

1-2 Febbraio 2022 Bologna Royal Hotel Carlton



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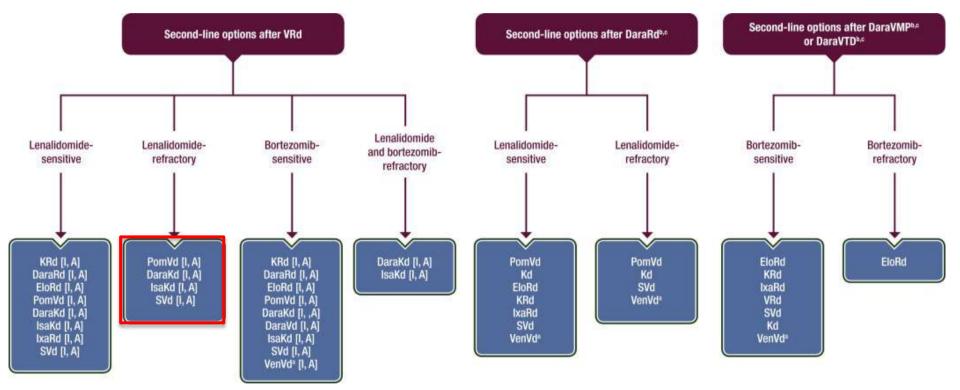
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BMS Celgene Sanofi Janssen Amgen Takeda

1-2 Febbraio 2022 Bologna Royal Hotel Carlton



Recommendations for the first relapse of myeloma



Dimopoulos et al, Annals of Oncology 2021

Results

(Table 1)

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P-224

Pomalidomide, bortezomib, and dexamethasone after 1 prior line of therapy in relapsed or refractory multiple myeloma: a safety subanalysis of the phase 3 OPTIMISMM trial

Katja Weisel, * Meletios Dimopoulos, * Albert Oriol, * Meral Beksac, * Fredrik Schjesvold, * Anna Marina Liberati, * Jindriska Lindsay, * Darrell White, * Jesus San Miguel, * Philippe Moreau, ** Larry D. Anderson, Jr, ** Alessandra Lorocca,11 Pawel Robak,11 Prisca Vogel,14 Rulyun Jiang,15 Lara Grote,15 Teresa Peluso,14 Paul Richardson1

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Introduction

- Patients with newly disgnosed multiple myeloms (ROWW) are routinely created with lensil demide (LEN) uncil disease progression, thus, at first relapse, many patients have LEN-ref ractory closese?
- Patients with relapsed or refractory multiple myelionia (RRWH) need proven effective therapies that no only help achieve classes control[®] but also have a manageable safety prefile
- Pomolidomide (POW) is an immunemodulatory drug with antitumor activity and immune-enhancing effects in patients with #W, including those with LDN-refractory disease¹¹
- The European Convision approved the FOM, bortaxonito (BORT), desimethesiane (BS2) (PVd) treatment for patients with IRWA after first nelapies, supported by data from the phase 3 OPTIMENAN treal (NCTOT14923)*
- Median progression free survival (#FS) at first relapse: 20.7 vs 11.6 months: HR, 0.54 (#58.0), 0.36-0.62); P = 0.0027⁴
- The individual safety profiles for PGW, BORT, and GEX' were consistent with adverse events (dEs) reported with PVd in the overall population of the OPTIMEWH trial.

Objective

To report a safety analysis of treatment emergent adverse events (TEAEs) in the events of interest (EOE) casegory for PMI vs BORT and DEX (Vd) administered at first relapse in the DPTIW64W trial

Methods

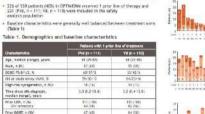
Patients with RRWM were randomized 1:1 to receive PVd or Vd in the OPTIWISMW trial (Figure 1) Figure 1. OPTINISMM study design



Theorem with FS during the way or within 40 days of the last state of a FSRS' partnering therapy when the approval during periodial of L1 regime before seeily were excluded. "Officery restanted move? If shale 1.1 days 1 with the accounted days to be the territory." and the population of population of a state of the sta

