Phase 3 BOSTON Study Results Presented at 2020 ASCO Annual Meeting

May 29, 2020

On Today's Call

Prepared Remarks

- **Ian Karp, MBA**, *Vice President, Investor and Public Relations*
- **Michael G. Kauffman, MD, PhD**, *Chief Executive Officer*
- **Jatin Shah, MD**, *Chief Medical Officer*
- **Paul Richardson, MD**, *Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, Dana Farber Cancer Institute and R.J. Corman Professor of Medicine at Harvard Medical School*

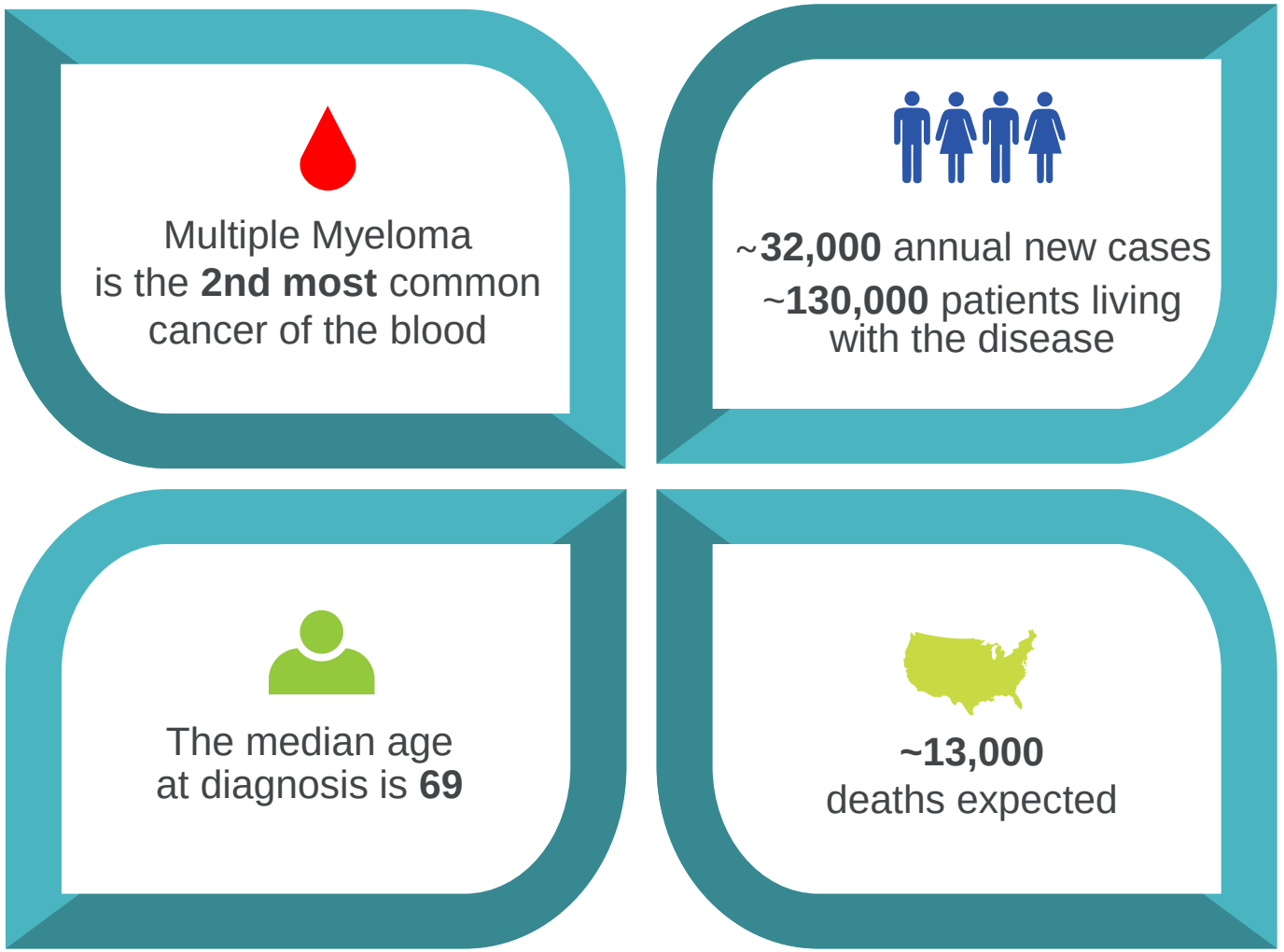
Joining for Q&A Session

- **Sharon Shacham, PhD, MBA**, *President and Chief Scientific Officer*
- **John Demaree, MBA**, *Chief Commercial Officer*

