresholds Used to Determine High Risk for Progression from SMM to Active MM

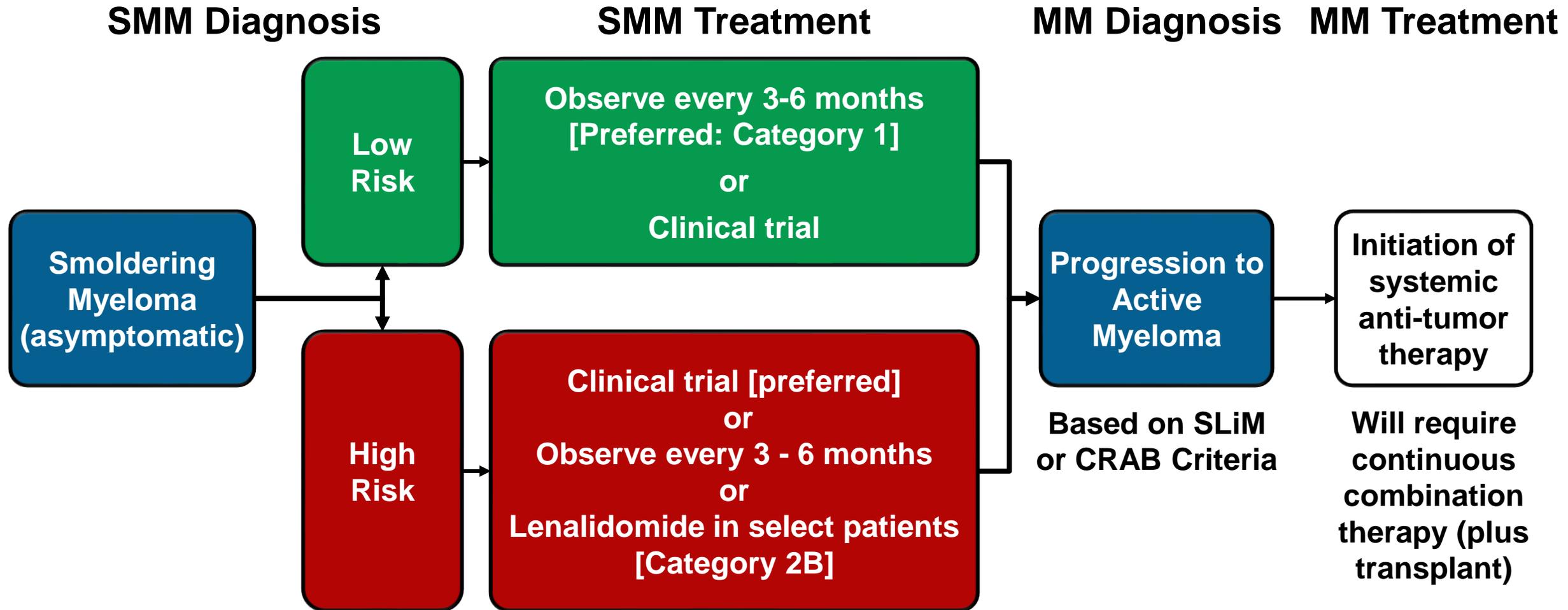
Markers Used to Determine High-Risk SMM	PETHEMA (2007) <sup>1</sup>	Mayo (2008) <sup>2</sup>	Rajkumar Consensus paper (2015) <sup>3</sup>	Mayo 2018 20/2/20
Serum M-Protein		✓	✓	✓
Abnormal FLC ratio		✓	✓	✓
IgA SMM			✓	
Immunoparesis	✓		✓	
Clonal BMPC			✓	✓
<b>2-year risk of progression in high-risk</b>	50%	52%	50%	47%

**AQUILA  
(2017)**

BMPC: clonal bone marrow plasma cells; FLC: free light chain ratio

1. Perez-Persona, 2007; 2. Dispenzieri, 2008; 3. Rajkumar, 2015

# SMM Standard of Care (NCCN)



# Preliminary Data Support Early Treatment Delays Progression in MM Continuum

Study	N	Response	OS (HR, 95% CI)	3-Year Progression to MM
<b>QuiRedex<sup>1,2</sup></b> (Rd vs observation)	119	ORR: 90%	0.57 (0.34, 0.95)	77%
<b>ECOG<sup>3</sup></b> (R vs observation)	182	PR or better: 50%	-	91%

## Study limitations

- No advanced imaging to exclude active MM at baseline (QuiRedex)
- Toxicity of lenalidomide (ECOG)
  - 40% of patients discontinued due to an AE
  - Median duration of treatment only 2 years

Rd = lenalidomide, dexamethasone; R = lenalidomide

1. Mateos 2016; 2. Mateos 2022; 3. Lonial 2019

# Patients with High-Risk SMM Likely to Progress to MM

- Observation is current standard of care for SMM
  - Risk of therapeutic intervention being initiated only after detection of end-organ damage
- Patients and providers want option of proactive treatment for high-risk SMM rather than watching and waiting for disease progression
- Treatment decision to be made between patient and provider

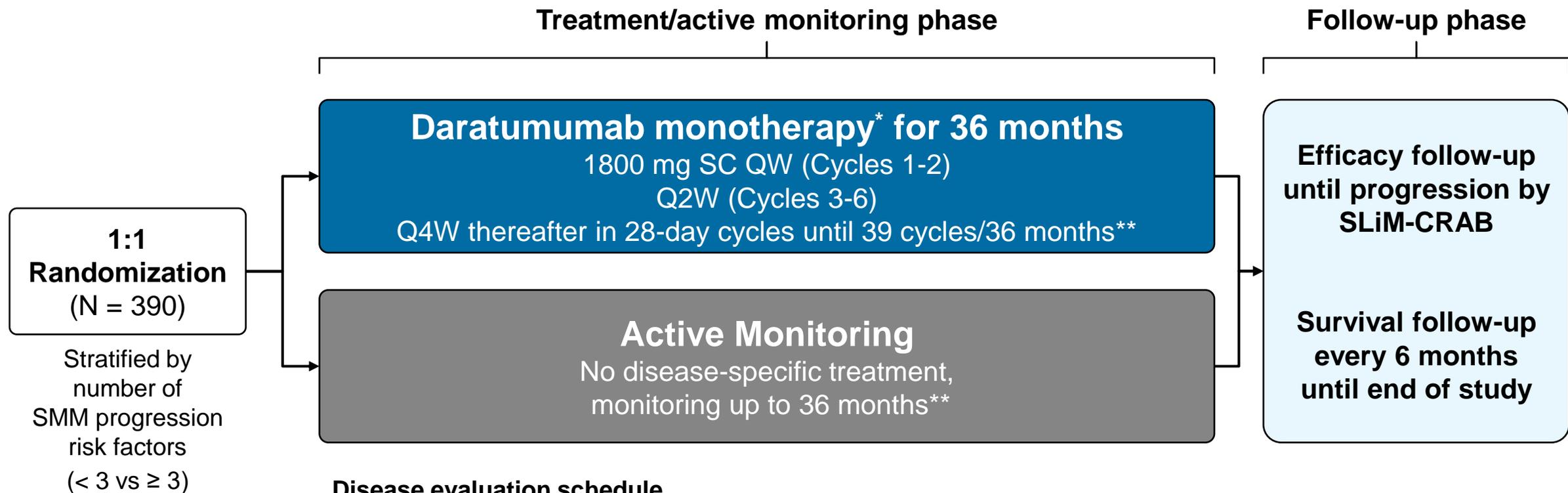


## Clinical Efficacy

**Robin Carson, MD**

Vice President, Oncology Research & Development  
Clinical Leader, Daratumumab  
Johnson & Johnson

# Phase 3 AQUILA (Study SMM3001): Study Design



## Disease evaluation schedule

- **Laboratory efficacy** – Every 12 weeks by central lab until disease progression
- **Imaging (CT/PET-CT, MRI)** – Yearly (central review)
- **Bone marrow** – At least every 2 years

\* Same dose as recommended to treat active MM

\*\* Or confirmed disease progression (whichever occurred first)

# AQUILA: Enrollment Criteria

- High-risk SMM based on predefined criteria
- Confirmed SMM diagnosis (per IMWG criteria) for  $\leq 5$  years
- $\geq 18$  years of age
- ECOG PS score of 0 or 1
- Absence active myeloma defined by SLiM-CRAB criteria or amyloidosis
  - Confirmed by CT/PET-CT and MRI imaging during screening to exclude bone disease

# AQUILA: Thresholds Used to Define High-Risk SMM

- BMPC  $\geq 10\%$  AND  
 $\geq 1$  of the following
  - Serum M-Protein  $\geq 3$  g/dL
  - Abnormal FLC ratio  $\geq 8$  and  $< 100$  (serum involved: uninvolved)
  - Immunoparesis (reduction of 2 uninvolved immunoglobulin isotypes below normal reference range)
  - IgA SMM
  - Clonal BMPCs  $> 50\%$  to  $< 60\%$

# Primary Endpoint - PFS: Progression to Active Myeloma Assessed by IRC per IMWG Criteria, or Death

<b>SLiM criteria</b>	<b>Clonal BMPCs</b>	$\geq 60\%$ BMPCs
	<b>Modified serum FLC</b>	Involved:uninvolved serum FLC ratio $\geq 100$ , involved light chain $\geq 100$ mg/L, and difference of involved – uninvolved light chain $\geq 25\%$ from lowest value (nadir)
	<b>Focal lesions</b>	$> 1$ focal lesions on MRI studies
<b>CRAB criteria</b>	<b>Calcium elevation</b>	Serum calcium $> 0.25$ mmol/L ( $> 1$ mg/dL) higher than the upper limit of normal of $> 2.75$ mmol/L ( $> 11$ mg/dL)
	<b>Renal insufficiency</b>	Creatinine clearance $< 40$ mL/min or serum creatinine $> 177$ $\mu$ mol/L ( $> 2$ mg/dL)
	<b>Anemia</b>	Hemoglobin $> 2.0$ g/dL below the limit of normal or $< 10.0$ g/dL
	<b>Bone disease</b>	$\geq 1$ osteolytic lesions on skeletal radiography, CT, or PET-CT