- + A subgroup of patients who received only 1 prior line of treatment were selected for this safety analysi Patients were included who received a 1 dose of study drug
- The NDI CICAE (version 4.0 or Higher) and Med0IA dictionary (version 30.0) were used to summarize AEs by system organ class and preferred term and assign AE grades
- Time to onset, duration, cycle timing, and supportive care for TEAE EDB were explored
- * Exposure-adjusted incidence rates were calculated in 100 × n/T n + the number of patients with the selected AE - T = the total patient-years (PY)
- · Grouped TEAE EOK were used to enhance AE detection and present
- clinically relevant AE terms Patients with > 1 occurrence of the same TEAE EOI were counted once in that category by the highest grade experience

Presented at the International Washing Workshop (WWI): September 8-11, 2021; Wesser, Autoli



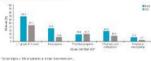




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At the data cutoff (25 Dctober 2017), the median duration of treatment, was longer in the (PK 3 am (47.4 weeks; range, 4.7.347.0) than the Vd arm (27.1 weeks; range, 0.4.162.0) Grade 3/4 TEAE EDIs accurred to 57.58 of patients (127/221).

 More grade 3/4 neutroperia, infections and infestations, and peripheral neuropathy events were present in the Pid vs vd arms (Pigure 2) Figure 2. Grade 3/4 TEAE EON



- To adjust for the longer treatment duration in the PVd arm than the Vd arm, incidence rates per 100 PVs were calculated for each of these grade 3/4 TEAE ECIS (TBAILE 2)
- The incidences of grade 3/4 neutropertia and infections and infestations were greater with Pvid vs Vd, whereas the incidence of grade 3/4 thrombocytopenia was greater with Vd Neutropenia was mostly grade 3/4 (Figure 3), began in the first cycle of sreatment (Figure 4), and lasted a median of 8 days (Figure 5)
- All febrile neutropersie cases (n + 4) were grade 3/4

Infections and infectations and peripheral rescopathy were mostly grade 1/2 (Figure 3), began in the first 2 cycles of treatment (Figure 4), and had median durations of 12 and 19 days, respectively (Figure 9)

Table 2. Grade 3/4 TEAE EOI incidence rates per 100 PYs¹





Figure 3. Grade of TEAE EOIs in each cycle of PVd treatment



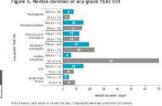
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Figure 4. Median time to onset of any-grade TEAE EOI PROVINE and the second

Tenteri

Figure 5. Median duration of any-grade TEAE EOI



Dose modifications ------

- TEAE EDIs were mainly managed with dose reductions and interruptions of any drug in the PVd and Vd arms (Table 3) PON discontinuations due to 2.1 TEAE EDI of any grade were low (9.65)
- 15.5% of patients had POM interruptions and +5.9% of patients had POM dose reductions - The mechan relative POV dose intensity was 0.9 (range, 0.3-1.0)
- Infections and infestations were the primary cause of Pvd doke interruptions (04.15) (Table 3)

 Perpheral neuropathy was the most common TEAE EDI leading to dose reduction (32,46) and discontinuation (16,25) with PVd (Table 3) Table 3. Dose modifications of any drug due to TEAE EOB

	due to 1	desa Any dese Any de ctian internaction discontinuet EAE 201, due to TEAE 200, to TEAE 30, s (%) n (%)		due to TEAE EDI.		EAE EOL	
	(1 - 111)	V6 (n - 112)	1944 (1 - 111)	(1-116)	PMd (6 = 111)	V0 (1 - 110)	
a 1 TEAC CO beaching to dow modifications of any drug	60 (38.8)	43 (39.1)	85 (79.3)	40 (54.5)	24 (21.1)	7 (13.3)	
Mistracente	15 (11.7)	1 (0.1)	72 (19.89	2 (1.8)	a	đ	
Transforstepente	17 (10.0)	1015	11 (1.3)	0.01.6	1.01.9	+ (0.9)	
Infections and Infestigations	8 (7.2)	40.6	60 (54-1)	-4 (36.4)	1(3.6)	÷ (0.5)	
Perspheral seuropathy	16 (32 m)	24 (25 4	34 (21,6)	18 (16:4)	18.06.2)	71 (10.6)	
terrelaria (relading derivies and contation)	±(7.2)	1.42.90	8(7.3)	10.7)	1.03.9	1 (0.5)	

