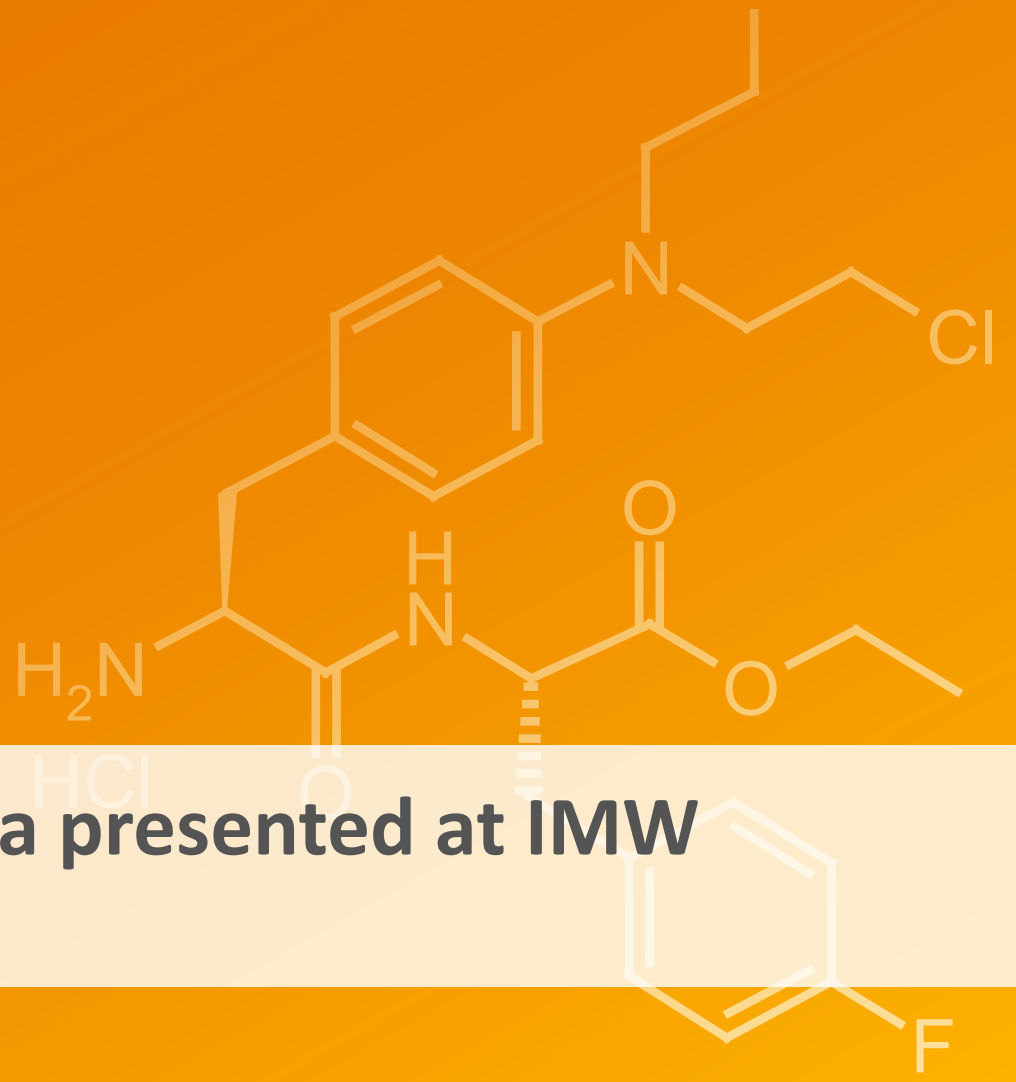

Webcast presentation of data presented at IMW

September 12, 2021

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Disclaimer

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On 26 February 2021, the U.S. Food and Drug Administration ("FDA") approved PEPAXTO® (melphalan flufenamide, also known as melflufen), in combination with dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. This indication has been granted under accelerated approval based upon data from the HORIZON study. Melflufen is not approved by any other registration authorities.

Melflufen is an abbreviated form of the international non-proprietary name (INN) melphalan flufenamide

The Information contains forward-looking statements. All statements other than statements of historical fact included in the Information are forward-looking statements. Forward-looking statements give the Company's current expectations and projections relating to its financial condition, results of operations, plans, objectives, future performance and business. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Such forward-looking statements involve known and unknown risks, uncertainties and other important factors beyond the Company's control that could cause the Company's actual results, performance or achievements to be materially different from the expected results, performance or achievements expressed or implied by such forward-looking statements. Such forward-looking statements are based on numerous assumptions regarding the Company's present and future business strategies and the environment in which it will operate in the future.

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Agenda

- **Introduction – Marty J Duvall, CEO, Klaas Bakker, CMO**
  - Welcome
  - Introduction of Fredrik Schjesvold, MD, PhD
- **Presentation of OCEAN data – Fredrik Schjesvold, MD, PhD**
  - Q&A on OCEAN data – Fredrik Schjesvold, Klaas Bakker
- **Oncopeptides' view on OCEAN data, opportunity and regulatory update – Klaas Bakker**
- **Presentation of data from PORT – Klaas Bakker**
- **Closing remarks – Marty J Duvall**
  - Q&A – Oncopeptides

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FDA regulatory update

- Melphalan flufenamide (referred to hereinafter as “melflufen”) plus dexamethasone received **accelerated approval** by the US FDA (under tradename Pepaxto®) for the treatment of adult patients with RRMM who have received ≥4 prior lines of therapy and whose disease is refractory to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 monoclonal antibody[1,2]
- In the confirmatory OCEAN trial, melflufen plus dexamethasone was superior compared with pomalidomide plus dexamethasone in terms of PFS (primary endpoint), but not OS (key secondary endpoint) in the ITT population[3]
- The US FDA issued a **partial clinical hold** based on the differences in the frequency and management of adverse events between the melflufen plus dexamethasone arm and the pomalidomide plus dexamethasone arm and the OS data in favour of the pomalidomide plus dexamethasone arm (HR, 1.104) for the ITT population[3,4]
- On 28 July, the US FDA issued a safety alert regarding an increased risk of death associated with melflufen OCEAN[3,4]
- The US FDA has recently announced that a public advisory committee meeting of the **Oncologic Drugs Advisory Committee** discussing safety findings from OCEAN, will be held on **28 October 2021**[5]
- Oncopeptides is cooperating with the US FDA as OCEAN data are evaluated[3]

FDA, Food and Drug Administration; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

1. Oncopeptides. Press Release, 28 July 2021. https://www.oncopeptides.com/en/media/press-releases/regulatory-update-from-us-food-and-drug-administration. 2. PEPAXTO® (melphalan flufenamide). Prescribing Information. Oncopeptides; 2021. 3. Oncopeptides. Press Release, 8 July 2021. https://www.oncopeptides.com/en/media/press-releases/updated-results-from-phase-3-ocean-study-shows-melflufen-met-primary-endpoint-of-superior-pfs--overall-survival-data-lead-to-partial-clinical-hold. 4. US Food and Drug Administration. FDA Drug Alert, 28 July 2021. https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-patients-and-health-care-professionals-about-clinical-trial-results-showing-increased. 5.US FDA. Oncologic Drug Advisory Committee. https://public-inspection.federalregister.gov/2021-19024.pdf Accessed 2 September 2021.

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Fredrik Schjesvold, MD, PhD

Head of Myeloma Center at Oslo University Hospital

- Head of Oslo Myeloma Center, in Oslo, Norway
- Head of the Norwegian myeloma association; president of the Nordic Myeloma Study Group and a member of the European Myeloma Network board
- National investigator of 36 clinical trials in multiple myeloma, and principal investigator for 4 academic trials
- Co-author of ESMO and IMWG guidelines, and lead author of the Norwegian myeloma guidelines
- Peer-reviewer of several international journals, and co-editor of the journal Hemato
- International expert on myeloma and has given talks in Europe, America and Asia

OCEAN (OP-103): A Phase 3, Randomized, Global, Head-to-Head Comparison Study of Melflufen and Dexamethasone Versus Pomalidomide and Dexamethasone in Relapsed Refractory Multiple Myeloma

Fredrik Schjesvold[1,2]; Meletios-Athanasios Dimopoulos[3]; Sosana Delimpasi[4]; Pawel Robak[5]; Daniel Coriu[6]; Wojciech Legiec[7]; Luděk Pour[8]; Ivan Spicka[9]; Tamas Masszi[10]; Vadim Doronin[11]; Jiri Minarik[12], Galina Salogub[13,14]; Yulia Alexeeva[13,15]; Antonio Lazzaro[16]; Vladimir Maisnar[17]; Gábor Mikala[18]; Victoria Moody[19]; Marcus Thuresson[19]; Catriona Byrne[19]; Johan Harmenberg[19]; Roman Hájek[20]; Maria-Victoria Mateos[21]; Paul G. Richardson[22]; Pieter Sonneveld[23]