# Key Secondary Endpoints

- Type 1 error- controlled secondary endpoints
  - Overall response rate (ORR)
  - Progression-free survival on first-line multiple myeloma treatment (PFS2)
  - Overall survival (OS)
- Other secondary endpoints
  - Time to first subsequent treatment for MM
  - Health-related quality of life measures

# Baseline Demographics Balanced Between Arms

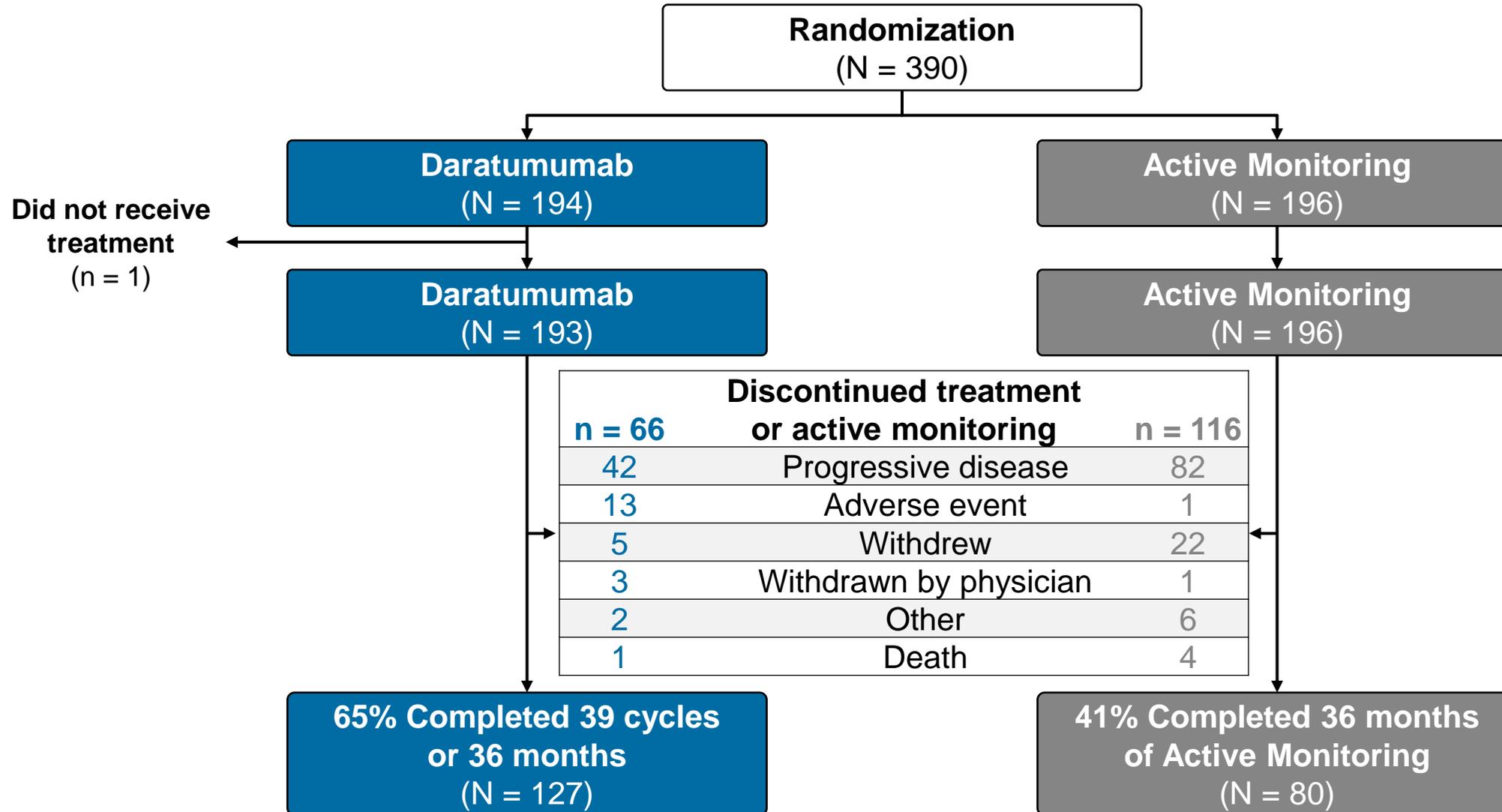
		Daratumumab (N = 194)	Active Monitoring (N = 196)
	<b>Median (range)</b>	<b>63.0 (31, 86)</b>	<b>64.5 (36, 83)</b>
<b>Age (years)</b>	<b>18 to &lt; 65, %</b>	<b>55%</b>	<b>50%</b>
	<b>65 to &lt; 75, %</b>	<b>35%</b>	<b>38%</b>
	<b>≥ 75 years, %</b>	<b>11%</b>	<b>12%</b>
<b>Sex, %</b>	<b>Female</b>	<b>51%</b>	<b>53%</b>
	<b>White</b>	<b>83%</b>	<b>83%</b>
<b>Race</b>	<b>Black</b>	<b>2%</b>	<b>4%</b>
	<b>Asian</b>	<b>9%</b>	<b>7%</b>
	<b>Other / NR</b>	<b>6%</b>	<b>7%</b>
<b>ECOG PS score, %</b>	<b>0</b>	<b>85%</b>	<b>82%</b>
	<b>1</b>	<b>15%</b>	<b>18%</b>

# Disease Characteristics Balanced and Representative of Patients with High-Risk SMM

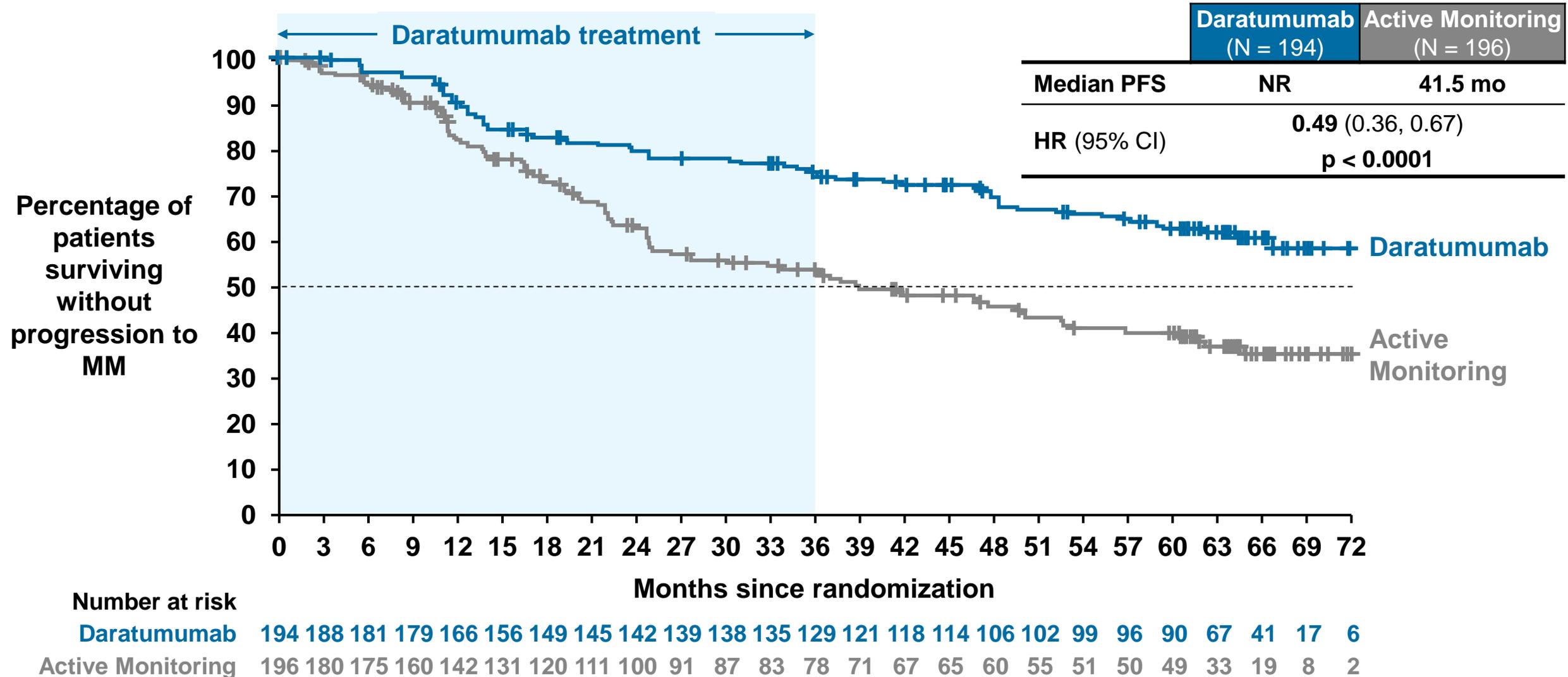
		Daratumumab (N = 194)	Active Monitoring (N = 196)
<b>Median time from SMM diagnosis to randomization (range)</b>		<b>0.80 years</b> (0, 4.7)	<b>0.67 years</b> (0, 5.0)
<b>Time from diagnosis &lt; 2 years</b>		77%	76%
<b>Median BMPCs (range)</b>		<b>20%</b> (8, 60)	<b>20%</b> (10, 55)
<b>Risk Factors for High-Risk SMM</b>			
<b>Serum M Protein <math>\geq</math> 3 g/L</b>		<b>18%</b>	<b>20%</b>
<b>Serum Involved: uninvolved FLC Ratio <math>\geq</math> 8 and &lt; 100</b>		<b>70%</b>	<b>75%</b>
<b>Immunoparesis with reduction of <math>\geq</math> 2 uninvolved immunoglobulin isotypes</b>		<b>60%</b>	<b>59%</b>
<b>IgA SMM</b>		<b>28%</b>	<b>21%</b>
<b>Clonal BMPCs &gt; 50% to &lt; 60%</b>		<b>3%</b>	<b>2%</b>
<b>Number of risk factors for progression</b>	<b>&lt; 3*</b>	<b>81%</b>	<b>82%</b>
	<b><math>\geq</math> 3</b>	<b>19%</b>	<b>18%</b>
<b>Cytogenetic risk profile</b>			
<b><math>\geq</math> 1 of del(17p), t(4;14), and/or t(14;16)</b>		<b>n = 167</b> <b>17%</b>	<b>n = 170</b> <b>13%</b>