Medical interventions of TEAE EOIs

 Antibiotics, antifrangais, antiprotocoals, and antivirals were used to treat.
 995 of patients in the PVd arm who experienced infections and infestations (Table 4)

- G-CSF treatments were used for patients with neutropenia (62.0%) and febrile neutropenia (66.7%) in the PVd erm (3ble 4)
- Anthrinkl and G-CSF prophyliskes were recommended by study protocol and carnot be obtinguished from supportive treatments after AE ensor
- Among patients with thrombocytopenia, 29.05 (9/31) in the PVd arm and 28.1% (9/32) in the Vd arm received plateix transfisions
- Among patients with anemia, 57.76 of patients (13.126) in the PVd ann and 45.5% of patients (10/22) in the Vd ann received red blood cell transfusions

Table 4. Medications for TEAE management used in the PVd arm

Nedications	FYG. n OG
Artivited user in partnerss with a 1 indections and indestations event in ϵ Sty	90 (16.5)
Antibiodics, antifyingsis, an antiprotesses use in patients with a 1 infactions and infactiants exent $(\tau=91)$.87 (65.6)
G-CSF use in patients with a 1 neutrapovia event (n < 50)	31 (62.7)
G-CSF use in patients with a 1 febrie reatropenia event is = 3)*	1 (05.7)
Programmedication in patients with a 1 DVT event (in = 4): Antyrearcy is adapt timesporty soften Termsporty	3 (73.0) 1 (73.0) 1 (73.0)

Conclusions

. The safety profile for PVd at first relapse in patients with RRMM is consistent with previous reports**

+ Grade 3/4 TEAEs of neutropenia, peripheral neuropathy, and infections and infestations were more frequent with PVd vs Vd

- Exposure-adjusted incidence rates were higher per 100 PVs in the PVd group than the Vd group

Treatment durations were longer for patients who received PVd than Vd. and POM discontinuations. were infrequent.

· TEAE EOIs generally occurred in early cycles of treatment and were monaged with dose modifications or appropriate supportive care

. The higher efficacy of PVd and consequent use of supportive strategies is recommended to minimize toxicity and maximize effect

References

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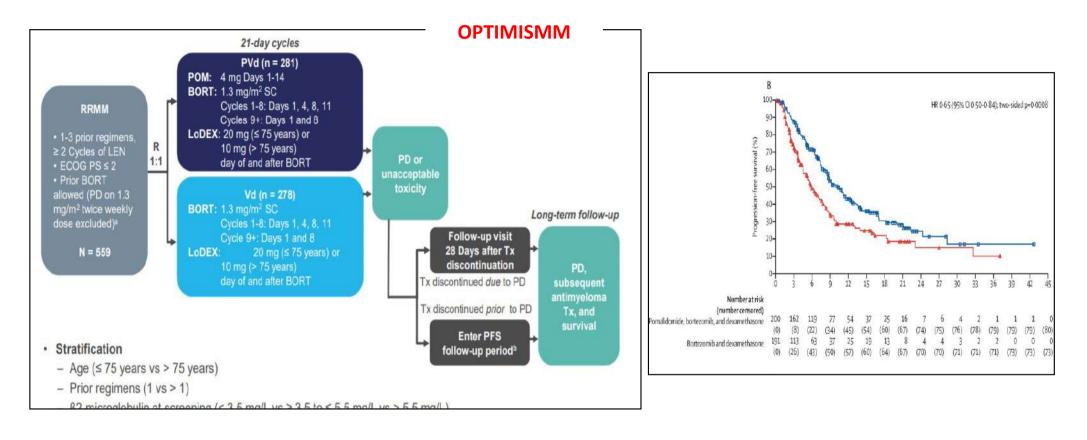
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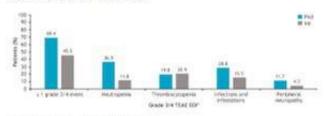
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Safety