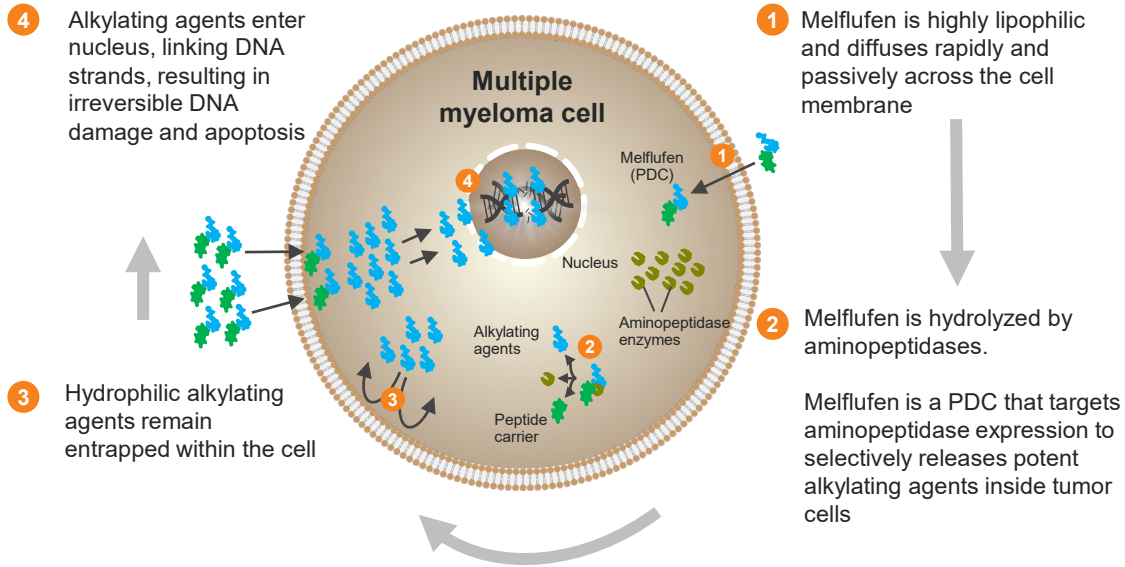
[1]Oslo Myeloma Center, Department of Hematology, Oslo University Hospital, Oslo, Norway; [2]KG Jebsen Center for B Cell Malignancies, University of Oslo, Oslo, Norway; [3]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Alexandra General Hospital, Athens, Greece; [4]Department of Hematology and Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece; [5]Department of Hematology, Medical University of Lodz, Nicolaus Copernicus Memorial Hospital, Lodz, Poland; [6]Center of Hematology and Bone Marrow Transplantation, Fundeni Clinical Institute, Bucharest, Romania; [7]St. John of Dukla Oncology Center of Lublin Land, Department of Hematology and Bone Marrow Transplantation, Lublin, Poland [8]Department of Internal Medicine, University Hospital Brno, Brno, Czech Republic; [9]Charles University and General Hospital, Prague, Czech Republic; [10]Department of Hematology, Semmelweis University, 3rd Department of Internal Medicine, Budapest, Hungary; [11]Department, State Budget Healthcare Institution of Moscow, City Clinical Hospital #40 of Moscow Healthcare Department, Moscow, Russian Federation; [12]Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Olomouc, Czech Republic; [13]V.A. Almazov National Medical Research Centre, St. Petersburg, Russian Federation; [14]V.A. Almazov Chemotherapy of Oncohematology Diseases and Bone Marrow Transplantation Department #2; [15]V.A. Almazov Chemotherapy of Oncohematology Diseases and Bone Marrow Transplantation Department #1; [16]Division of Hematology and Bone Marrow Transplant Center, Hospital Guglielmo da Saliceto, Piacenza, Italy; [17]4th Department of Medicine - Haematology, Charles University Hospital, Hradec Králové, Czech Republic; [18]South-Pest Central Hospital, National Institute for Hematology and Infectious Diseases, Budapest, Hungary; [19]Oncopeptides AB, Stockholm, Sweden; [20]Department of Hemato-oncology, University Hospital Ostrava, Ostrava, Czech Republic; [21]Institute of Cancer Molecular and Cellular Biology, University Hospital of Salamanca, Salamanca, Spain; [22]Dana-Farber Cancer Institute, Boston, MA, USA; [23]Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Disclosures

Fredrik Schjesvold, MD, PhD

- **Consulting/Advisory**: Amgen, Celgene/Brystol Myers Squibb, Janssen, Novartis, Oncopeptides, Sanofi
- **Honoraria**: AbbVie, Amgen, Celgene/Brystol Myers Squibb, Janssen, Novartis, Oncopeptides, Sanofi, Schain, SkyliteDX, Takeda
- **Stocks**: Nordic Nanovector, Oncopeptides
- **Research Funding**: Celgene, GlaxoSmithKline, Janssen, Oncopeptides, Sanofi

Melflufen in Relapsed/Refractory Multiple Myeloma



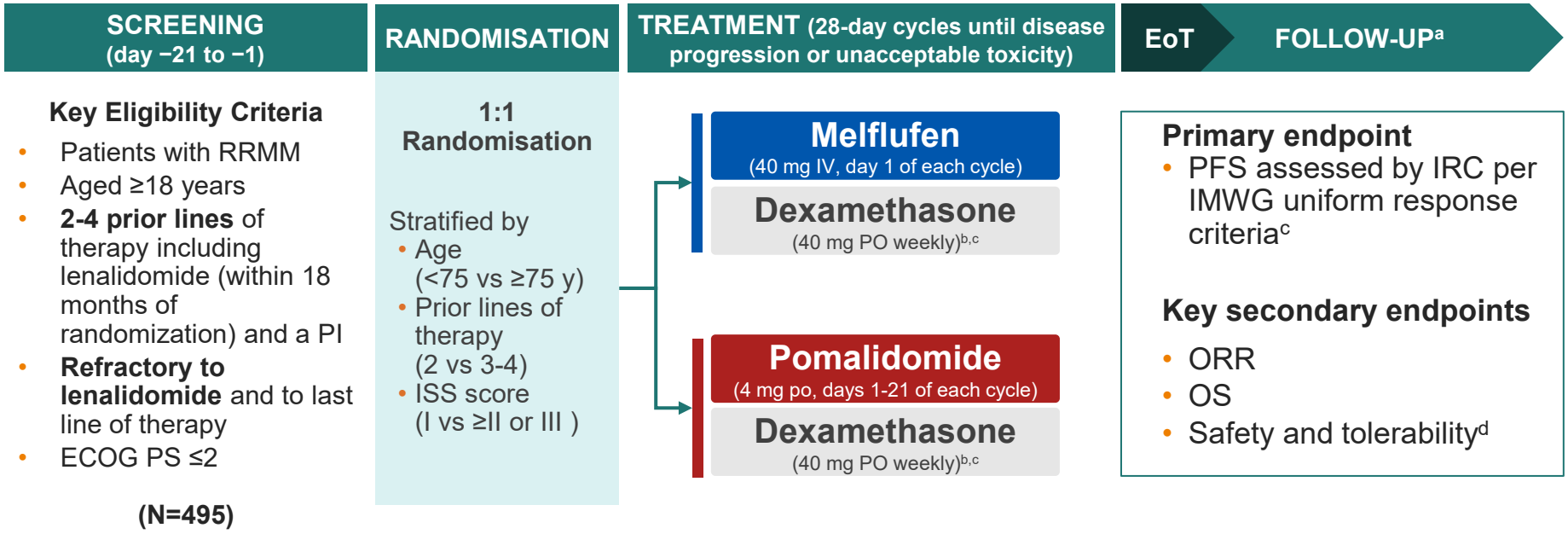
Melphalan flufenamide (melflufen) is a first-in-class peptide-drug conjugate (PDC) that targets aminopeptidases and thereby rapidly releases alkylating agents inside tumor cells.[1-6]

[a]Refractory to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 monoclonal antibody.

1. PEPAXTO (melphalan flufenamide). [package insert]. Waltham, MA: Oncopeptides (publ); 2021. 2. Chauhan D, et al. *Clin Cancer Res*. 2013;19:3019-3031. 3. Wickström M, et al. *Oncotarget*. 2017;8:66641-66655. 4. Wickström M, et al. *Biochem Pharmacol*. 2010;79:1281-1290. 5. Gullbo J, et al. *J Drug Target*. 2003;11:355-363. 6. Ray A, et al. *Br J Haematol*. 2016;174:397-409.

OCEAN (OP-103): Study Design and Key Eligibility Criteria

Phase 3, Randomised, Open-Label, Controlled, Head-to-Head, Comparison Study



ECOG, Eastern Cooperative Oncology Group; EoT, end of treatment; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; melflufen, melphalan flufenamide; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PO, orally; PS, performance status; RRMM, relapsed/refractory multiple myeloma.

[a]PFS follow-up every month until progressive disease; OS follow-up every 3 months for up to 24 months. [b]The starting dexamethasone dose was reduced to 20 mg in patients aged ≥75 years. [c]The study was powered to measure superiority using a log-rank test to determine the *P* value for the treatment comparison, and noninferiority (ie, if the upper limit of the 95% CI for the hazard ratio was below 1.2). [d]An independent data safety monitoring committee monitored the benefit-risk ratio at regular intervals.

Patient Characteristics

Characteristics	Melflufen + Dex (N=246)	Pom + Dex (N=249)
Age, median (IQR), years	68 (60-72)	68 (61-72)
<65 years, n (%)	96 (39)	85 (34)
65 to <75 years, n (%)	113 (46)	125 (50)
≥75 years, n (%)	37 (15)	39 (16)
Male sex, n (%)	139 (57)	140 (56)
ECOG PS (0 / 1 / 2), %	37 / 53 / 11	37 / 55 / 8
ISS score (I / II / III) at study entry, %	48 / 38 / 13	50 / 38 / 12
High-risk cytogenetics at study entry[a]	83 (34)	86 (35)
EMD at study entry	31 (13)	31 (12)
Previous lines of therapy, median (IQR), n	3 (2-3)	3 (2-3)
2 vs 3 or 4, %	46 / 54	45 / 55
Previous ASCT, n (%)	125 (51)	120 (48)
Refractory to previous line of therapy, n (%)		
Alkylator	78 (32)	75 (30)
Lenalidomide	245 (>99)	248 (>99)
Lenalidomide in last line of therapy	213 (87)	217 (87)
Proteasome inhibitor	163 (66)	163 (65)
Anti-CD38 monoclonal antibody	48 (20)	39 (16)
Triple-class–refractory disease[b]	39 (16)	30 (12)
Last line of therapy[c]	245 (>99)	247 (99)

ASCT, autologous stem cell transplant; dex, dexamethasone; ECOG, Eastern Cooperative Oncology Group; EMD, extramedullary disease; IQR, interquartile range; ISS, International Staging System; melflufen, melphalan flufenamide; pom, pomalidomide; PS, performance status.

[a]Defined as t(4;14), t(14;16), t(14;20), del(17p), gain(1q21), or gain 1q(+1q) by fluorescence in situ hybridization. [b]Refractory to ≥1 immunomodulatory drug, ≥1 proteasome inhibitor, and ≥1 anti-CD38 monoclonal antibody. [c]Failure to achieve at least a minimal response or progression on therapy within 60 days of the last dose of treatment.