Forward-looking Statements and Other Important Information

This presentation contains forward-looking statements within the meaning of the “safe harbor” provisions of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm’s beliefs regarding XPOVIO’s ability to treat patients with multiple myeloma and expectations related to other XPOVIO regulatory submissions. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm’s drug candidate portfolio will result in stock price appreciation. Management’s expectations and, therefore, any forward-looking statements in this presentation could also be affected by risks and uncertainties relating to a number of other factors, including the following: the risk that the COVID-19 pandemic could disrupt Karyopharm’s business more severely than it currently anticipates, including by reducing sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm’s drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm’s drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm’s competitors for indications in which Karyopharm is currently developing its drug candidates; and Karyopharm’s ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on May 5, 2020, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

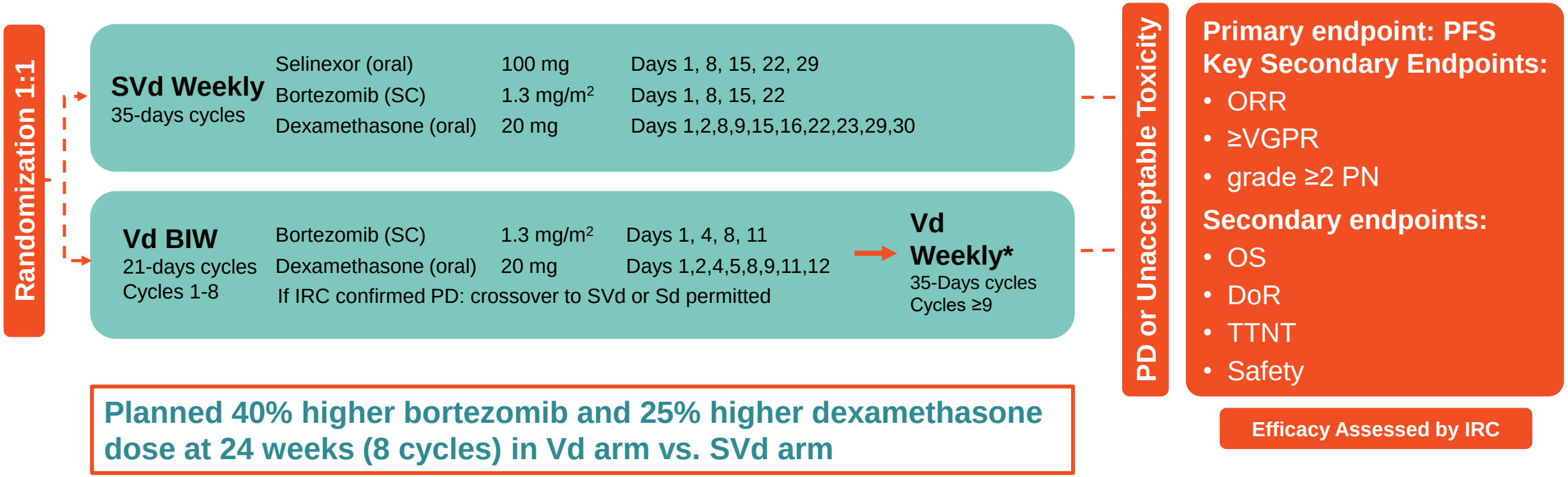
Multiple Myeloma (MM) Remains an Incurable Disease Where Patients are in Need of New Treatment Options



Source: SEER Cancer Stat Facts, May 2020. National Cancer Institute.

U.S. Statistics

BOSTON Trial: Phase 3, Global, Randomized, Open Label, Controlled Study in Patients with Multiple Myeloma who Had Received 1-3 Prior Therapies



Planned 40% higher bortezomib and 25% higher dexamethasone dose at 24 weeks (8 cycles) in Vd arm vs. SVd arm

CR= complete response, DoR = duration of response, IMWG = International Myeloma Working Group, IRC = Independent Review Committee, OS = overall survival, PD = progressive disease, PFS = progression free survival, PR = partial response, PN = peripheral neuropathy, sCR = stringent complete response, TTNT = time to next therapy, VGPR = very good partial response. PFS defined as: Time from date of randomization until the first date of progressive disease, per IMWG response criteria, or death due to any cause, whichever occurred first, as assessed by IRC. ORR: Any response ≥PR (ie, PR, VGPR, CR, or sCR) based on the IRC's response outcome assessments, according to IMWG response criteria (Kumar et al. Lancet oncology 2016). All changes in MM disease assessments were based on baseline MM disease assessments.
*Vd weekly dosing and schedule for cycles≥ 9 as per SVd arm description.