\*Median number of risk factors was 2

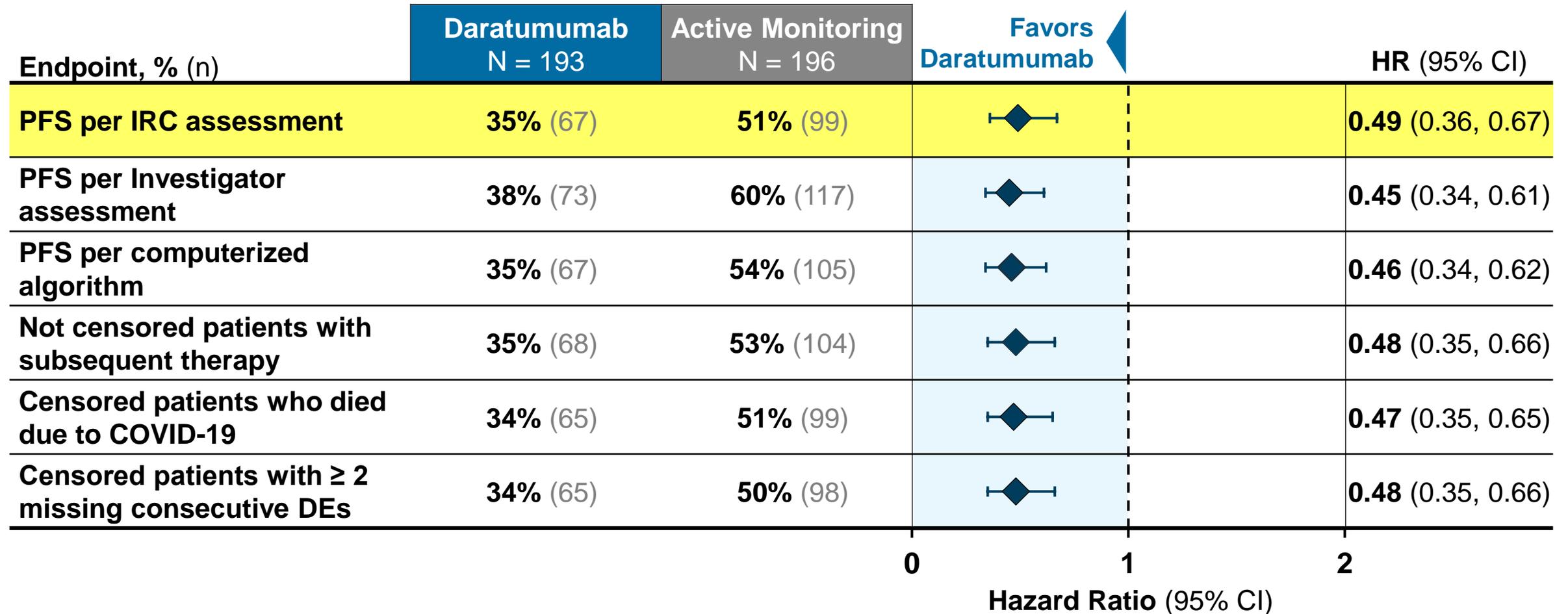
# Disposition: More Patients Completed Study Treatment in Daratumumab Arm



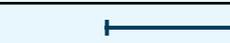
# Primary Endpoint of PFS Met, Daratumumab Significantly Reduced Risk of Progression to MM



# Sensitivity / Supplementary Analyses Strongly Support the Robustness of Primary PFS Results



# PFS Benefit Consistent Across Preplanned Subgroups

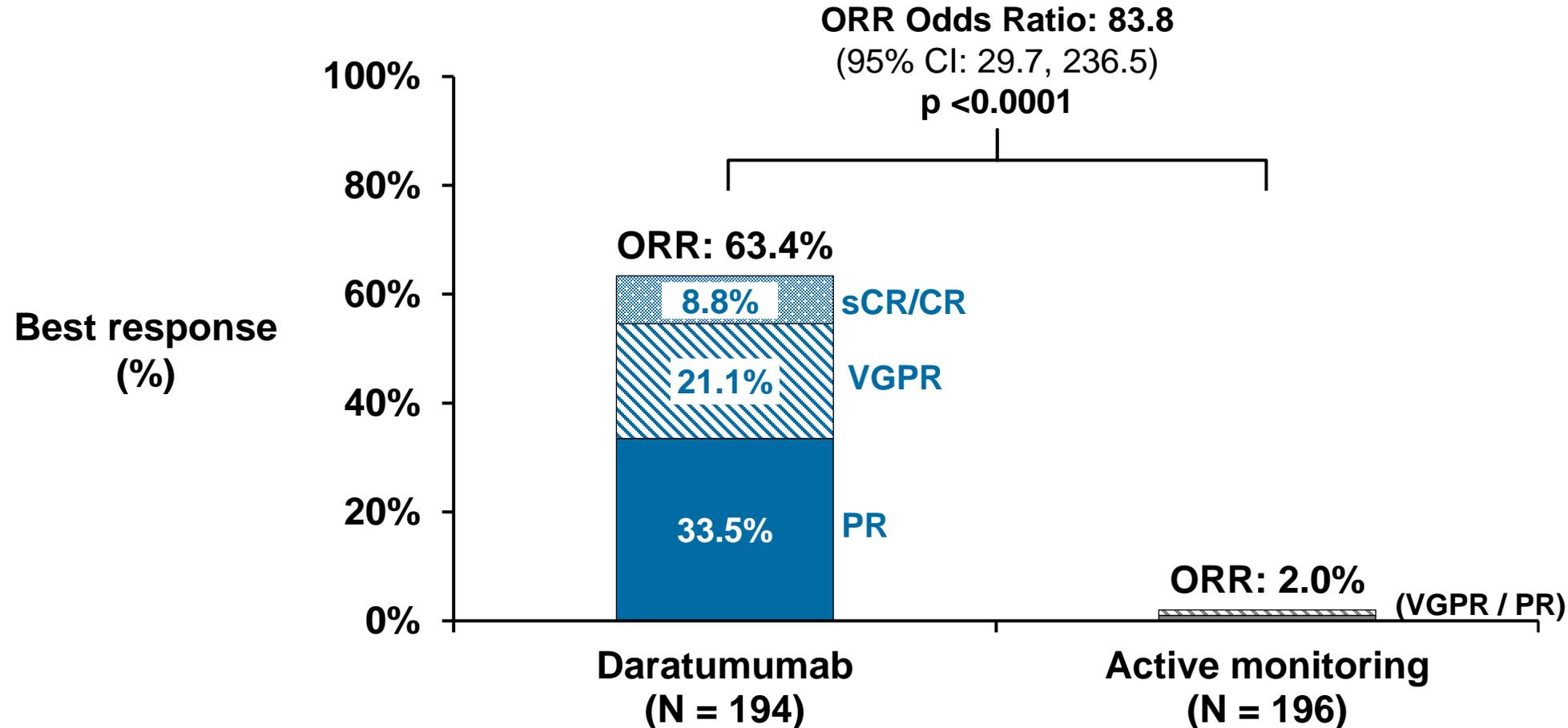
Subgroup		Disease progression or death, events / patients		Favors Daratumumab 	HR (95% CI)
		Daratumumab	Active Monitoring		
Age	< 65 years	34/106	45/98		<b>0.51</b> (0.32, 0.79)
	≥ 65 years	33/88	54/98		<b>0.50</b> (0.32, 0.77)
Sex	Male	37/95	48/93		<b>0.52</b> (0.34, 0.80)
	Female	30/99	51/103		<b>0.47</b> (0.30, 0.74)
Race	White	53/161	79/162		<b>0.49</b> (0.34, 0.69)
	Non-White	14/33	20/34		<b>0.57</b> (0.28, 1.12)
Region	EU	39/97	50/95		<b>0.62</b> (0.41, 0.94)
	North America	7/32	9/33		<b>0.53</b> (0.19, 1.42)
	Other	21/64	40/68		<b>0.36</b> (0.21, 0.62)
Baseline ECOG	0	53/165	80/160		<b>0.44</b> (0.31, 0.63)
PS score	1	14/29	19/36		<b>0.95</b> (0.48, 1.91)
Baseline renal function	Normal	17/54	27/58		<b>0.52</b> (0.28, 0.96)
	Abnormal	50/140	72/138		<b>0.49</b> (0.34, 0.70)
Risk factors	< 3	51/157	78/161		<b>0.48</b> (0.34, 0.69)
	≥ 3	16/37	21/35		<b>0.54</b> (0.28, 1.04)
Cytogenetic risk at study entry	Yes	13/29	14/22		<b>0.37</b> (0.17, 0.82)
	No	39/116	59/118		<b>0.52</b> (0.35, 0.78)