Data cut-off date: 3 Feb. 2021

Melflufen Had a Numerically Higher Response Rate Compared With Pomalidomide

Key secondary endpoint

	Melflufen + Dex (N=246)	Pomalidomide + Dex (N=249)
ORR, % (95% CI)[a]	**33 (27-39)**	**27 (22-33)**
CBR, % (95% CI)[b]	50 (43-56)	41 (35-47)
Best confirmed response[c], n (%)		
Stringent complete response	0 (0)	0 (0)
Complete response	7 (3)	3 (1)
Very good partial response	23 (9)	18 (7)
Partial response	50 (20)	46 (18)
Minimal response	42 (17)	35 (14)
Stable disease	68 (28)	72 (29)
Progressive disease	36 (15)	60 (24)
Not evaluable	20 (8)	15 (6)
Time to best response, median (IQR), months	2.1 (1.1-3.7)	2.0 (1.1-2.9)

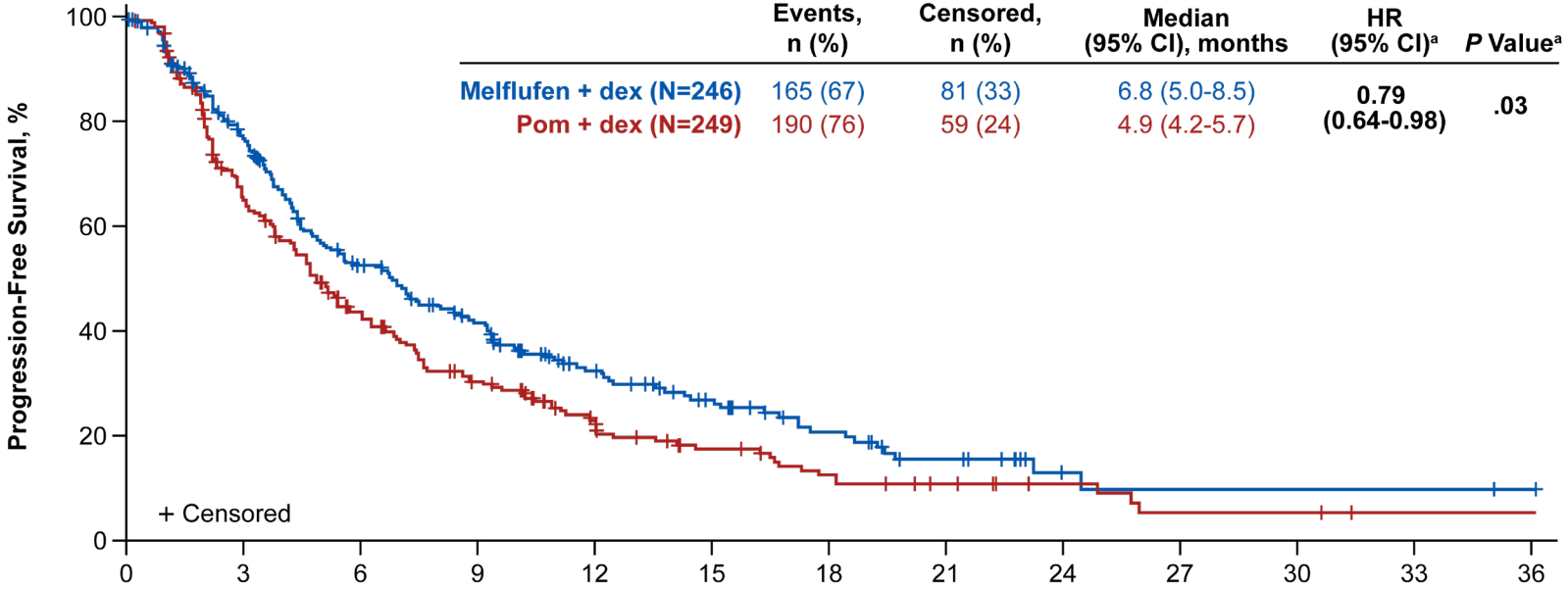
CBR, clinical benefit rate; dex, dexamethasone; IQR, interquartile range; melflufen, melphalan flufenamide; ORR, overall response rate.

[a]Defined as the proportion of patients with a partial response or better. [b]Defined as the proportion of patients with a minimal response or better. [c]Assessed by an independent review committee per the International Myeloma Working Group Uniform Response Criteria. All response categories required 2 consecutive assessments.

Data cut-off date: 3 Feb. 2021

Melflufen Met the Primary Endpoint of Superior PFS as Assessed by the IRC

Primary endpoint



	Events, n (%)	Censored, n (%)	Median (95% CI), months	HR (95% CI)[a]	*P* Value[a]
Melflufen + dex (N=246)	165 (67)	81 (33)	6.8 (5.0-8.5)	0.79 (0.64-0.98)	.03
Pom + dex (N=249)	190 (76)	59 (24)	4.9 (4.2-5.7)		

Patients at risk, n													
Melflufen + dex	246	168	109	80	50	34	22	13	5	3	3	3	2
Pom + dex	249	150	90	58	37	23	15	10	6	3	3	1	1

Median follow-up: 15.5 months (melflufen + dex) vs 16.3 months (pom + dex).

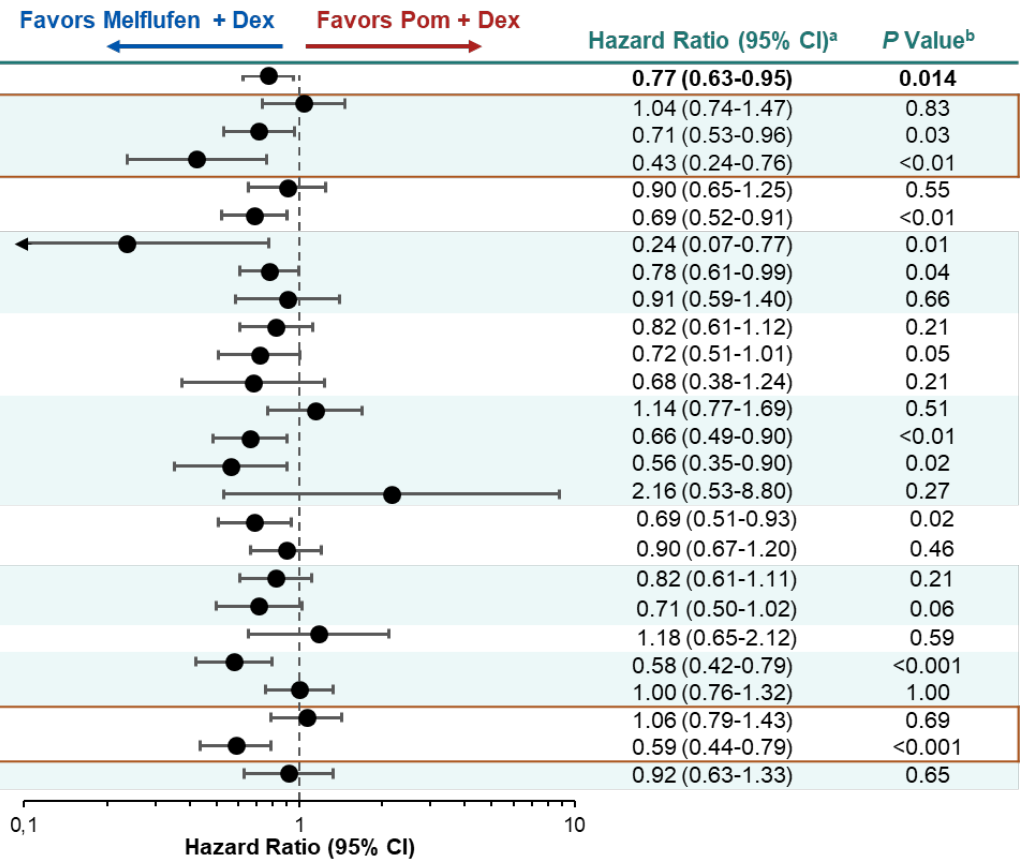
dex, dexamethasone; HR, hazard ratio; IRC, independent review committee; melflufen, melphalan flufenamide; pom, pomalidomide; PFS, progression-free survival.
[a]Stratified hazard ratio. [b]Log-rank *P* value.

Data cut-off date: 3 Feb. 2021

PFS was Generally in Favor of Melflufen in Subgroups

Prespecified analysis

Subgroup		Melflufen+ Dex, n	Pom + Dex, n	Hazard Ratio (95% CI)[a]	*P* Value[b]
Overall		**246**	**249**	**0.77 (0.63-0.95)**	**0.014**
Age category, years	<65	96	85	1.04 (0.74-1.47)	0.83
	65-74	113	125	0.71 (0.53-0.96)	0.03
	≥75	37	39	0.43 (0.24-0.76)	<0.01
Sex	Female	107	109	0.90 (0.65-1.25)	0.55
	Male	139	140	0.69 (0.52-0.91)	<0.01
Region	USA	11	15	0.24 (0.07-0.77)	0.01
	Europe	180	176	0.78 (0.61-0.99)	0.04
	ROW	55	58	0.91 (0.59-1.40)	0.66
ISS score	I	112	119	0.82 (0.61-1.12)	0.21
	II	88	95	0.72 (0.51-1.01)	0.05
	III	28	29	0.68 (0.38-1.24)	0.21
Creatinine clearance (mL/min)	≥90	76	69	1.14 (0.77-1.69)	0.51
	≥60 to <90	119	112	0.66 (0.49-0.90)	<0.01
	≥45 to <60	44	58	0.56 (0.35-0.90)	0.02
	<45	6	10	2.16 (0.53-8.80)	0.27
Median BSA	≤1.855 m^2	116	128	0.69 (0.51-0.93)	0.02
	>1.855 m^2	126	117	0.90 (0.67-1.20)	0.46
Cytogenetic risk group	Standard	128	130	0.82 (0.61-1.11)	0.21
	High[c]	83	86	0.71 (0.50-1.02)	0.06
EMD at baseline		30	26	1.18 (0.65-2.12)	0.59
Number of prior regimens	2	114	111	0.58 (0.42-0.79)	<0.001
	3-4	132	138	1.00 (0.76-1.32)	1.00
Previous ASCT	Yes	125	120	1.06 (0.79-1.43)	0.69
	No	121	129	0.59 (0.44-0.79)	<0.001
Refractory to prior alkylator		78	75	0.92 (0.63-1.33)	0.65



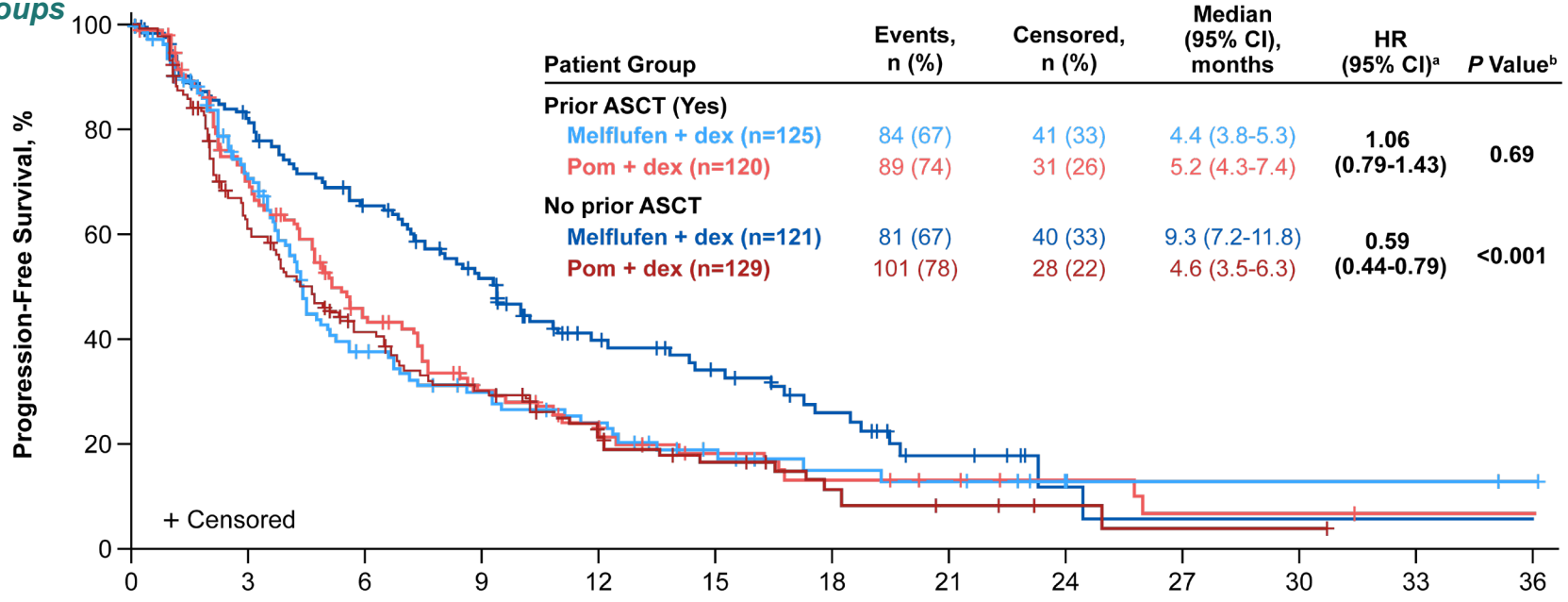
ASCT, autologous stem cell transplant; dex, dexamethasone; EMD, extramedullary disease; ISS, International Staging System score; melflufen, melphalan flufenamide; pom, pomalidomide; ROW, rest of world, USA, United States of America.