Baseline Characteristics

Patient and Disease Characteristics Well Balanced Between Treatment Arms

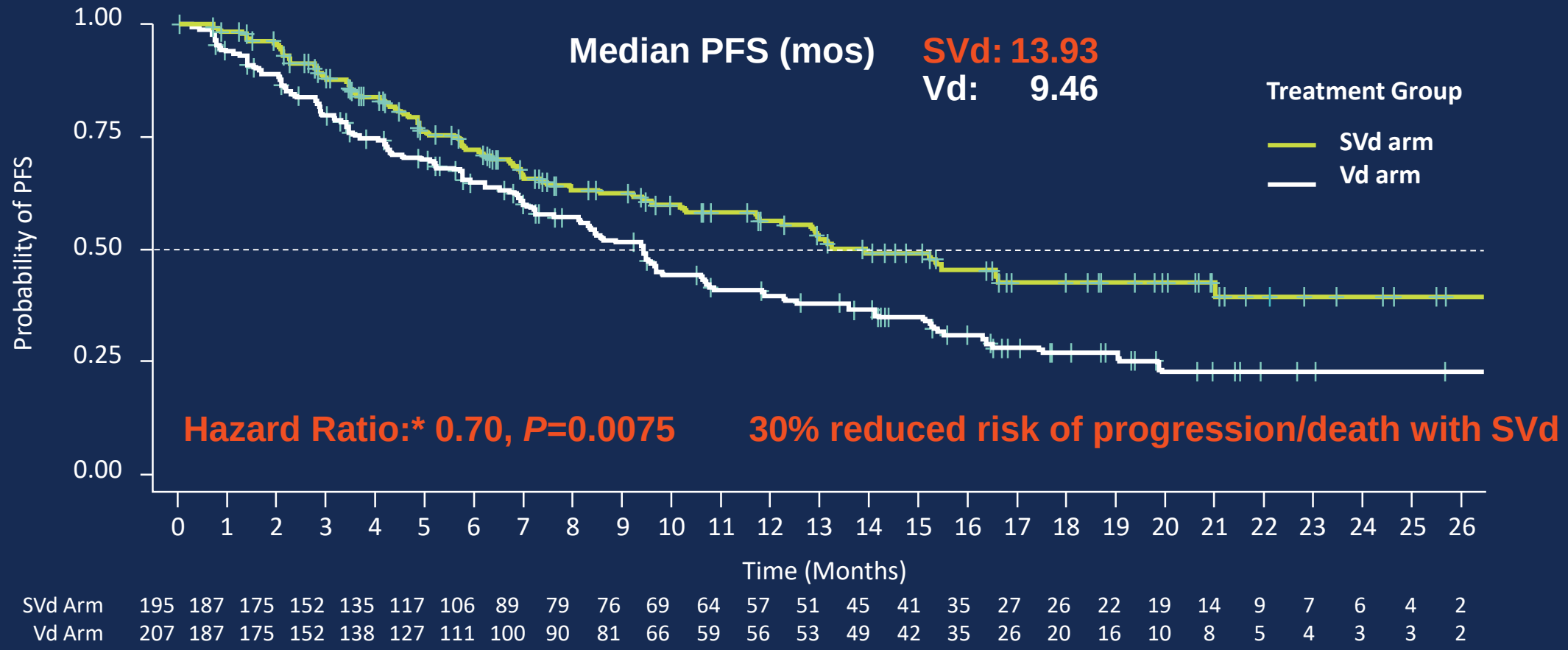
Characteristic	SVd arm (n=195)	Vd arm (n=207)
Median age, years (range)	66 (40, 87)	67 (38, 90)
≥75 years, n (%)	34 (17)	47 (23)
Male, n (%)	115 (59)	115 (56)
Creatinine clearance, mL/min, n (%)		
<30	3 (2)	10 (5)
30-60	53 (27)	60 (29)
Time since initial diagnosis, years, (range)	3.8 (0.4, 23.0)	3.6 (0.4, 22.0)
High risk cytogenetic, [del (17p) or t (14;16) or t (4;14) or amp 1q21] n (%)*	97 (50)	95 (46)
R-ISS disease stage at screening, n (%)		
I or II	173 (89)	177 (86)
III	12 (6)	16 (8)
Unknown	10 (5)	14 (7)
Number of prior lines of therapy, n (%)		
1	99 (51)	99 (48)
2	65 (33)	64 (31)
3	31 (16)	44 (21)
Prior therapies, n (%)		
Bortezomib	134 (68.7) } 79.0%	145 (70.0) } 80.1%
Carfilzomib	20 (10.3)	21 (10.1)
Daratumumab	11 (5.6)	6 (2.9)
Lenalidomide	77 (39.5)	77 (37.2)

*Fluorescence in-situ hybridization was performed at a central laboratory and used to assess cytogenetic risk status. 1q21 required at least 3 copies.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Progression Free Survival (PFS) Significantly Longer with SVd Compared to Vd

Early and Sustained PFS Benefit (Assessed by IRC)