- At the data cutoff (26 October 2017), the median duration of treatment was longer in the PVd arm (47.4 weeks; range, 4.7-147.0) than the Vd arm (27.1 weeks; range, 0.4-162.0)
- Grade 3/4 TEAE EOIs occurred in 57.5% of patients (127/221)
- More grade 3/4 neutropenia, infections and infestations, and peripheral neuropathy events were present in the PVd vs Vd arms (Figure 2)

Figure 2. Grade 3/4 TEAE EOIs



Occurring in + 10% of patients in either Insatraint arm.

- To adjust for the longer treatment duration in the PVd arm than the Vd arm, incidence rates per 100 PYs were calculated for each of these grade 3/4 TEAE EOIs (Table 2)
- The incidences of grade 3/4 neutropenia and infections and infestations were greater with PVd vs Vd, whereas the incidence of grade 3/4 thrombocytopenia was greater with Vd
- Neutropenia was mostly grade 3/4 (Figure 3), began in the first cycle of treatment (Figure 4), and lasted a median of 8 days (Figure 5)
- All febrile neutropenia cases (n = 4) were grade 3/4
- Infections and infestations and peripheral neuropathy were mostly grade 1/2 (Figure 3), began in the first 2 cycles of treatment (Figure 4), and had median durations of 12 and 19 days, respectively (Figure 5)

Table 2. Grade 3/4 TEAE EOI incidence rates per 100 PYs*

Patients with 1 prior line of treatment	Neutropenia	Thrombocy- topenia	Infections and Infestations	Peripheral neuropathy
PVd (n = 111)	46.25	21.30	32.91	11.31
Vd (n = 110)	18,14	32.96	23.71	6.39

Occurring in + 325 of patients in either inlatment arts.

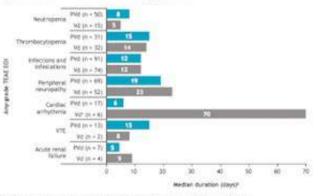
Peripheral neuropathy

Figure 4. Median time to onset of any-grade TEAE EOI

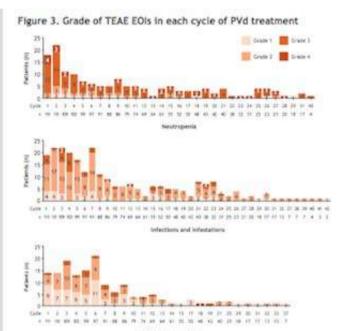
Prit (n = 3/2 0.76 No. concerts. we in + the NY11 PNd (n + 31) Thrombocytopenia WE (0 - 32) 1.00 Proj an - 91. 1.10 infestations. WE IN - TH PVd (n + kit) 3.0 Sector stat Wi etc = 32 Phil (n = 17 Canthal arity Chiefe 101 101 - 311 Prizi in - Thi 1.0 MTC. VE IN + ZI Acute result . INC m > 7) Witted Hectien time to impat (months)

VTE, venue thrundacerebolism.

Figure 5. Median duration of any-grade TEAE EOI



Yorly 2 events, with values of 14 and 126 days; "Orgoing AEs were excluded from calculations.