[a]Unstratified hazard ratio. [b]Log-rank *P* value. [c]High-risk defined as t(4;14), t(14;16), t(14;20), del(17p), gain(1q21), or gain 1q(+1q) by fluorescence in situ hybridization.

Data cut-off date: 3 Feb. 2021

PFS Benefit in the Melflufen Arm Mainly Driven by Patients Who Had Not Received a Prior ASCT

Prespecified subgroups



Patient Group	Events, n (%)	Censored, n (%)	Median (95% CI), months	HR (95% CI)[a]	*P* Value[b]
Prior ASCT (Yes)					
Melflufen + dex (n=125)	84 (67)	41 (33)	4.4 (3.8-5.3)	**1.06 (0.79-1.43)**	**0.69**
Pom + dex (n=120)	89 (74)	31 (26)	5.2 (4.3-7.4)		
No prior ASCT					
Melflufen + dex (n=121)	81 (67)	40 (33)	9.3 (7.2-11.8)	**0.59 (0.44-0.79)**	**<0.001**
Pom + dex (n=129)	101 (78)	28 (22)	4.6 (3.5-6.3)		

Patients at risk, n													
Prior ASCT (Yes)													
Melflufen + dex	74	36	26	19	11	7	6	3	2	2	2	1	0
Pom + dex	77	45	26	18	11	8	6	4	2	2	1	1	1
No prior ASCT													
Melflufen + dex	94	73	54	31	23	15	7	2	1	1	1	1	0
Pom + dex	73	45	32	19	12	7	4	2	1	1	0	0	0

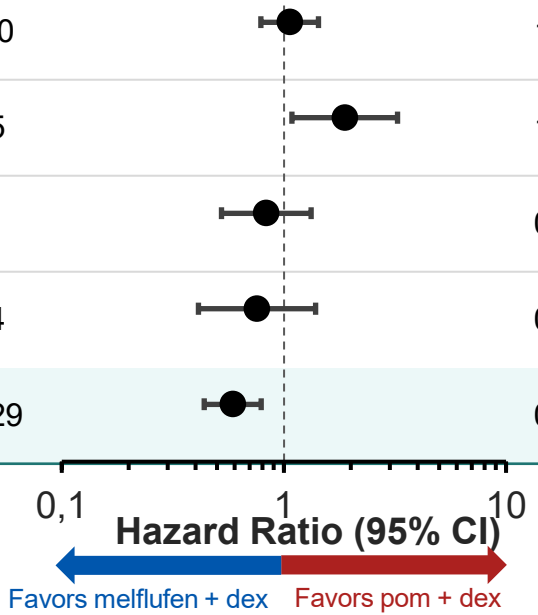
ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; PFS, progression-free survival; pom, pomalidomide.
[a]Unstratified HR. [b]Log-rank *P* value.

Data cut-off date: 3 Feb. 2021

Time From Prior ASCT Impacts Progression-Free Survival

Post-hoc analysis

	Events/Patients, n/N			
	Melflufen + Dex	Pom + Dex	HR (95% CI)[a]	*P* Value[b]
Prior ASCT (Overall)	84/125	89/120	1.06 (0.79-1.43)	0.694
ASCT <2.5 years ago	33/43	23/35	1.88 (1.09-3.25)	0.022
ASCT 2.5 to 5 years ago	32/48	41/51	0.83 (0.52-1.32)	0.442
ASCT >5 years ago	19/34	25/34	0.76 (0.41-1.39)	0.367
No prior ASCT	81/121	101/129	0.59 (0.44-0.79)	<0.001

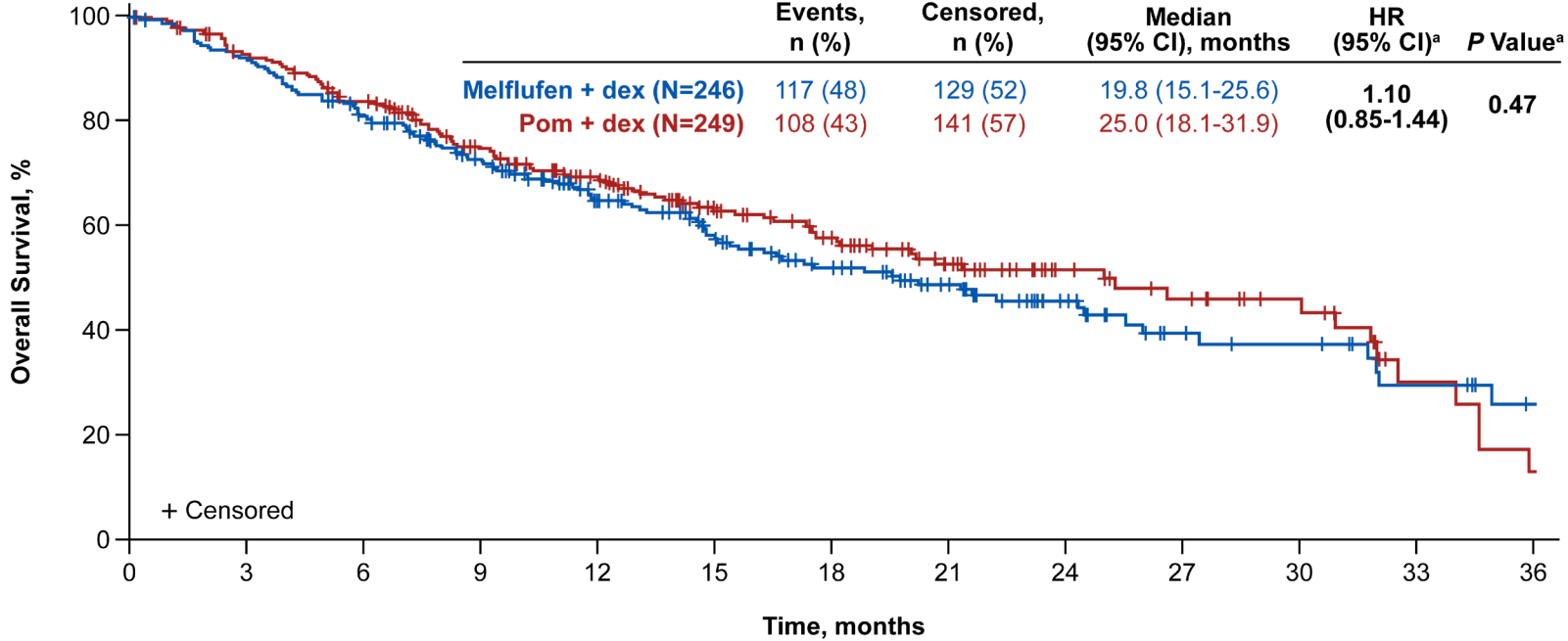


ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; PFS, progression-free survival; pom, pomalidomide.
[a]Unstratified hazard ratio. [b]Log-rank *P* value.

Data cutoff date: 3 Feb, 2021

Overall Survival by Treatment Group

Key secondary endpoint



	Events, n (%)	Censored, n (%)	Median (95% CI), months	HR (95% CI)[a]	*P* Value[a]
Melflufen + dex (N=246)	117 (48)	129 (52)	19.8 (15.1-25.6)	1.10 (0.85-1.44)	0.47
Pom + dex (N=249)	108 (43)	141 (57)	25.0 (18.1-31.9)		

Patients at risk, n													
Melflufen + dex	246	223	192	160	119	91	70	53	34	20	17	11	6
Pom + dex	249	225	196	157	129	95	75	53	31	24	18	7	3

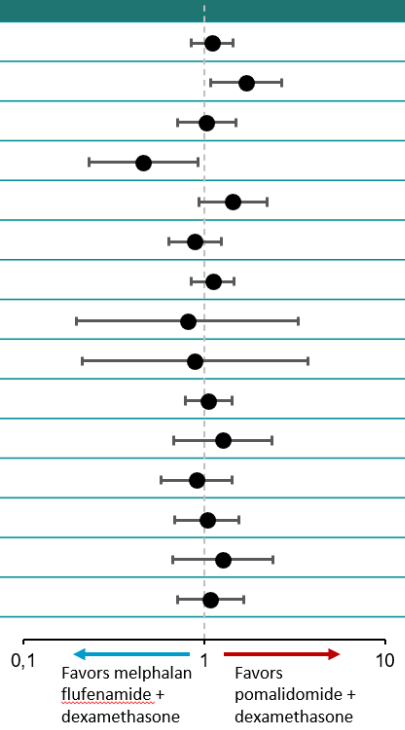
dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; pom, pomalidomide.
[a]Stratified hazard ratio. [b]Log-rank *P* value.