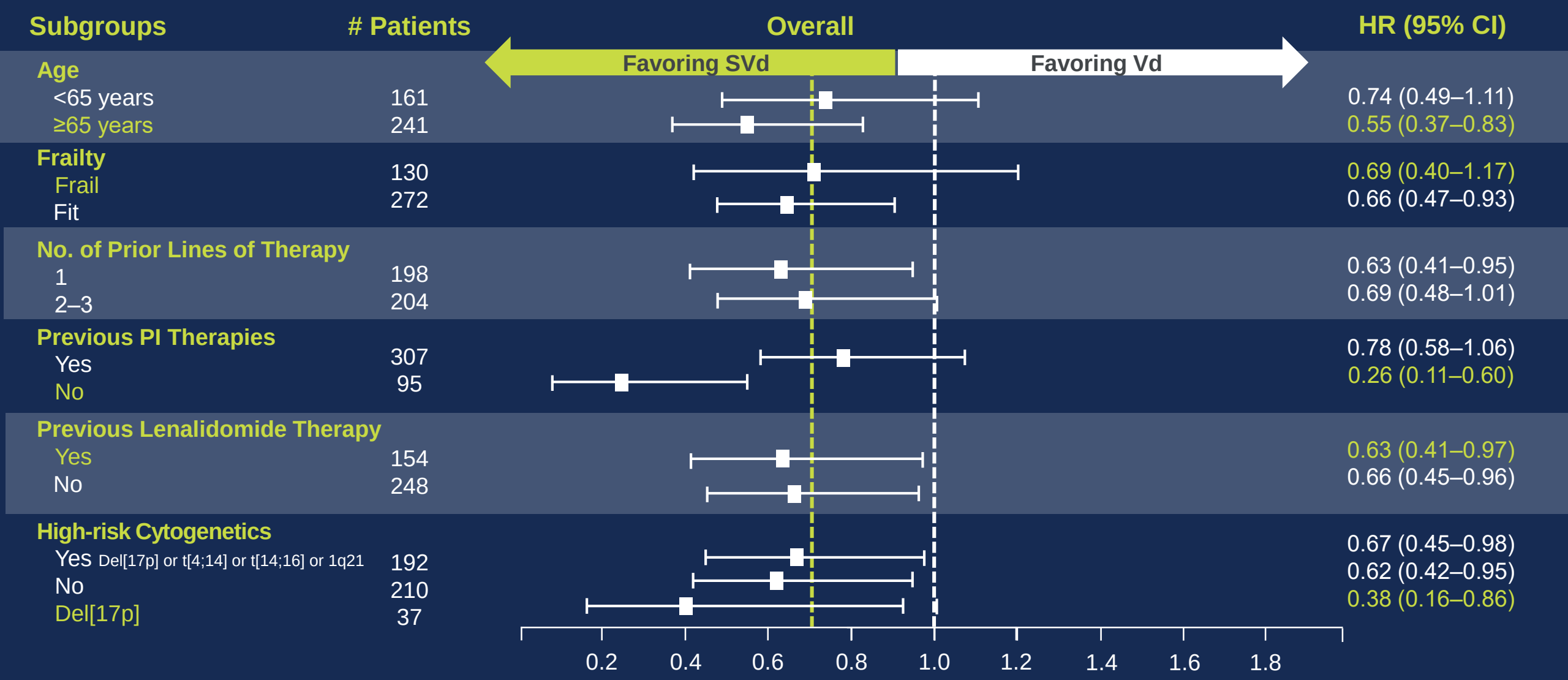


Intention-to-treat (ITT) population N=402, Data cut-off February 18, 2020
*HR=Hazard Ratio 95% CI=0.53–0.93 one-sided *P* value

Median follow-up: 13.2 and 16.5 months in SVd and Vd arms, respectively

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

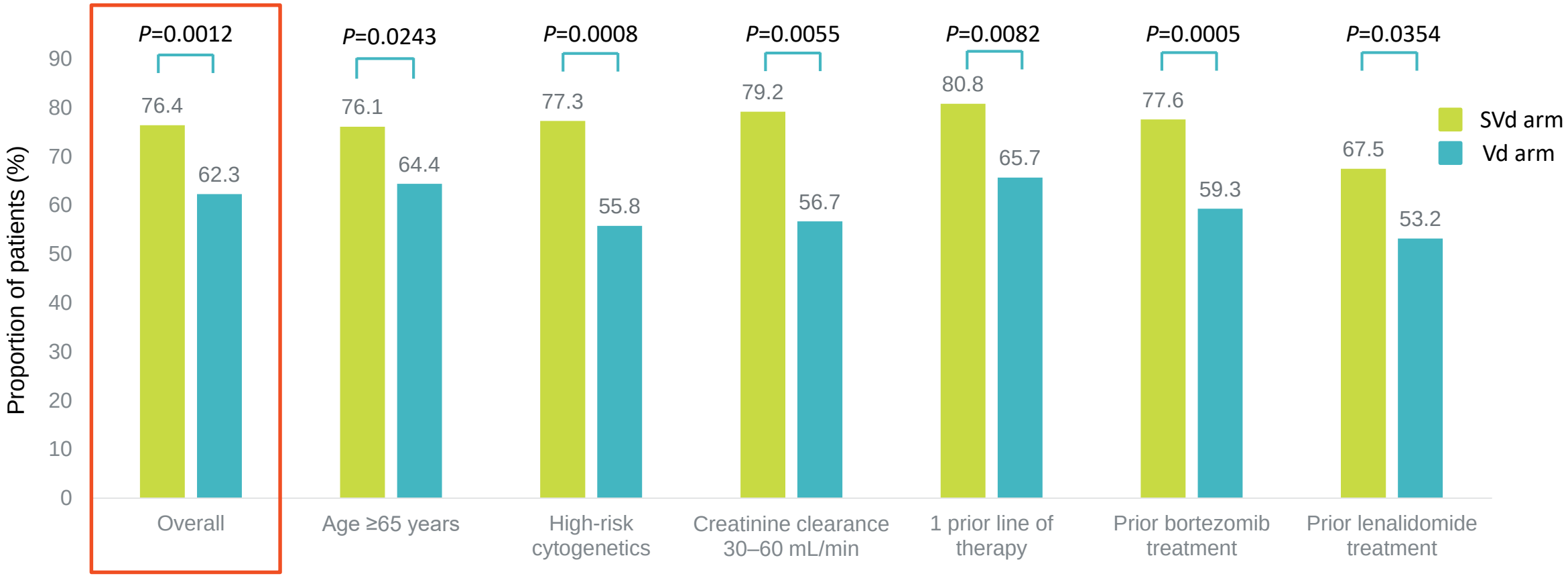
Consistent PFS Benefit for SVd Across Subgroups