0.1

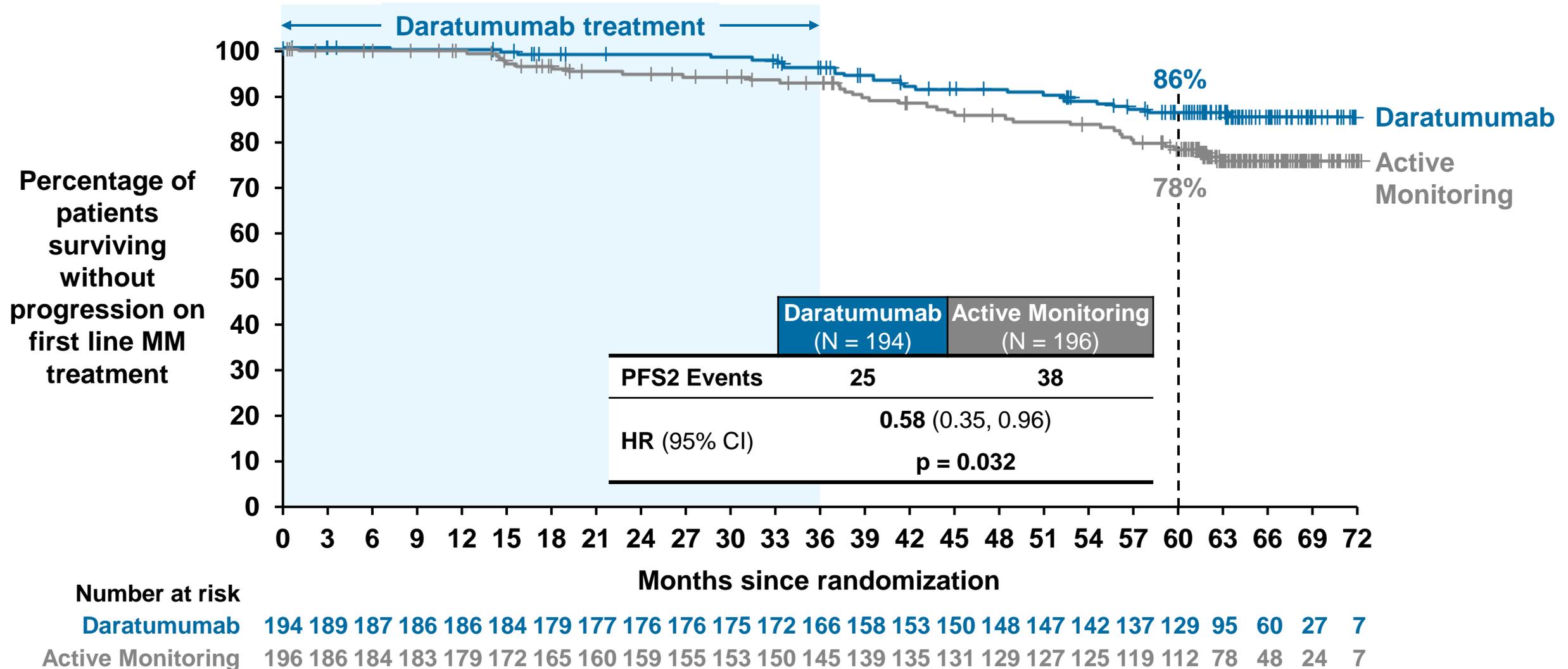
Hazard Ratio (95% CI)

1

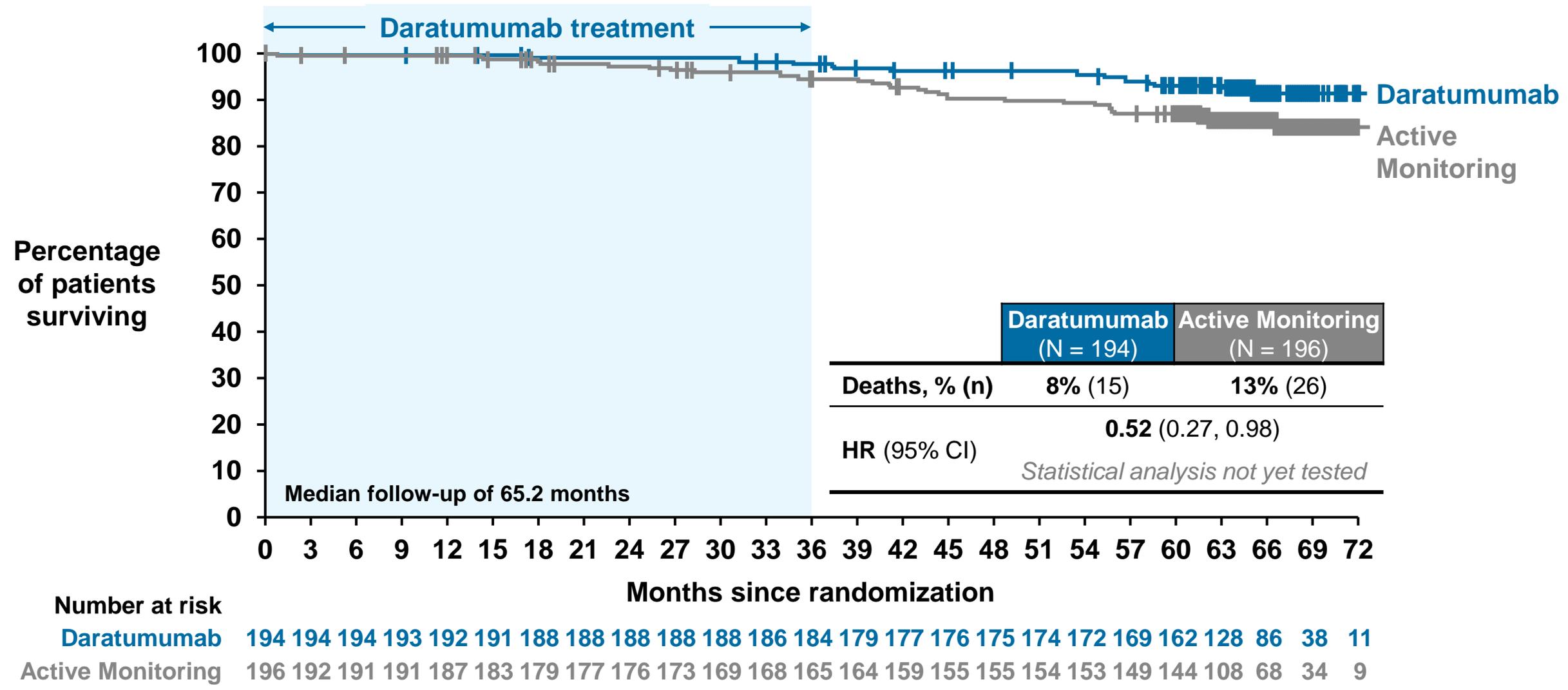
# Secondary Endpoint: ORR Shows Statistically Significant and Clinically Meaningful Daratumumab Response



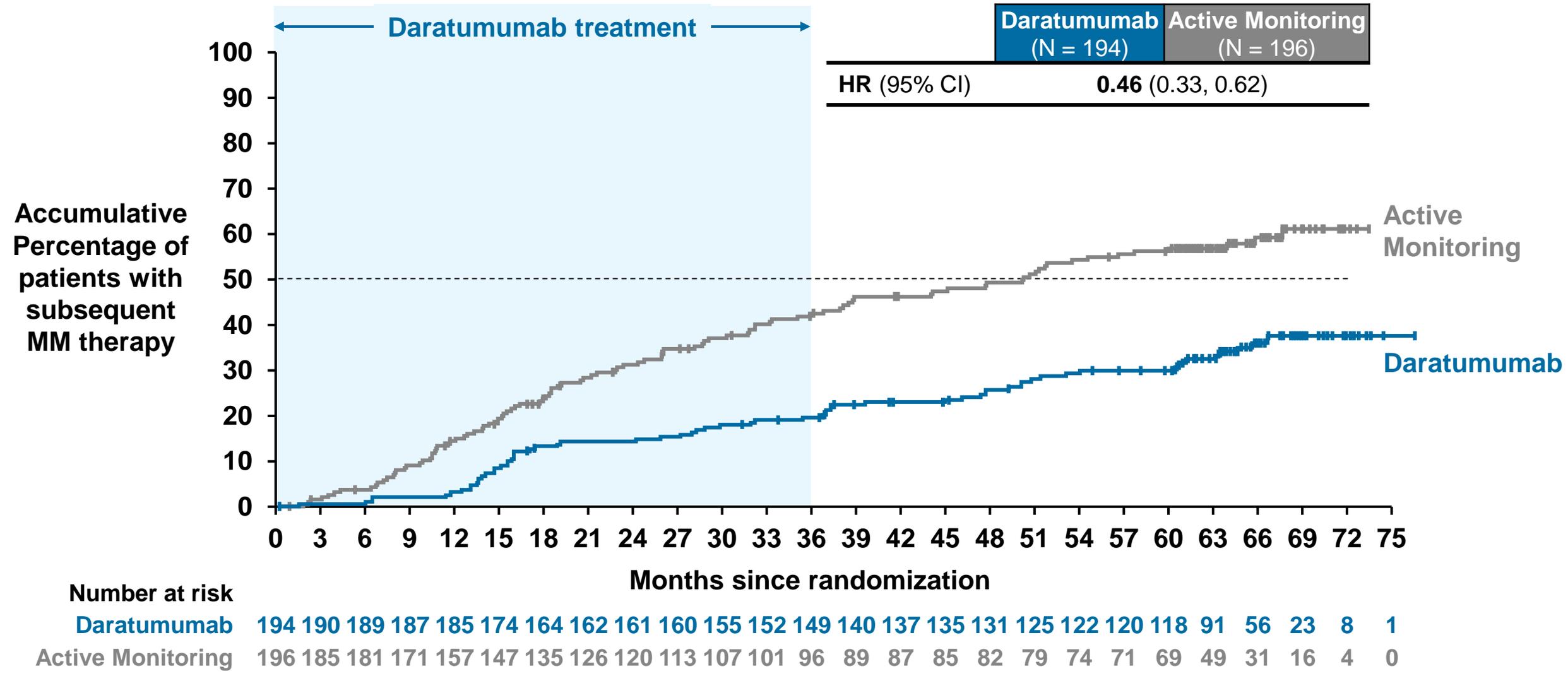
# Secondary Endpoint: PFS2 (From Randomization to Progression After First-Line Treatment for Active MM or Death)