Data cut-off date: 3 Feb. 2021

Subgroup Analyses: OS

Prespecified analysis

Subgroup		N	OS Hazard Ratio (95% CI)[a]
Overall		495	1.10 (0.85-1.44)
Age, years	<65	181	1.71 (1.09-2.69)
	65-74	238	1.03 (0.71-1.50)
	≥75	76	0.46 (0.23-0.92)
Sex	Female	216	1.44 (0.94-2.22)
	Male	279	0.89 (0.64-1.25)
Race	White	446	1.12 (0.85-1.47)
	All other	30	0.81 (0.20-3.30)
Region	USA	26	0.89 (0.21-3.73)
	Europe	356	1.06 (0.79-1.42)
	ROW	113	1.27 (0.68-2.36)
International Staging System score	I	231	0.91 (0.58-1.42)
	II	183	1.04 (0.69-1.55)
	III	57	1.27 (0.67-2.41)
High-risk cytogenetics[b]		169	1.08 (0.71-1.65)



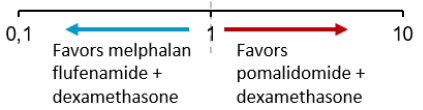
[a]Unstratified hazard ratios for subgroups; stratified hazard ratios for overall. [b]Classified by the presence of t(4;14), t(14;16), t(14;20), del(17p), or gain(1q); determined by FISH.
FISH, fluorescence in situ hybridization; OS, overall survival; PFS, progression-free survival; ROW, rest of the world.
Oncopeptides: Unpublished data (data on file).

Data cut-off date: 3 Feb. 2021

Subgroup Analyses: OS (cont.)

Prespecified analysis

Subgroup		N	OS Hazard Ratio (95% CI)[a]
Extramedullary disease at baseline		56	1.45 (0.71-2.97)
Prior regimens	2	225	0.87 (0.60-1.27)
	3-4	270	1.30 (0.90-1.88)
Previous autologous stem cell transplant	Yes	245	1.61 (1.09-2.40)
	No	250	0.78 (0.55-1.12)
Refractory to previous therapy			
Alkylator		153	0.87 (0.55-1.40)
Anti-CD38 monoclonal antibody		87	1.62 (0.82-3.21)
Immunomodulatory agent			
Lenalidomide in last line		430	1.07 (0.81-1.41)
Double refractory disease		256	1.03 (0.72-1.47)
Creatinine clearance (mL/min)			
≥90		145	1.67 (0.97-2.88)
≥60 to <90		231	0.99 (0.68-1.44)
≥45 to <60		102	0.84 (0.47-1.48)
<45		16	1.34 (0.36-5.08)



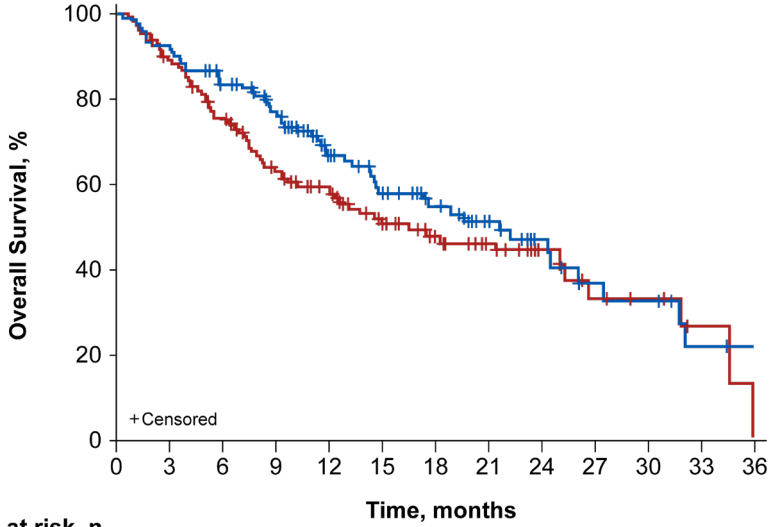
[a]Unstrat
OS, over

Data cut-off date: 3 Feb. 2021

OS Trended in Favor of Melflufen in Patients Without a Prior ASCT, and Favored Pom in Patients With a Prior ASCT

Prespecified subgroups

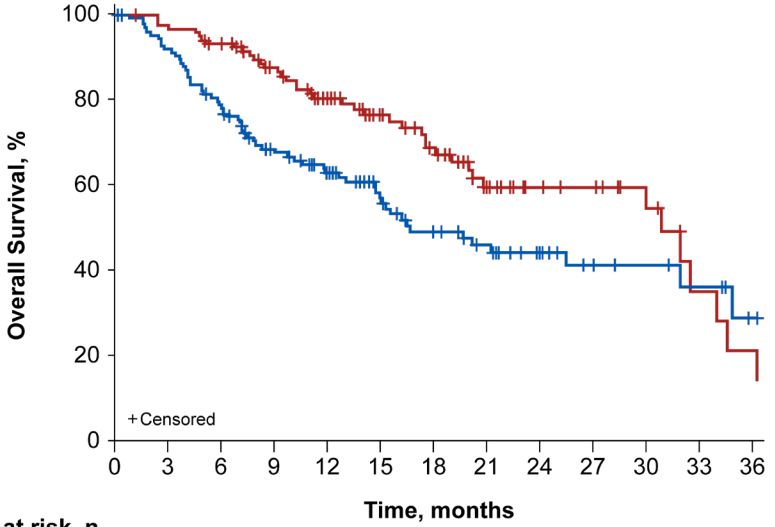
No Prior ASCT



Patients at risk, n													
Melflufen + dex	121	111	97	84	55	45	34	25	14	9	8	4	3
Pom + dex	129	112	91	70	59	43	32	24	13	8	6	2	0

No Prior ASCT	Patients, n: Events	Patients, n: Censored	Median (95% CI), months	HR (95% CI)[a]; *P* Value[b]
Melflufen + dex (n=121)	56	65	21.6 (14.6-26.0)	0.78 (0.55-1.12) *P*=0.1766
Pom + dex (n=129)	67	62	16.5 (10.3-25.3)	

Prior ASCT (Yes)



Patients at risk, n													
Melflufen + dex	125	112	95	76	64	46	36	28	20	11	9	7	3
Pom + dex	120	113	105	87	70	52	43	29	18	16	12	5	3

Prior ASCT (Yes)	Patients, n: Events	Patients, n: Censored	Median (95% CI), months	HR (95% CI)[a]; *P* Value[b]
Melflufen + dex (n=125)	61	64	16.7 (14.8-32.0)	1.61 (1.09-2.40) *P*=0.0170
Pom + dex (n=120)	41	79	31.0 (20.2-34.1)	

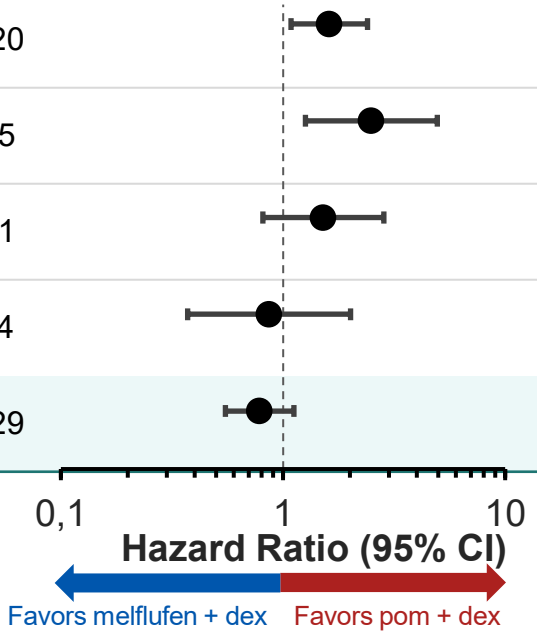
ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; pom, pomalidomide. [a]Unstratified HR. [b]Log-rank *P* value.

Data cut-off date: 3 Feb. 2021

Time From Prior ASCT Impacts Overall Survival

Post-hoc analysis

	Events/Patients, n/N				
	Melflufen + Dex	Pom + Dex		HR (95% CI)[a]	*P* Value[b]
Prior ASCT (Overall)	61/125	41/120		1.61 (1.09-2.40)	0.017
ASCT <2.5 years ago	27/43	12/35		2.50 (1.26-4.94)	0.007
ASCT 2.5 to 5 years ago	22/48	18/51		1.52 (0.81-2.84)	0.190
ASCT >5 years ago	12/34	11/34		0.87 (0.37-2.01)	0.737
No prior ASCT	56/121	67/129		0.78 (0.55-1.12)	0.177



ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; NE, not estimable; OS, overall survival; pom, pomalidomide.
[a]Unstratified hazard ratio. [b]Log-rank *P* value.

Data cutoff date: 3 Feb, 2021

Efficacy in Non- ASCT Alkylator Refractory Patients

Efficacy differential versus Pom holds in Non-ASCT patients who are refractory to alkylators

	Non-ASCT Patients Full Subset		Non-ASCT Patients Alkylator Refractory Only	
	Melflufen+dex n=121	Pomalidomide+dex n=129	Melflufen +dex n=44	Pomalidomide+dex n=46
Median PFS, mo (95% CI)	9.33 (7.23-11.79)	4.63 (3.48-6.28)	8.30 (5.6-13.8)	3.80 (2.9-7.6)
Median OS, mo (95% CI)	21.62 (14.55-26.02)	16.53 (10.25-25.30)	24.30 (14.6-NA)	13.10 (9.3-NA)

Data cutoff date: 3 Feb, 2021

Deaths on Study

		Melflufen + Dex	Pom + Dex
Patients randomized (intention-to-treat population), n		**246**	**249**
Total number of deaths in the intention-to-treat population, n (%)		117 (48)	108 (43)
Patients randomized and who received ≥1 dose of study drug (safety population), n		**228**	**246**
Total of deaths in the safety population, n (%)		106 (46)	106 (43)
Death ≤30 days after last dose, n (%)		23 (10)	33 (13)
Primary cause of death (death ≤30 days after last dose), n (%)	Adverse event	16 (7)	23 (9)
	Progressive disease	7 (3)	8 (3)
	Unknown	0	2 (1)
Death >30 days after last dose, n (%)		83 (36)	73 (30)
Primary cause of death (death >30 days after last dose), n (%)	Progressive disease	53 (23)	46 (19)
	Other	11 (5)	11 (4)
	Unknown	13 (6)	13 (5)
	Adverse event	6 (3)	3 (1)
Deaths attributed to COVID-19, n (%)		7 (3)	4 (2)

dex, dexamethasone; melflufen, melphalan flufenamide; pom, pomalidomide.

Data cut-off date: 3 Feb. 2021

Treatment-Emergent Adverse Events of Special Interest

Treatment-Emergent Adverse Events of Special Interest, n (%)[a]	Melflufen + Dex (n=228)	Pom + Dex (n=246)
Thrombocytopaenia	198 (87)	58 (24)
Grade 3/4	174 (76)	31 (13)
Haemorrhage	36 (16)	16 (7)
Grade 3/4 haemorrhage and concomitant grade 3/4 thrombocytopaenia	2 (1)	0
Neutropoenia	161 (71)	135 (55)
Grade 3/4	147 (64)	121 (49)
Infection	114 (50)	137 (56)
Grade 3/4	30 (13)	53 (22)
Grade 3/4 infection and concomitant grade 3/4 neutropoenia	7 (3)	16 (7)
Infective pneumonia	38 (17)	60 (24)
Grade 3/4	12 (5)	30 (12)
Grade 3/4 infective pneumonia and concomitant grade 3/4 neutropoenia	2 (1)	8 (3)
Febrile neutropoenia	6 (3)	4 (2)
Anaemia	153 (67)	93 (38)
Second primary malignancy	3 (1)	6 (2)
Myelodysplastic syndromes or acute myeloid leukaemia	1 (<1)	1 (<1)

dex, dexamethasone; melflufen, melphalan flufenamide; pom, pomalidomide.