HR = Hazard Ratio, Data cut-off February 18, 2020.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

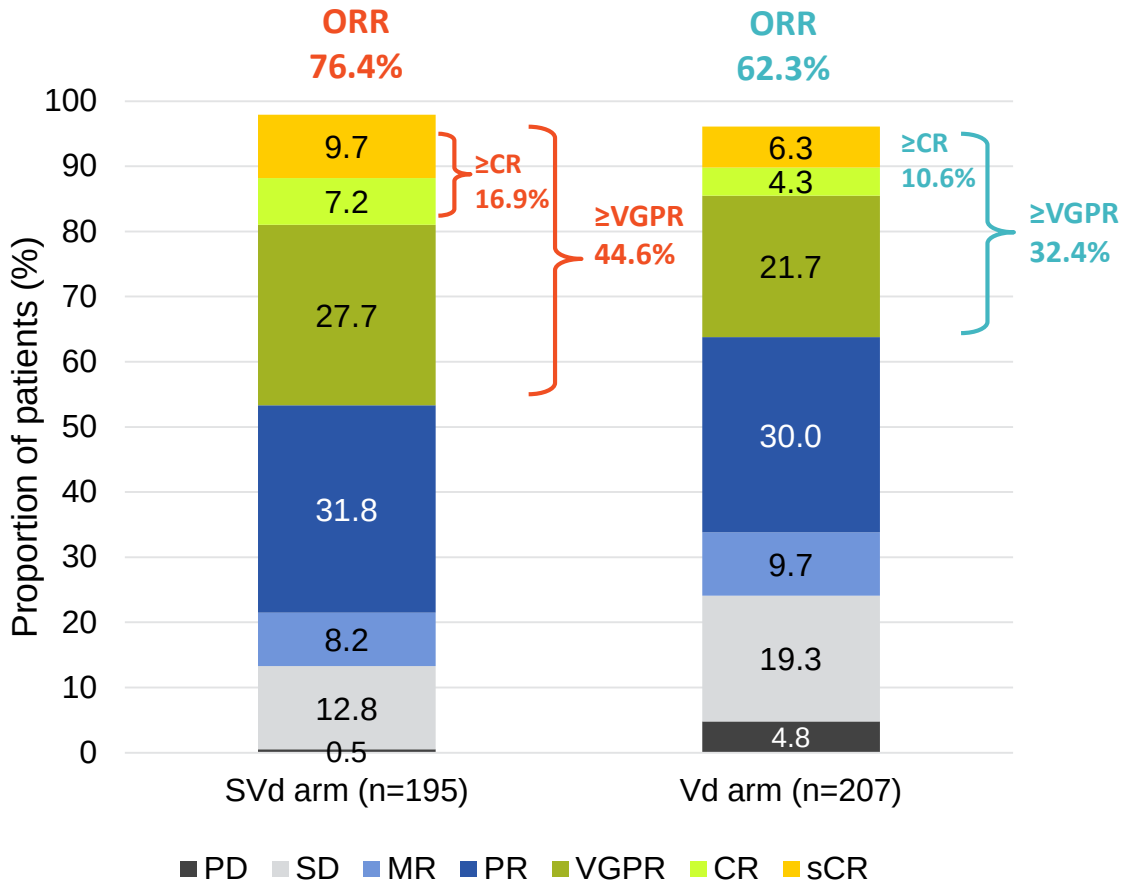
SVd Was Associated With a Significantly Higher ORR Overall and Across Patient Subgroups



One-sided P values for the Cochran-Mantel-Haenszel Test based on unstratified model. Data cut-off February 18, 2020.
ORR = Overall Response, based on Independent Review Committee's (IRC) response outcome assessments, according to IMWG response criteria (Kumar et al. Lancet Oncology 2016).
All changes in MM disease assessments were based on baseline MM disease assessments.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