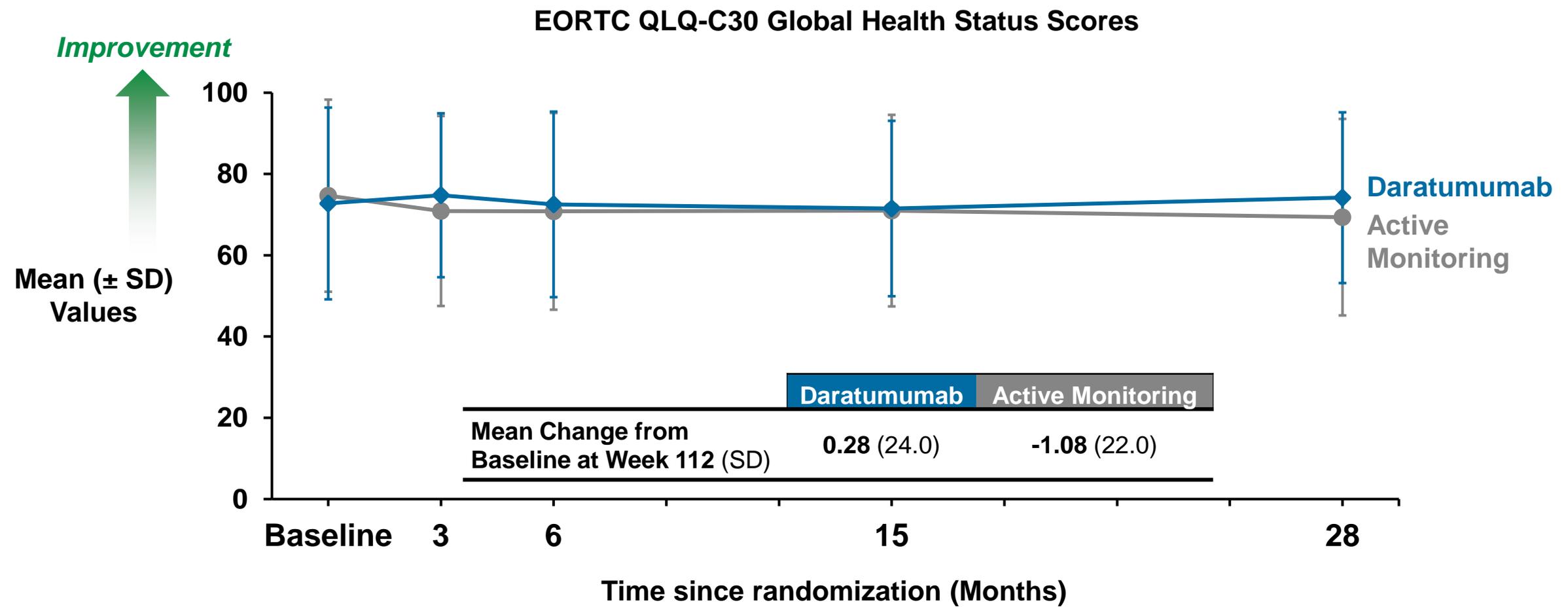
# Secondary Endpoint: Evidence of Positive Overall Survival Trend



# Secondary Endpoint: Daratumumab Delayed Time to First Treatment for Multiple Myeloma



# Secondary Endpoint: Health Related QoL Comparable Between Arms Over Course of the Study



Number of patients

Daratumumab	185	178	168	153	121
Active Monitoring	153	177	155	135	83

# AQUILA Strongly Favored Early Intervention with Daratumumab in Patients with High-risk SMM

- Statistically significant and clinically meaningful improvements in PFS
- Benefit observed across secondary endpoints, including early evidence of positive OS
- Health-related quality of life for daratumumab-treated patients comparable to active monitoring
- Daratumumab offers an opportunity to delay disease progression



## Clinical Safety

**Robyn Dennis, MD**

Senior Medical Director Oncology Research &  
Development

Johnson & Johnson

# Exposure to Daratumumab

	<b>Daratumumab (N = 193)</b>	<b>Active Monitoring (N = 196)</b>
<b>Median duration of treatment or monitoring (range), months</b>	<b>35.0</b> (0.03, 36.1)	<b>25.9</b> (0.1, 36.0)
<b>Median number of treatment cycles (range)</b>	<b>38</b> (1, 39)	n/a

# Daratumumab 1800 mg SC Dosing Schedule and Predose Medications

QW (Cycles 1-2)	Q2W (Cycles 3 - 6)	Q4W (Cycles 7 - 39)											
Months													
1	3	6	9	12	15	18	21	24	27	30	33	36	
*****	*****	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *	* * * * *
Doses													

- Medications given 1 – 3 hours prior to each daratumumab dose
  - Antipyretic
  - Antihistamine
  - Corticosteroid
- Leukotriene inhibitor recommended on Cycle 1 Day 1

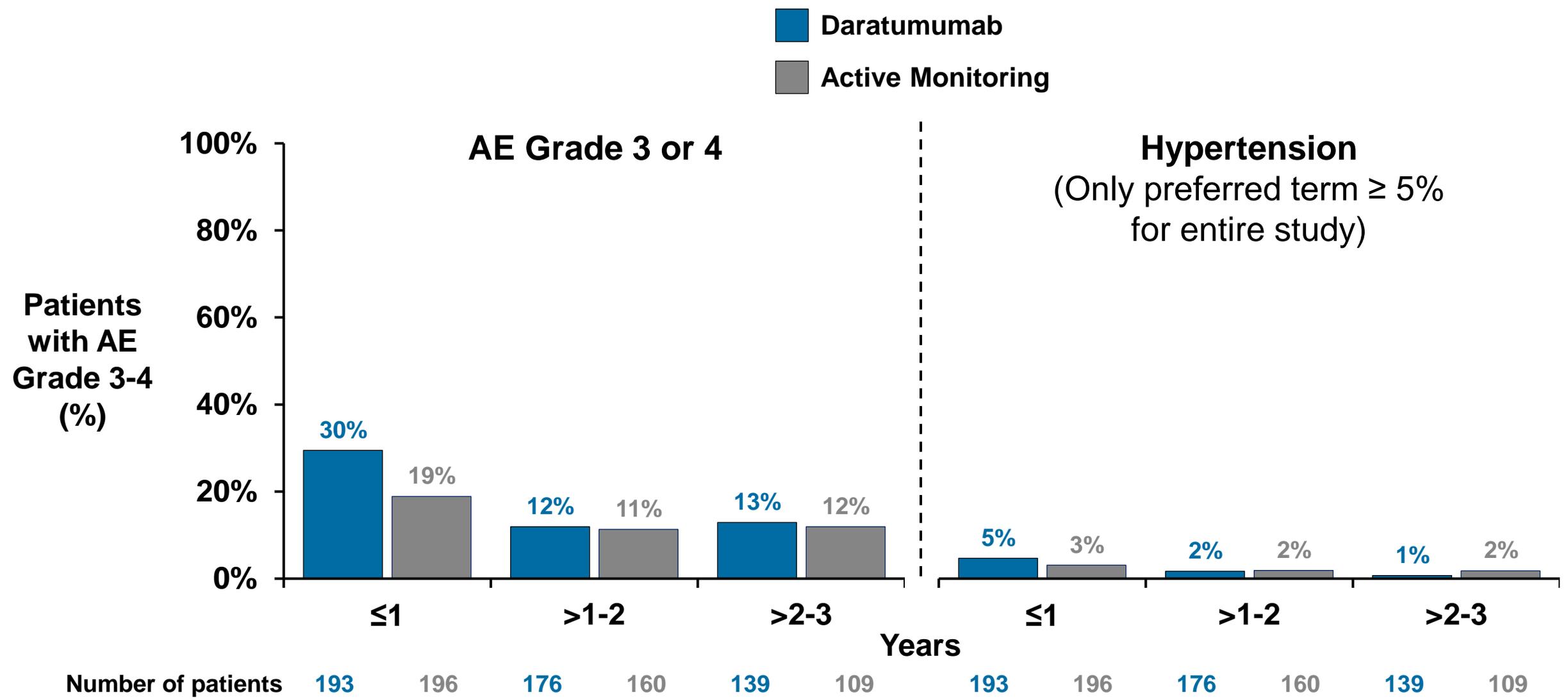
# AQUILA: Most Adverse Events were Low Grade