[a]Treatment-emergent adverse events of special interest are categorized by standardized MedDRA query (SMQ); anaemia includes Haematopoietic erythropenia (SMQ); neutropoenia includes neutropoenia, febrile neutropoenia, neutrophil count decreased, neutropenic sepsis, neutropenic infection, cyclic neutropoenia, band neutrophil count decreased, band neutrophil percentage decreased, neutrophil percentage decreased, agranulocytosis, granulocyte count decreased, and granulocytopenia; thrombocytopaenia includes haematopoietic thrombocytopaenia (SMQ); haemorrhages includes haemorrhage terms (excl laboratory terms) (SMQ) and haemorrhage laboratory terms (SMQ) narrow were combined; second primary malignancy includes the high level term myelodysplastic syndromes or any term in malignant or unspecified tumours (SMQ), but will exclude high level group term plasma cell neoplasm; and myelodysplastic syndromes includes the high level term myelodysplastic syndromes.

Data cut-off date: 3 Feb. 2021

Safety Overview

Treatment-Emergent Adverse Events (TEAEs), n (%)	Melflufen + Dex (n=228)	Pom + Dex (n=246)
Any TEAE	226 (99)	241 (98)
Any grade ≥3 TEAE	206 (90)	189 (77)
Non-haematologic grade 3/4 TEAEs occurring in ≥2% of patients overall		
Pneumonia	10 (4)	21 (9)
Muscular weakness	5 (2)	5 (2)
Hyperglycaemia	4 (2)	7 (3)
Asthenia	4 (2)	6 (2)
COVID-19 pneumonia	4 (2)	4 (2)
Hypertension	4 (2)	4 (2)
Bronchitis	3 (1)	5 (2)
Acute kidney injury	2 (1)	6 (2)
Any treatment-related TEAE	216 (95)	209 (85)
Any serious TEAE	95 (42)	113 (46)
Any serious treatment-related TEAE	42 (18)	52 (21)
Any TEAE leading to dose modifications of melflufen or pom	178 (78)	144 (59)
Dose delays	137 (60)	109 (44)
Reductions[a]	107 (47)	37 (15)
Permanent discontinuation	60 (26)	54 (22)

dex, dexamethasone; melflufen, melphalan flufenamide; pom, pomalidomide.

[a]Dose reductions of melflufen were allowed for drug-related toxicities from 40 mg to 30 mg or 20 mg. Treatment was discontinued in patients unable to tolerate the 20-mg dose. Dose reductions of pomalidomide were also allowed for drug-related toxicities from 4 mg to 3 mg to 2 mg. Treatment was discontinued in patients unable to tolerate the 2-mg dose.

Data cut-off date: 3 Feb. 2021

Conclusions

- The phase 3 OCEAN study enabled a direct head-to-head comparison of melflufen plus dexamethasone versus pomalidomide plus dexamethasone in RRMM
- Melflufen plus dexamethasone was superior to pomalidomide plus dexamethasone for the primary endpoint of PFS
- OS trended in favour of melflufen plus dexamethasone in patients without a prior ASCT, and favoured pomalidomide plus dexamethasone in patients with a prior ASCT
- The safety of melflufen plus dexamethasone primarily consisted of haematologic adverse events that were manageable with dose modifications, which is consistent with previous reports[1-3]
- Results from OCEAN suggest that melflufen plus dexamethasone may become a potential treatment for patients with lenalidomide-refractory RRMM who have received 2-4 previous lines of therapy and who have not received a prior ASCT

ASCT, autologous stem cell transplant; melflufen, melphalan flufenamide; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

1. Richardson PG, et al. *Lancet Haematol*. 2020;7:e395-e407. 2. Bringhen S, et al. *Br J Haematol*. 2021;193:1105-1109. 3. Richardson PG, et al. *J Clin Oncol*. 2021;39:757-767.

OCEAN data Q&A

Oncopeptides' view on OCEAN data, opportunity and regulatory update

Klaas Bakker

oncopeptides

FDA to hold an ODAC meeting on October 28 on OCEAN

- The committee will hear an update where the confirmatory trial demonstrated a worse overall survival in the melphalan flufenamide treatment arm compared to the control arm. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval.
- Based on the update provided, the committee will have a general discussion focused on next steps for the product including whether the indication should remain on the market while additional trial(s) are conducted

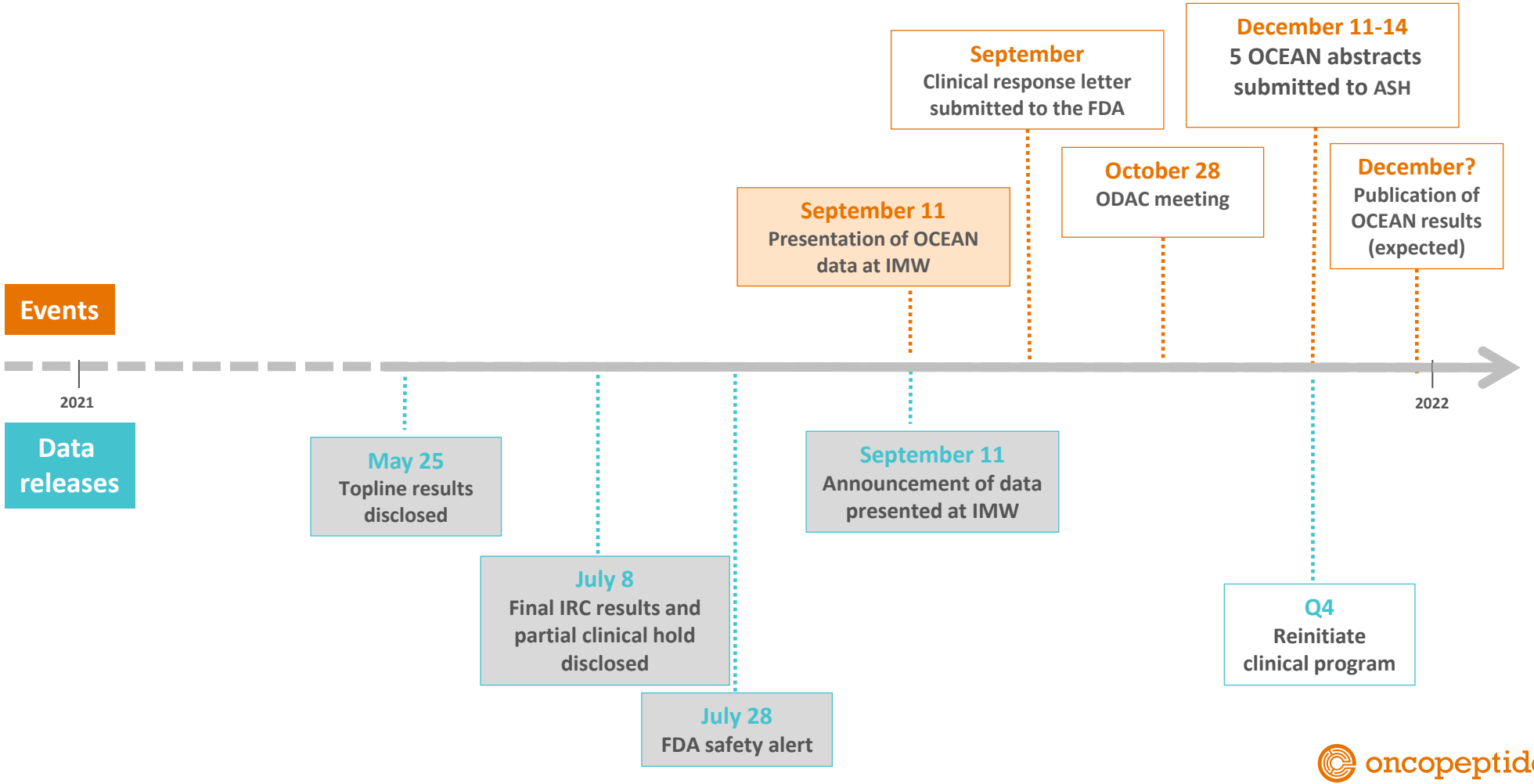
What is an ODAC meeting?

- Reviews and evaluates data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer and makes appropriate recommendations to the Commissioner of Food and Drugs
- Consists of a core of 13 voting members including the Chair
- Members and the Chair are selected by the Commissioner or designee from among authorities knowledgeable in the fields of general oncology, pediatric oncology, hematologic oncology, immunologic oncology, biostatistics, and other related professions
- The core of voting members may include one technically qualified member
- The vote is considered to be informative to the FDA but non-binding

Potential outcomes of the FDA review including ODAC

- OCEAN data results have generated a level of concern around OS that may challenge the continued accelerated approval of Pepaxto. Still various outcomes possible:
  - OCEAN data review at FDA results in a label that includes 3rd and 4th line
  - OCEAN data is viewed as “hypothesis generating” and that we need to confirm in our clinical development program
  - Withdrawal of Pepaxto from the US market
- Safety update on current HORIZON label possible

OCEAN study – regulatory timeline and upcoming events



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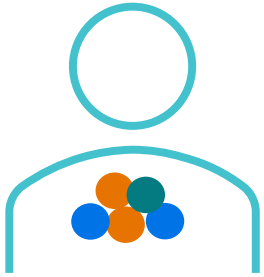
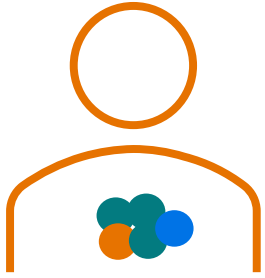
Profiles of non-transplanted and transplanted patients