SVd Was Associated With Significantly Higher Rate of Deep Responses (≥VGPR, p=0.0082)



Longer Duration of Response with SVd

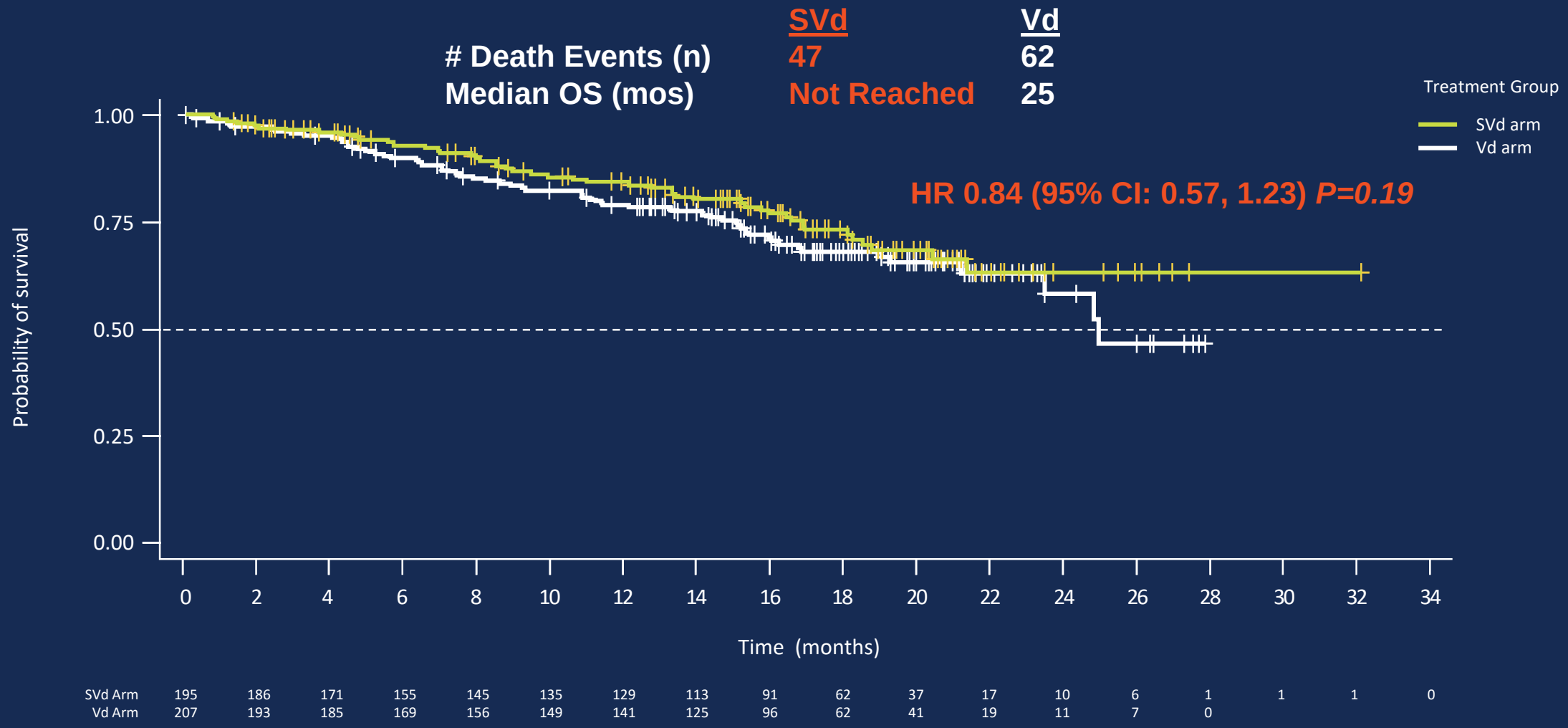
	SVd arm (n=165)	Vd arm (n=149)
Median Time to Response (months)†	1.1	1.4
Median Duration of Response (months)*	20.3	12.9

Fewer Patients with Progressive Disease: SVd (n=1, 0.5%) vs Vd (n=10, 4.8%)

CR= complete response, MR = minimal response, PD = progressive disease, PR = partial response, sCR = stringent complete response, SD = stable disease, VGPR = very good partial response. All responses assessed by an Independent Review Committee (IRC), according to the IMWG criteria (Kumar et all. Lancet Oncology 2016). †Unadjusted Time from date of randomization until first response per IMWG response criteria.
*Duration of the time interval between the first IRC-confirmed PR or better response and the first IRC-confirmed PD or death due to any cause, whichever occurred first. Data cut-off February 18, 2020.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Overall Survival Interim Analysis (109 Deaths [27%])



OS = Overall Survival, Data cut-off February 18, 2020.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Peripheral Neuropathy Rates were Significantly Lower with SVd than with Vd