	Daratumumab (N = 193)	Active Monitoring (N = 196)
<b>Any AE</b>	<b>97%</b>	<b>83%</b>
<b>Grade 3 or 4</b>	<b>40%</b>	<b>30%</b>
<b>Any SAE</b>	<b>29%</b>	<b>19%</b>
<b>AEs leading to discontinuation, % (n)</b>	<b>6% (11)</b>	n/a
<b>AEs with outcome of death, % (n)</b>	<b>1% (2)</b>	<b>2% (4)</b>

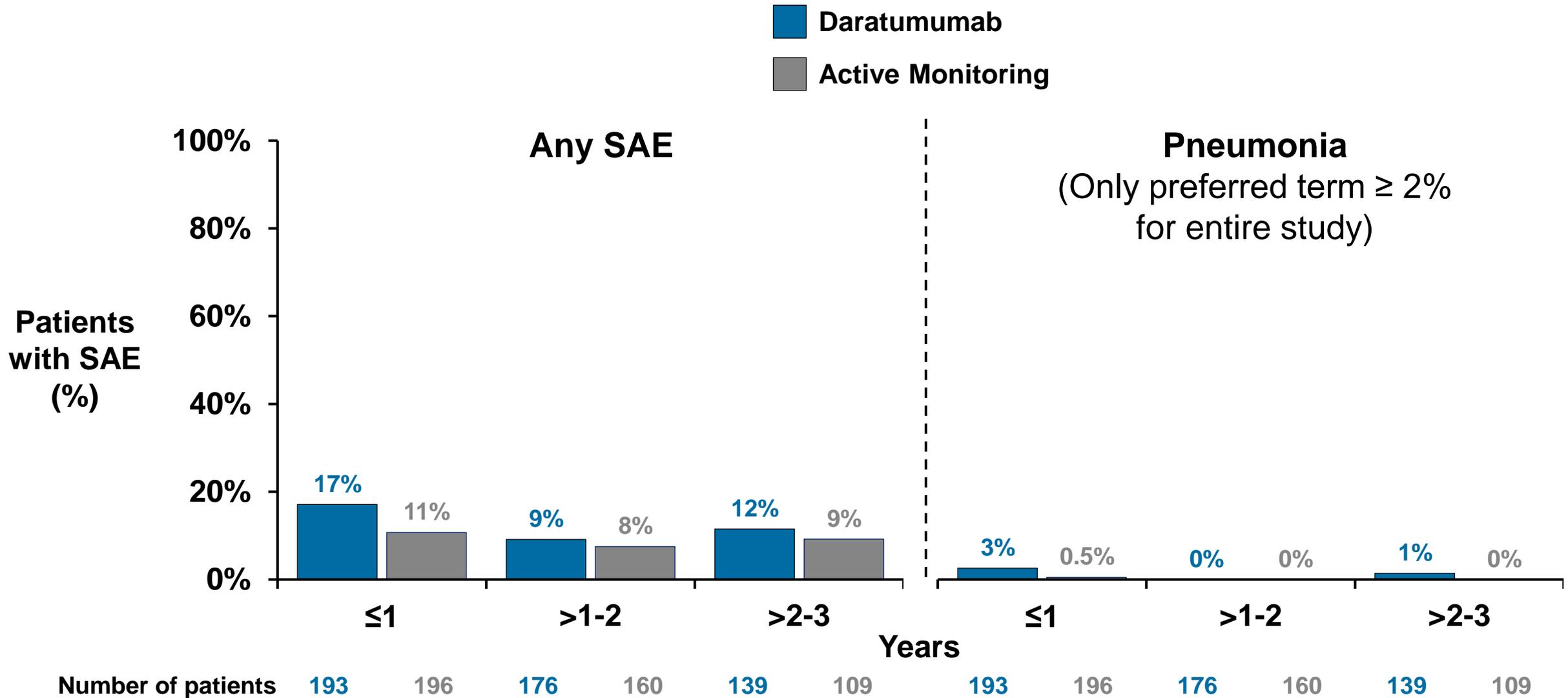
# AQUILA: Common AEs ( $\geq 10\%$ in Either Arm) Align with Current Daratumumab Label

	Daratumumab (N = 193)	Active Monitoring (N = 196)
<b>Any AE, %</b>	<b>97%</b>	<b>83%</b>
<b>Fatigue</b>	<b>34%</b>	<b>13%</b>
<b>Upper respiratory tract infection</b>	<b>30%</b>	<b>8%</b>
<b>Diarrhea</b>	<b>28%</b>	<b>5%</b>
<b>Arthralgia</b>	<b>27%</b>	<b>18%</b>
<b>Nasopharyngitis</b>	<b>25%</b>	<b>12%</b>
<b>Back pain</b>	<b>24%</b>	<b>19%</b>
<b>Insomnia</b>	<b>22%</b>	<b>3%</b>
<b>Nausea</b>	<b>19%</b>	<b>5%</b>
<b>Headache</b>	<b>18%</b>	<b>7%</b>
<b>Cough</b>	<b>17%</b>	<b>6%</b>
<b>Pyrexia</b>	<b>17%</b>	<b>3%</b>
<b>Injection site erythema</b>	<b>16%</b>	<b>0</b>
<b>Pain in extremity</b>	<b>15%</b>	<b>8%</b>
<b>Dyspnea</b>	<b>15%</b>	<b>5%</b>
<b>Pneumonia</b>	<b>11%</b>	<b>5%</b>
<b>Hypertension</b>	<b>10%</b>	<b>10%</b>
<b>Myalgia</b>	<b>10%</b>	<b>5%</b>
<b>Edema Peripheral</b>	<b>10%</b>	<b>2%</b>

# AQUILA: Incidence of Grade 3 or 4 AEs was Highest within the First Year



# AQUILA: Incidence of Serious Adverse Events



# AQUILA: Dose Delay Recommended As Primary Method For Managing Toxicities

	Daratumumab (N = 193)
<b>AEs leading to dose modification, %</b>	<b>47%</b>
<b>Cycle delays</b>	<b>38%</b>
<b>Dose skips</b>	<b>18%</b>
<b>Dose delay within cycle</b>	<b>4%</b>
<b>By preferred term (≥ 5%)</b>	
<b>Upper respiratory tract infection</b>	<b>7%</b>
<b>Pneumonia</b>	<b>6%</b>
<b>COVID-19</b>	<b>5%</b>

# AQUILA: AEs Leading to Discontinuation $\geq 1\%$ Patients

	Daratumumab (N = 193)	
	Any Grade	Grade 3 or 4
Treatment discontinuation due to AEs % (n)	6% (11)	3% (5)
<b>By Preferred Term <math>\geq 1\%</math></b>		
Fatigue	1% (2)	0.5% (1)
Anxiety	1% (2)	0.5% (1)
Dyspnea	1% (2)	0.5% (1)

# AQUILA: Deaths

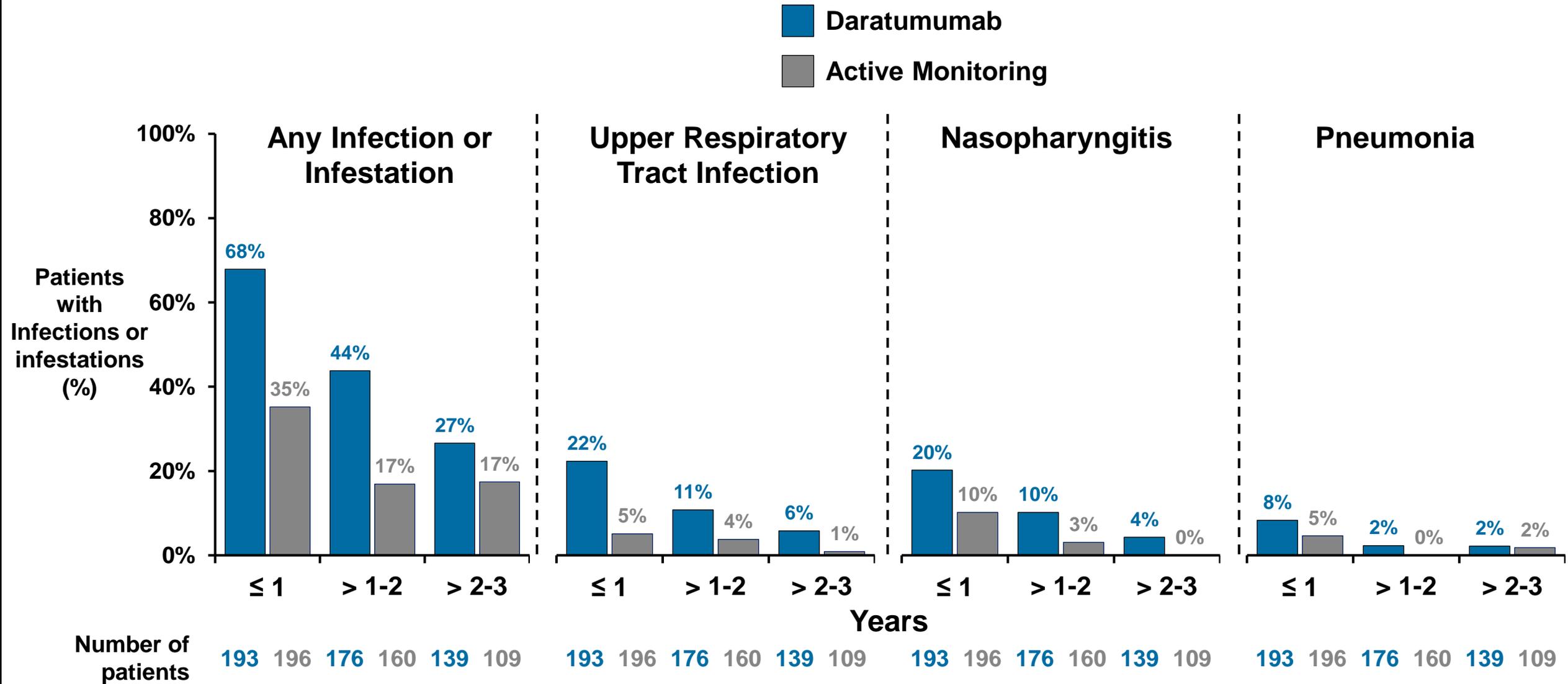
	Daratumumab (N = 193)	Active Monitoring (N = 196)
<b>Deaths, % (n)</b>	<b>8% (15)</b>	<b>13% (26)</b>
<b>Progressive disease</b>	<b>2% (3)</b>	<b>5% (9)</b>
<b>Adverse event</b>	<b>1% (2)</b>	<b>2% (4)</b>
<b>COVID-19</b>	<b>1% (2)</b>	<b>0</b>
<b>Pulmonary</b>	<b>0</b>	<b>1% (2)</b>
<b>Cardiac</b>	<b>0</b>	<b>1% (2)</b>
<b>Other*</b>	<b>5% (10)</b>	<b>7% (13)</b>
<b>Unknown, n</b>	<b>5</b>	<b>5</b>
<b>Cardiac events, n</b>	<b>3</b>	<b>3</b>
<b>Infection, n</b>	<b>1</b>	<b>3</b>
<b>Respiratory failure, n</b>	<b>1</b>	<b>1</b>
<b>General deterioration, n</b>	<b>0</b>	<b>1</b>