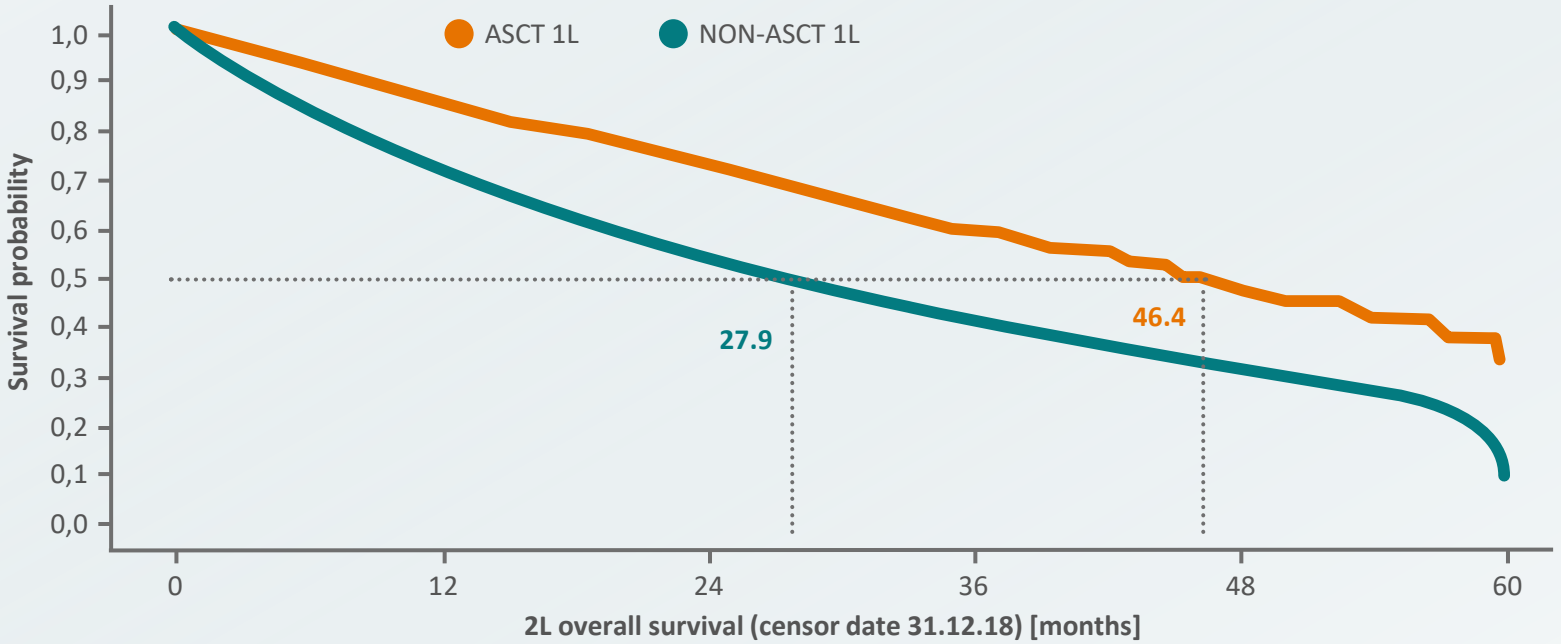
Non-Transplanted	
Age	Older
Performance Status	Lower
Co-morbidities	Higher
Previous exposure in OCEAN	• Regular dose alkylators • Len refractory • PI • CD38



Transplanted	
Age	Younger
Performance Status	Higher
Co-morbidities	Lower
Previous exposure in OCEAN	• High dose alkylators • Len refractory • PI • CD38

Higher unmet need for non-transplanted patients

OS in transplanted vs non-transplanted patients[1]



Number at risk

3454	2162	1287	640	234	0
9533	5139	2833	1379	542	0

Cyrille Touzeau & Nadia Quignot & Jie Meng & Heng Jiang & Artak Khachatryan & Moushmi Singh & Vanessa Taieb & Jean-Vannak Chauny & Gaëlle Désaméricq
Received: 8 February 2021 /Accepted: 12 April 2021
Survival and treatment patterns of patients with relapsed or refractory multiple myeloma in France — a cohort study using the French National Healthcare database (SNDS)

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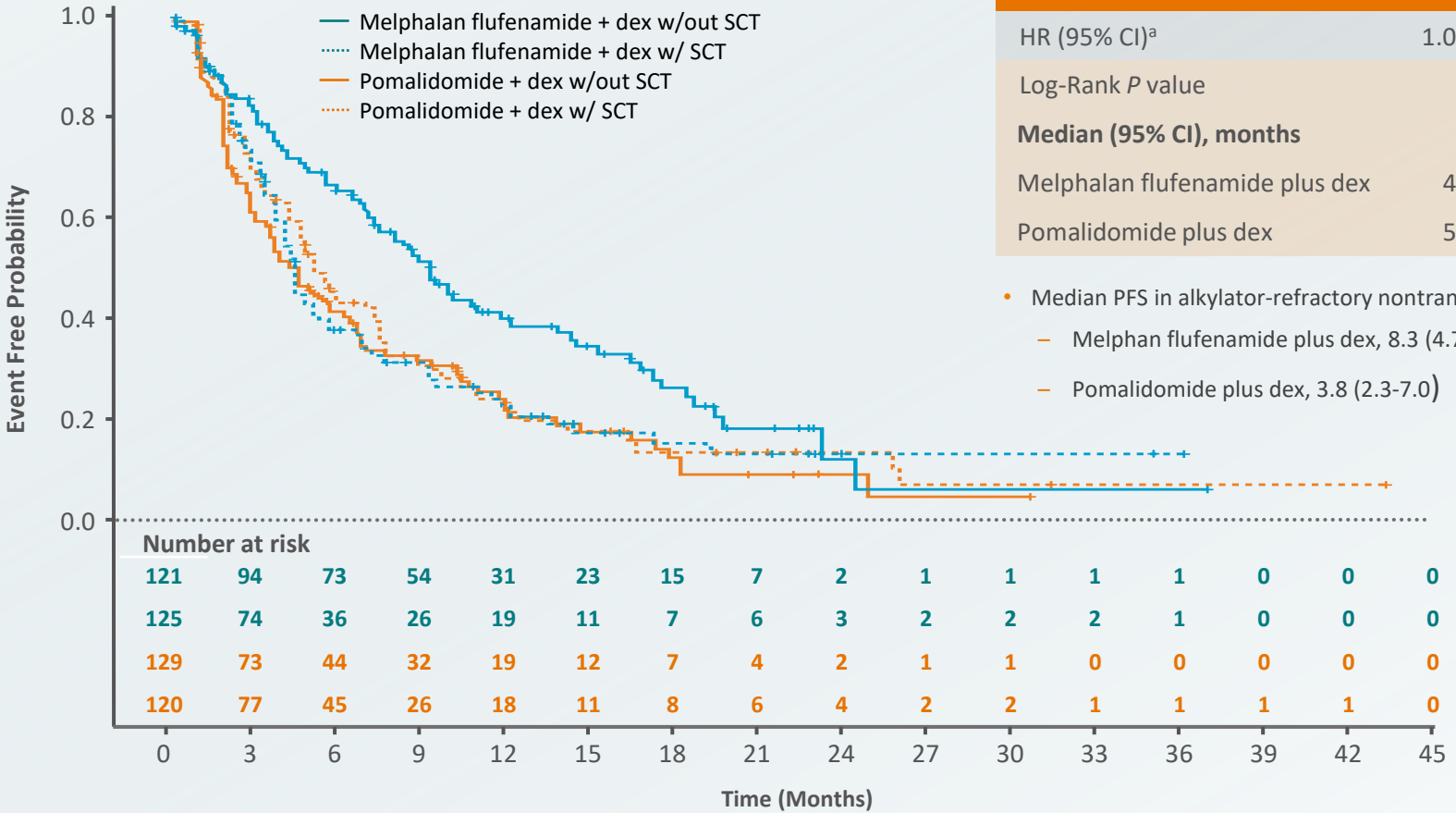
PFS in Transplanted vs Nontransplanted Patients



Statistic	Transplanted	Non-Transplanted
HR (95% CI)[a]	1.06 (0.79-1.43)	0.59 (0.44-0.79)
Log-Rank *P* value	0.6949	0.0004
Median (95% CI), months		
Melphalan flufenamide plus dex	4.4 (3.8-5.3)	9.3 (7.2-11.8)
Pomalidomide plus dex	5.2 (4.3-7.4)	4.6 (3.5-6.3)

- Median PFS in alkylator-refractory nontransplanted patients:
  - Melphan flufenamide plus dex, 8.3 (4.7-10.8)
  - Pomalidomide plus dex, 3.8 (2.3-7.0)

[a]Unstratified hazard ratio. SCT, stem cell transplant; dex, dexamethasone; PFS, progression-free survival. Oncopeptides: Unpublished data (data on file).

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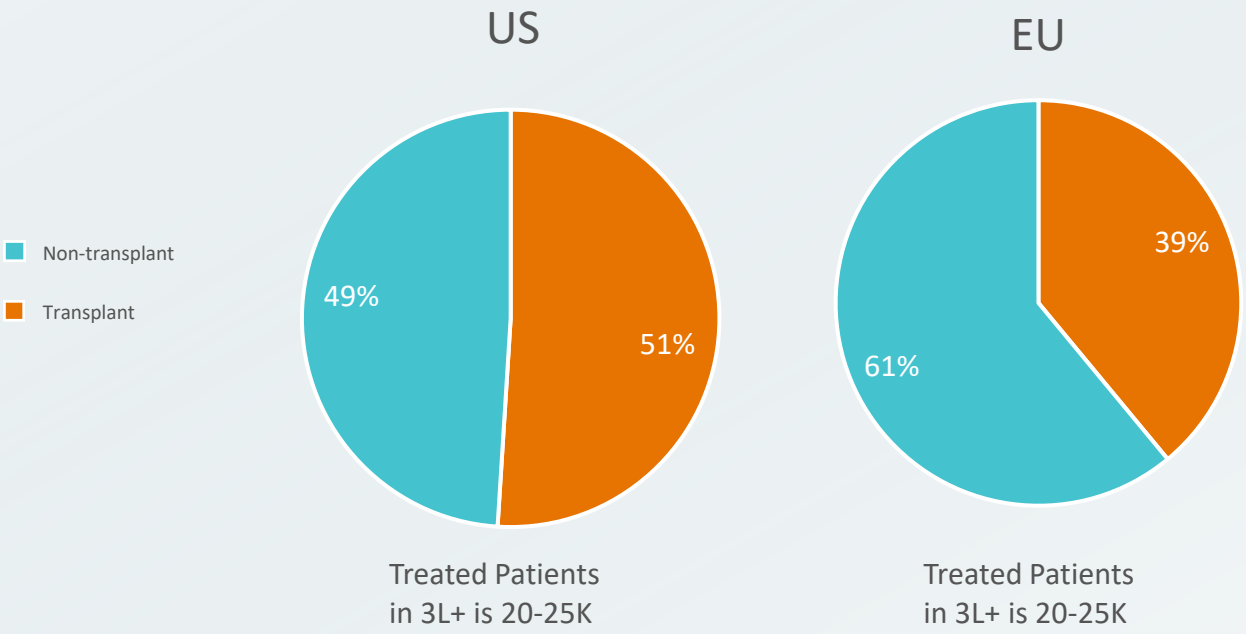
Addressable patient population

Large growing unmet need in a non-transplant setting

Transplant ineligible (non-transplant) patients make up 45%-60% in major markets across the US and EU