Peripheral neuropathy was the most common adverse event (AE) leading to treatment discontinuation: 4.6% on SVd, 7.4% on Vd

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Selected Hematological Treatment Emergent Adverse Events (TEAEs)*

	SVd (n=195)		Vd (n=204)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematological (%)				
Thrombocytopenia	60.0†	39.5	27.0	17.2
Grade ≥3 Bleeding		2.1		1.0
Anemia	36.4	15.9	23.0	9.8
Neutropenia	14.9	8.7	5.9	3.4
Febrile Neutropenia		0.5		0.5

- Thrombopoietin receptor agonists were used to mitigate thrombocytopenia in 35 patients on SVd and 2 patients on Vd, and reduced dose interruptions and reductions
- 12 patients on SVd and 13 patients on Vd received platelet transfusions to manage thrombocytopenia

*Shown are adverse events that occurred in at least 10% of patients and had a >5% difference between treatment arms. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. For patients who crossed over, adverse events that occurred after the crossover are not included.
†Includes 3 fatal events. Data cut-off February 18, 2020.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Selected Non-Hematological TEAEs*

	SVd (n=195)		Vd (n=204)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Non-hematological (%)				
Nausea	50.3	7.7	9.8	0
Fatigue	42.1	13.3	18.1	1.0
Decreased Appetite	35.4	3.6	5.4	0
Diarrhea	32.3	6.2	25.0	0.5
Peripheral Neuropathy†	32.3	4.6	47.1	8.8
Upper Respiratory Track Infection‡	29.2	3.6	21.6	1.5
Weight decreased	26.2	2.1	12.3	1.0
Asthenia	24.6	8.2	13.2	4.4
Cataract§	21.5	8.7	6.4	1.5
Vomiting	20.5	4.1	4.4	0

*Shown are adverse events that occurred in at least 15% of patients and had a >5% difference between treatment arms. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. For patients who crossed over, adverse events that occurred after the crossover are not included. †Includes high-level term Peripheral Neuropathies NEC. ‡Includes upper respiratory infection, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis and viral upper respiratory tract infection. §Per ophthalmology exam during which 24% of patients on the SVd arm versus 8.5% of patients on the Vd arm had new-onset cataracts and worsening of cataracts on study was noted in 20.5% patients on the SVd arm versus 7.9% on the Vd arm. Data cut-off February 18, 2020.

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

BOSTON Trial Conclusions

- Once-weekly SVd significantly prolonged PFS (median PFS improvement of 47%, HR 0.70, *P*=0.0075) vs Vd
  - SVd was superior to Vd across key efficacy endpoints (PFS, ORR, ≥VGPR, and DoR) including in patients over the age of 65, those that were frail, those treated with prior lenalidomide and those with del[17p]
  - Median OS not reached with SVd versus 25 months with Vd
- Once-weekly dosing used in the SVd arm was associated with significantly lower rates and severity of Velcade-induced peripheral neuropathy compared with twice-weekly Vd
- AEs associated with SVd were manageable and reversible
  - The most common AEs were cytopenias, along with gastrointestinal and constitutional symptoms and were consistent with those previously reported from other selinexor studies
  - Discontinuation rate due to AEs was 17% (SVd) and 11% (Vd)

In patients with MM who have received 1-3 prior therapies, including prior lenalidomide or a proteasome inhibitor, once-weekly SVd offers patients an effective, convenient, IMiD-free, novel triplet regimen, requiring ~40% fewer clinic visits and reduced rate of peripheral neuropathy

Additional XPOVIO Triplet Regimens Indicate Additive or Synergistic Activity Compared to Benchmark Doublet Regimens

- Selinexor is currently being studied in the ongoing STOMP Phase 1b/2 trial evaluating selinexor and low-dose dexamethasone in combination with one of several standard approved myeloma therapies in patients with relapsed or refractory multiple myeloma

STOMP Trial			Benchmark Data	
STOMP Triplet Regimen	**# of Patients Treated to Date**	**Efficacy Data**	**Benchmark Regimen**	**Efficacy Data**
Selinexor + Kyprolis + dex	24 (median 3 lines of prior therapy)	ORR = 71%[1]	Kyprolis + dex	ORR = 23%[5]
Selinexor + Darzalex + dex	30 (Darzalex-naïve)	ORR = 73%[2]	Darzalex	ORR = 29%[6]
Selinexor + Pomalyst + dex	32 (Pomalyst–naïve and Revlimid relapsed or refractory	ORR = 56%[3] PFS = 12.2 months[3]	Pomalyst + dex	ORR = 29%[7] PFS = 3.6 months[7]
Selinexor + Revlimid + dex	12 (Revlimid-naïve)	ORR = 92%[4]	Revlimid + dex	ORR = 67%[8]

Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies[9]

Note: The STOMP study does not include any arms studying current myeloma backbone therapies without the combination of selinexor. The purpose of displaying the "Benchmark" data above is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