\*Events that occurred >30 days after discontinuation of daratumumab or active monitoring, or after the start of subsequent therapy

# AQUILA: Median Duration of Infections/Infestations was Comparable Between Arms

	Daratumumab (N = 193)		Active Monitoring (N = 196)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
<b>Patients with Infections and infestations, %</b>	<b>80%</b>	<b>16%</b>	<b>45%</b>	<b>5%</b>
<b>Duration of infections</b>				
<b>Median, days (Q1, Q3)</b>	<b>14 (7, 28)</b>	<b>5 (4, 15)</b>	<b>14 (8, 31)</b>	<b>9 (6, 12)</b>

# AQUILA: Infections/Infestations Risk Over Time (with Preferred Terms $\geq 10\%$ )



# Daratumumab Well-tolerated in Patients with High-Risk SMM, with Clinically Manageable Side Effects

- AEs observed were expected for daratumumab
- Majority AEs were low grade
- Highest incidence of AEs primarily occurred within the first year
- Treatment discontinuations low (6%)
- Most infections were low grade and 98% of infections resolved with a median duration of 14 days



## Clinical Perspective

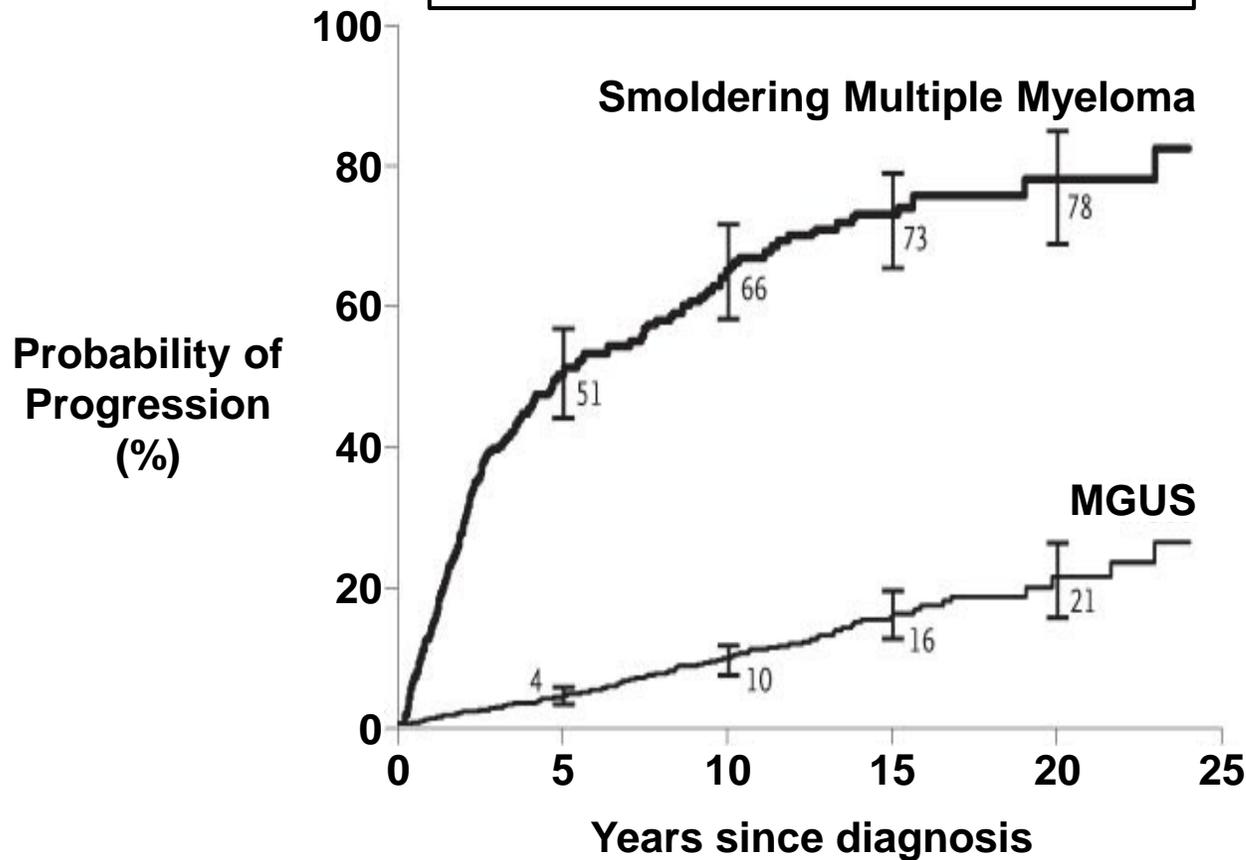
**S. Vincent Rajkumar, MD**

Edward W. and Betty Knight Scripps Professor of Medicine  
Mayo Clinic

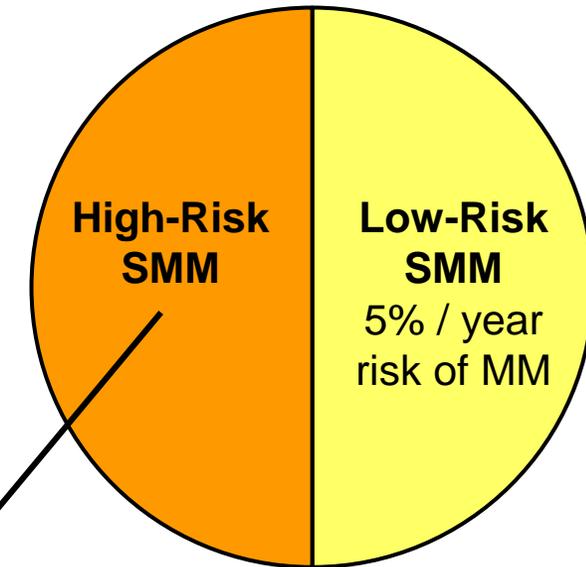
# High-Risk SMM is Appropriate Group for Early Intervention; NOT a Premalignancy (MGUS)



The NEW ENGLAND  
JOURNAL of MEDICINE



Kyle RA...Rajkumar SV. N Engl J Med 2007



≥10% Plasma Cells plus:

- M protein ≥3 g/dL
- Immunoparesis
- Abnormal FLC ratio 8-100
- IgA type

Rajkumar SV, Landgren O, Mateos MV. Blood 2015

# Challenges with Active Monitoring

- Don't want to treat too early but risk treating too late
- Close observation as done in AQUILA is likely not feasible in real world settings
- Observation in reputed academic settings has not been able to intervene in a timely manner
- Intervention should be considered in the right patient population

# Early Intervention for High-Risk SMM Acknowledged by Myeloma Experts

- MM studies have already moved beyond observation as standard of care
- Observation is not a control arm in any current or ongoing phase III trials for high-risk patients
- MM clinicians acknowledge need for treatment of high-risk disease, defining that patient population has shifted over time

# While Definition of High-Risk Continues to Evolve, Patients Today Deserve an Effective and Safe Option

- Key considerations from FDA
  - Suggested heterogeneity of study population
  - PFS as an appropriate endpoint in SMM
  - Safety in an asymptomatic patient population
  - Potential impact on QoL

# AQUILA Enrolled Well-Defined High-Risk Population

- AQUILA has the best characterized high-risk group
  - 50% of active monitoring patients progressed by 3 years
  - Included same biomarkers as used in current Mayo 2018 criteria with different risk thresholds
  - AQUILA showed benefit regardless of subgroup
- Patients with SMM will progress to MM at variable rates