Melflufen offers benefits to address non-transplanted population

- Patients with high unmet need
- PDC mechanism offers novel approach against MM
- Striking efficacy in head-to-head trial versus pomalidomide
- Manageable safety profile (mostly hematologic toxicities)
- Convenient dosing for elderly population

SOURCE: CancerMPact, Kantar Nov 2020

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Presentation of data from PORT

Klaas Bakker

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Study design

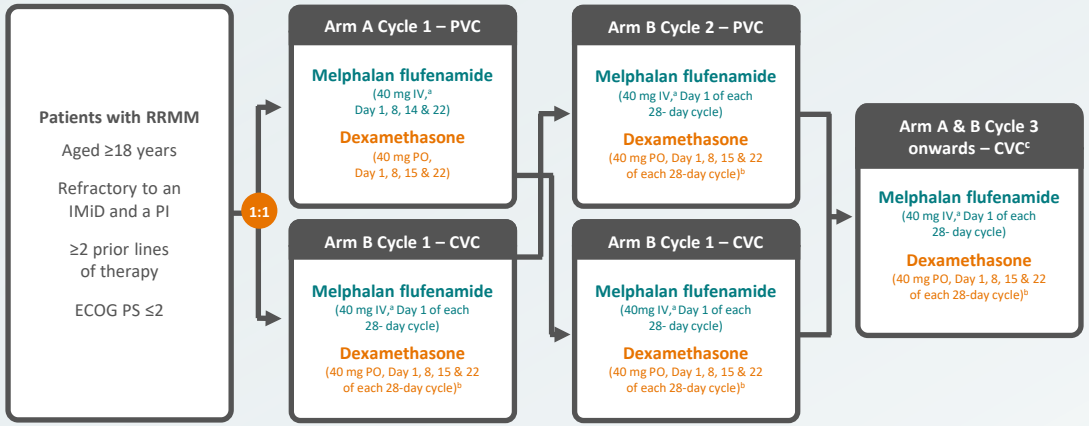
PRIMARY ENDPOINTS

- PK variables of melphalan (PVC vs CVC): maximum observed concentration (Cmax); area under the concentration–time profile from start of infusion to last measurable concentration (AUC0–t); and AUC from start of infusion to infinity (AUC0–inf)
- Frequency and severity of PVC-related local infusion-site reactions

SECONDARY ENDPOINTS

- PK variables of melflufen and desethyl-melflufen: Cmax; AUC0–t; AUC0–inf; and elimination half-life
- General safety and tolerability (treatment-emergent adverse events summarised by Medical Dictionary for Regulatory Activities v23.0)
- Efficacy outcomes – data to be presented at maturity

Figure 1. Phase 2 PORT Study Design (NCT04412707)



[a]30-minute infusion; [b]Dexamethasone 20 mg in patients aged ≥75 years; [c]A DSMC assessed safety and tolerability after six patients had received the PVC infusion and provided adequate PK data. The DSMC allowed continuation with PVC administration in Cycle 3 and onwards to further study local tolerability with repeat PVC administration, at the discretion of the investigator and in agreement with the patient.

CVC, central venous catheter; DSMC, Data and Safety Monitoring Committee; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; IV, intravenous; PI, proteasome inhibitor; PK, pharmacokinetics; PO, by mouth (orally); PVC, peripheral venous catheter; RRMM, relapsed/refractory multiple myeloma.

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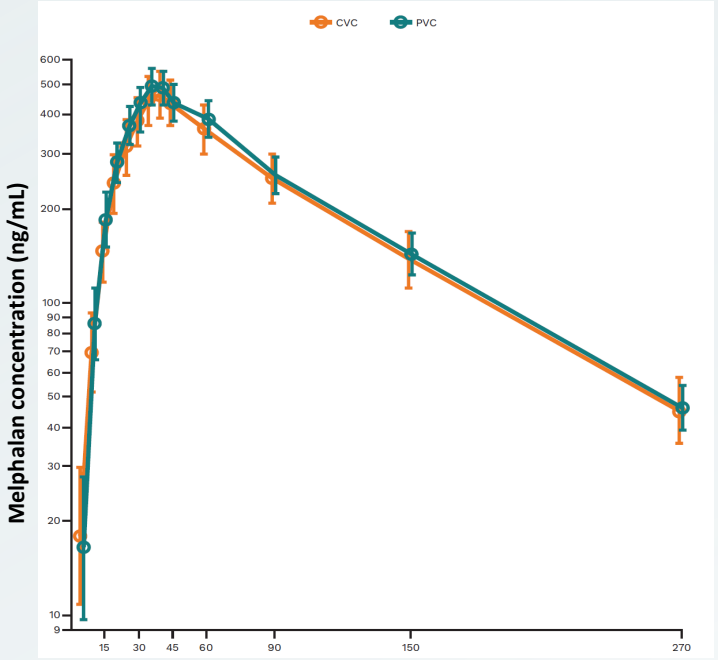
Results

Table 2. Melphalan PK Following PVC vs. CVC Administration of Melflufen

Parameter	Route	Geometric mean	Ratio % PVC/CVC (90% CI)[a]
C_{max} (ng/mL)	CVC	475	106 (95–118)
	PVC	504	
AUC_{0-t} (ng/mL• min)	CVC	49,908	106 (95–117)
	PCV	52,575	
AUC_{0-inf} (ng/mL• min)	CVC	54,961	105 (95–116)
	PVC	57,784	

- 19 patients were included in the PK population
- Melphalan: PK parameters were bioequivalent[a] after PVC and CVC administration *(Table 2; Figure 2)*

Figure 2. Geometric Mean Melphalan Concentration with 95% CI by Time Point & Route



CI, confidence interval; CVC, central venous catheter; PVC, peripheral venous catheter

[a]Bioequivalence criteria = 90% CI for the ratio of means within 80-125%.

AUC_{0-inf},area under the concentration-time profile from start of infusion to infinity; AUC_{0-t}, area under the concentration-time profile from start of infusion to last measurable concentration; CI, confidence interval; C_{max}, maximum observed concentration; CVC, central venous catheter; PK, pharmacokinetics; PVC, peripheral venous catheter.

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Conclusions

- In this Phase 2 Study of patients with RRMM, melphalan C_{max}, AUC_{O-t} and AUC_{inf}, were bioequivalent after PVC and CVC administration of melflufen
  - Melphalan C_{max} was observed on average 7–9 minutes after the end of melflufen infusion for both routes of administration, which reflects the delay in distribution of melphalan from tissues to plasma
  - Differences observed between some PVC- and CVC-related PK parameters for melflufen and the metabolite desethyl-melflufen (values slightly higher for PVC vs. CVC) are considered to have no clinical consequences, because the duration of their plasma exposure is short
  - There were no local reactions after PVC administration of melflufen, and no new safety signals were reported after melflufen PVC and CVC administration

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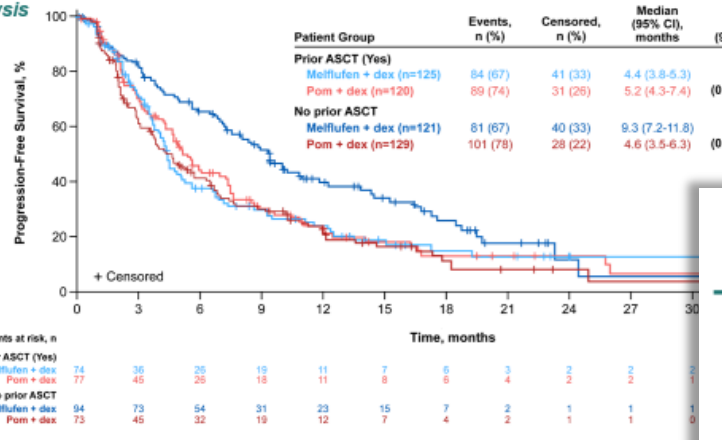
Concluding remarks

Marty J Duvall

OCEAN data summary – picture worth a thousand words

PFS Benefit in the Melflufen Arm Mainly Driven by Patients Who Had Not Received a Prior ASCT

Post-hoc analysis



Patient Group	Events, n (%)	Censored, n (%)	Median (95% CI), months	HR (95% CI)[a]	*P* Value[b]
Prior ASCT (Yes)					
Melflufen + dex (n=125)	84 (67)	41 (33)	4.4 (3.8-5.3)	1.06 (0.79-1.43)	0.69
Pom + dex (n=120)	89 (74)	31 (26)	5.2 (4.3-7.4)		
No prior ASCT					
Melflufen + dex (n=121)	81 (67)	40 (33)	9.3 (7.2-11.8)	0.59 (0.44-0.79)	<0.001
Pom + dex (n=129)	101 (78)	28 (22)	4.6 (3.5-6.3)		

Patients at risk, n											
Prior ASCT (Yes)											
Melflufen + dex	74	36	26	19	11	7	6	3	2	2	2
Pom + dex	77	45	26	18	11	8	6	4	2	2	1
No prior ASCT											
Melflufen + dex	94	73	54	31	23	15	7	2	1	1	1
Pom + dex	73	45	32	19	12	7	4	2	1	1	0

ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio; melflufen, melphalan flufenamide; PFS, progression-free survival; pom, pomalidomide.
[a]Unstratified HR. [b]Log-rank *P* value.

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Conclusions

- The phase 3 OCEAN study enabled a direct head-to-head comparison of melflufen plus dexamethasone versus pomalidomide plus dexamethasone in RRMM
- Melflufen plus dexamethasone was superior to pomalidomide plus dexamethasone for the primary endpoint of PFS
- OS trended in favour of melflufen plus dexamethasone in patients without a prior ASCT, and favoured pomalidomide plus dexamethasone in patients with a prior ASCT
- The safety of melflufen plus dexamethasone primarily consisted of haematologic adverse events that were manageable with dose modifications, which is consistent with previous reports[1-3]
- Results from OCEAN suggest that melflufen plus dexamethasone is a potential treatment for patients with lenalidomide-refractory RRMM who have received 2-4 previous lines of therapy and who have not received a prior ASCT

ASCT, autologous stem cell transplant; melflufen, melphalan flufenamide; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.
1. Richardson PG, et al. *Lancet Haematol*. 2020;7:e395-e407. 2. Bringhen S, et al. *Br J Haematol*. 2021;193:1105-1109. 3. Richardson PG, et al. *J Clin Oncol*. 2021;39:757-767.

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Summary

- Data presented at IMW encouraging
  - OCEAN Phase 3 study
  - PORT Phase 2 study
- Near-term focus is to reach an agreement with the FDA
  - ODAC meeting to be held on October 28
  - Various outcomes from FDA review possible
- Commercialization of Pepaxto in the US continues
- Regulatory process with the EMA proceeding according to plan
- ASH 2021 … more data to come

Q&A

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