[1] Gasparetto C, et al. ASCO 2020. Abstract 8530. [2] Gasparetto C, et al. EHA 2019. Abstract S1606. [3] Chen C, et al. ASH 2019. Abstract 141. [4] White D, et al. IMW 2019. Abstract 353. [5] Kyprolis Package Insert; Study PX-171-003 A1
[6] Lonial et al. Lancet 2016. [7] Pomalyst Package Insert. [8] Stewart et al. NEJM 2015. [9] Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

Next Steps

1. Support BOSTON sNDA submitted to FDA on May 19, 2020 requesting expansion of current XPOVIO label
2. MAA in Europe requesting XPOVIO label based on BOSTON data to be submitted in 2020
3. Depending on FDA review time, potential U.S. commercial launch before end of 2020

Clinical Perspective from Paul Richardson, MD,
Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, Dana Farber Cancer Institute and R.J. Corman Professor of Medicine at Harvard Medical School

Background on the Treatment of Multiple Myeloma

- **Main classes of MM drugs used across lines of therapy include:**
  - Proteasome inhibitors (PIs): Velcade® (bortezomib), Kyprolis® (carfilzomib)
  - Immunomodulatory agents (IMiDs): Revlimid® (lenalidomide), Pomylast® (pomalidomide)
  - Monoclonal antibodies (mAbs): Darzalex®(daratumumab), Empliciti® (elotuzumab)
  - Nuclear export inhibitor: XPOVIO® (selinexor) is the only drug in this class and is currently approved in heavily pretreated patients
- **Drugs with proven single-agent clinical activity are generally preferred by physicians, even when used in 2-4 drug-combination regimens**
  - Single agent (± steroids) activity: Revlimid®, Pomalyst®, Darzalex ®, Velcade®, Kyprolis®, XPOVIO®
  - Used in combination: Alkylators, Glucocorticoids, Empliciti®
- **Velcade®, a proteasome inhibitor, is a well-established treatment for patients in early and late lines of treatment, typically in combination with dexamethasone and either an IMiD or mAb**
- **Standard Velcade® therapy is dosed twice per week and administered as a subcutaneous injection**
  - Prolonged usage is often limited due to its main adverse reaction, peripheral neuropathy, or due to acquired resistance

Patients and physicians demand new options with increasing efficacy and novel mechanisms of action

Recent Studies Evaluating Vd and Vd-Combinations for Patients with Previously Treated Multiple Myeloma

Parameter	BOSTON		CASTOR[a]		PANORAMA-1[b]		OPTIMISMM[c]	
	SVd[d]	Vd	Dara-Vd	Vd	Pano-Vd	Vd	Pom-Vd	Vd
Efficacy								
mPFS (month)	13.9	9.5	~18	7.2	12.0	8.1	11.2	7.1
ORR (%)	76.4	62.3	82.9	63.2	60.7	54.6	82.2	50.0
≥CR (%)	16.9	10.6	19.2	9.0	10.8	5.8	15.7	4.0
≥VGPR (%)	44.6	32.4	59.2	29.1	~28[e]	~16[e]	37.0	18.3
PR (%)	31.8	30.0	23.8	34.2	33	38.8	29.5	31.7
Safety: All grade % (Grade ≥3 %)								
Thrombocytopenia	60.0 (39.5)	27.0 (17.2)	58.8 (45.3)	43.9 (32.9)	98 (67.9)	84.0 (31.0)	36.7 (27.3)	38 (29.3)
Neutropenia	14.9 (8.7)	5.9 (3.4)	17.7 (12.8)	9.3 (4.2)	75 (34.5)	36.0 (11.0)	46.7 (41.2)	10.7 (8.5)
Nausea	50.3 (7.7)	9.8 (0)	NR	NR	36 (5.5)	21.0 (0.5)	17.6 (<1)	20.0 (0.4)
PN	32.3 (4.6)	47.1 (8.8)	47.3 (4.5)	37.6 (6.8)	61 (17.6)	67.0 (15.0)	47.8 (8.3)	37.0 (4.4)
Serious AEs (SAE)	52	38	42	34	60	42	57	42

CR=complete remission; mPFS=median progression-free survival; ORR= objective response rate; PN=peripheral neuropathy; PR=partial remission; SVd=selinexor plus bortezomib plus low-dose dexamethasone; Vd=bortezomib plus low-dose dexamethasone; VGPR= very good partial response.

a. Palumbo A, et al. NEJM. 2016. (FDA Approved Regimen)
b. San-Miguel J, et al. Lancet Oncology. 2014. (FDA Approved Regimen)
c. Richardson P, et al. Lancet Oncology. 2019.
d. Bortezomib is given once weekly on SVd and is given twice weekly on *all* other arms in *all* studies including BOSTON
e. VGPR not reported; near CR reported (nCR=17%)

Note: Provided only to contextualize traditional twice weekly Vd-based dosing regimens and not to make cross regimen comparisons.

Questions?

Answers.