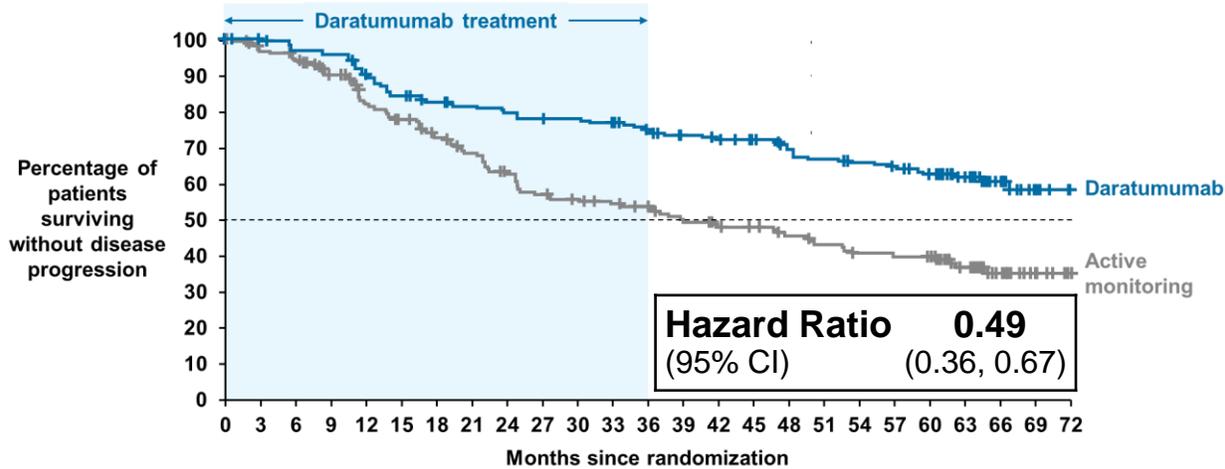
# PFS, as Defined in AQUILA, is an Appropriate Endpoint to Assess Benefit in SMM

- PFS in SMM is progression to MM or death
  - Stringent requirement for IMWG definition
- With progression comes life changing consequences
  - Life-long multi-drug regimens
  - Higher risk of morbidity and mortality
  - Worsening QoL
- Daratumumab monotherapy has low toxicity

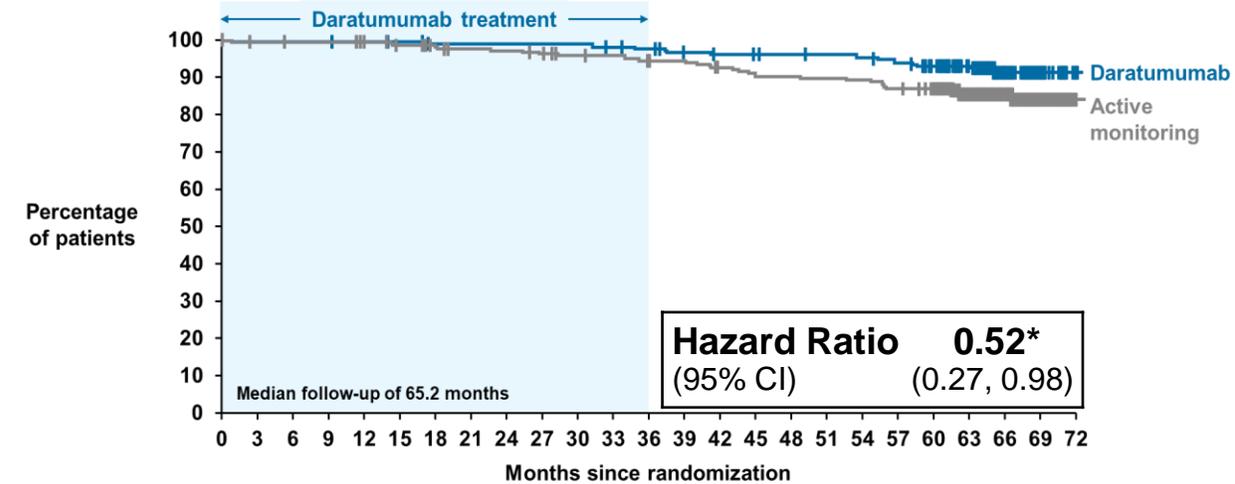
**Delaying time to progression of MM is a meaningful endpoint for high-risk SMM**

# AQUILA Provides Compelling Efficacy Data

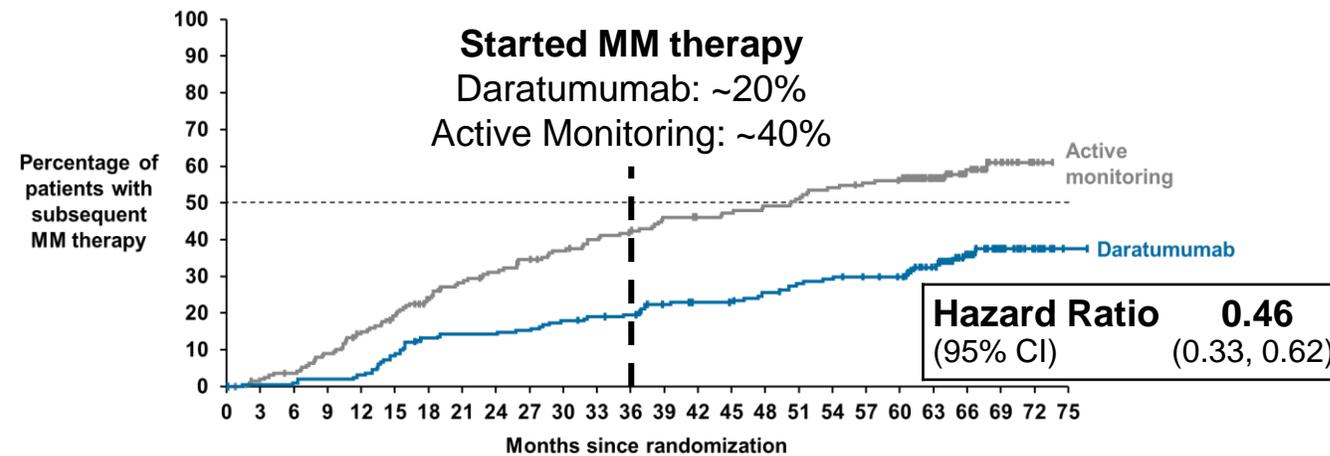
## PFS



## OS



## Time to subsequent therapy



\* Statistical analysis not yet tested

# AQUILA Shows Treatment with Single Agent Daratumumab for 36 Months is Safe

- Physicians diagnosing SMM familiar with daratumumab risks
- AEs mostly mild and occur early in treatment
  - Few discontinuations due to AEs
  - Mostly monitoring for infection risk
- QoL maintained in asymptomatic patients
- Daratumumab provides opportunity to delay more severe AEs associated with multi-drug myeloma therapy

# Daratumumab Offers Patients with High-Risk SMM an Early Intervention

- Meaningfully delay in progression to MM
- No negative impact to quality of life
- Manageable and well-understood adverse events
  - Daratumumab as standard of care for MM for >10 years
- Patients want ability to choose proactive treatments
  - With informed consent, in shared decision making, can determine their best treatment path
- Daratumumab can fundamentally change treatment landscape
  - Offering patients a choice that could extend their life

**DARZALEX FASPRO**  
(daratumumab and hyaluronidase)  
**for the Treatment of High-Risk  
Smoldering Multiple Myeloma**

**May 20, 2025**

Oncologic Drugs Advisory Committee

Johnson & Johnson



**Backup Slides Shown**

# FDA Table 10: First Line Subsequent Therapies for MM

	Dara SC N = 194 n (%)	ACTM N = 196 n (%)	Overall N = 390 n (%)
<b>Participants with first line therapy</b>	65 (34)	105 (54)	170 (44)
VRd	19 (10)	29 (15)	48 (12)
VCd	6 (3)	14 (7)	20 (5)
VTd	9 (5)	8 (4)	17 (4)
DVRd	4 (2)	10 (5)	14 (4)
DRd	3 (2)	10 (5)	13 (3)
Rd	5 (3)	7 (4)	12 (3)
DVMP	1 (0.5)	5 (3)	6 (2)
KRd	3 (2)	3 (2)	6 (2)
DVTd	2 (1)	2 (1)	4 (1)
Isa-VRd	1 (0.5)	3 (2)	4 (1)
Vd	2 (1)	1 (0.5)	3 (1)
Daratumumab	2 (1)	0 (0)	2 (0.5)
IRd	0 (0)	2 (1)	2 (0.5)
R	1 (0.5)	1 (0.5)	2 (0.5)
RCd	1 (0.5)	1 (0.5)	2 (0.5)
VMP	1 (0.5)	1 (0.5)	2 (0.5)
VMP-DRd	0 (0)	2 (1)	2 (0.5)
D-VTCd	0 (0)	1 (0.5)	1 (0.3)
Dara-Iber-d	1 (0.5)	0 (0)	1 (0.3)
DKRd	1 (0.5)	0 (0)	1 (0.3)
DVd	0 (0)	1 (0.5)	1 (0.3)
Elo-KRd	0 (0)	1 (0.5)	1 (0.3)
Isa	0 (0)	1 (0.5)	1 (0.3)
KCd	0 (0)	1 (0.5)	1 (0.3)
Venetoclax+VTd	0 (0)	1 (0.5)	1 (0.3)
VTCd	1 (0.5)	0 (0)	1 (0.3)
VRd, Isa-Kd, transplant	1 (0.5)	0 (0)	1 (0.3)
VRTd + melphalan, transplant	1 (0.5)	0 (0)	1 (0.3)
Any Daratumumab-containing regimen	14 (7)	31 (16)	45 (12)