Peripheral neuropathy

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Dose modifications

- TEAE EDIs were mainly managed with dose reductions and interruptions of any drug in the PVd and Vd arms (Table 3)
- POM discontinuations due to ≥ 1 TEAE EOI of any grade were low (9.0%) - 95.5% of patients had POM interruptions and 45.9% of patients had POM dose reductions
- The median relative POM dose intensity was 0.9 (range, 0.2-1.0)
- · Infections and infestations were the primary cause of PVd dose interruptions (54.1%) (Table 3)
- Peripheral neuropathy was the most common TEAE EOI leading to dose reduction (32, 4%) and discontinuation (15, 2%) with PVd (Table 3)

Table 3. Dose modifications of any drug due to TEAE EOIs

	due to T	dose Any dose interruption EAE EOI, (%) n (%)		uption TAE EOI,	Any dose discontinuation to TEAE EDI, n (%)	
	(n - 111)	Vđ (n - 110)	PVd (n = 111)	Vd (1 - 110)	Pvid (n = 111)	Vd (n - 110)
± 1 TEAE EOI leading to dose modifications of any drug	65 (58.6)	43 (39.1)	55 (79.3)	60 (54.5)	24 (21.6)	7 (15.5)
Neut/ope/sla	13 (11.7)	1 (0.9)	22 (19.8)	2 (1.8)	0	ø
Thronbocytopenia	12 (10.8)	8 (5.5)	11 (9.9)	13 (11.8)	1 (0.9)	1 (0.9)
Infections and Infestations	8 (7.2)	4 (3.6)	60 (54.1)	40 (36.4)	4 (3,6)	1 (0.9)
Peripheral neuropathy	36 (32.4)	29 (26.4)	24 (21.6)	38 (56.4)	18 (16.2)	11 (10.0)
Someolence (including distriness and confusion)	8 (7.2)	1 (0.9)	8 (7.2)	3 (2.7)	1 (0,9)	1 (0.9)

Medical interventions of TEAE EOIs

- Antibiotics, antifungals, antiprotozoals, and antivirals were used to treat > 95% of patients in the PVd anm who experienced infections and infestations (Table 4)
- · G-CSF treatments were used for patients with neutropenia (62.0%) and febrile neutropenia (66.7%) in the PVd arm (Table 4)
- Antiviral and G-CSF prophylaxes were recommended by study protocol and cannot be distinguished from supportive treatments after AE onset
- Among patients with thrombocytopenia, 29.0% (9/31) in the PVd arm and 28.1% (9/32) in the Vd arm received platelet transfusions
- Among patients with anemia, 57.7% of patients (15/26) in the PVd arm and 45.5% of patients (10/22) in the Vd arm received red blood cell transfusions.

Table 4. Medications for TEAE management used in the PVd arm

Medications	PVd , n (%)
Antivirel use in patients with \pm 1 infections and infestations event $(n \pm 91)^n$	90.(98.9)
Antibiotics, antifungals, or antiprotopoals use in patients with a 1 infections and infestations event $(n = 91)$	87 (95.6)
G-CSF use in patients with a 1 neutropenia event (n + 50)*	31 (62.0)
G-CSF use in patients with \pm 1 febrile neutropenia event (n + 3)*	2 (66.7)
Prophylaxis medication in patients with a 1 DVT event (n = 4): Acetylsaticytic acid Enoxoparin sodium Enoxoparin	3 (75.0) 1 (25.0) 1 (25.0)

Acyclore prophylaus was not mandetory, but was recommended per protocol, "G CIP prophylaus was not manifetory, but recommended per protocol, in the Pitt ann (n = 111), 4 patients had a 1 DPT event (J Ab) 2 had prior BPT events

Conclusions

- · The safety profile for PVd at first relapse in patients with RRMM is consistent with previous reports**
- Grade 3/4 TEAEs of neutropenia, peripheral neuropathy, and infections and infestations were more frequent with PVd vs Vd
- Exposure-adjusted incidence rates were higher per 100 PYs in the PVd group than the Vd group
- Treatment durations were longer for patients who received PVd than Vd, and POM discontinuations were infrequent
- · TEAE EOIs generally occurred in early cycles of treatment and were managed with dose modifications or appropriate supportive care
- · The higher efficacy of PVd and consequent use of supportive strategies is recommended to minimize toxicity and maximize effect

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Disclosures

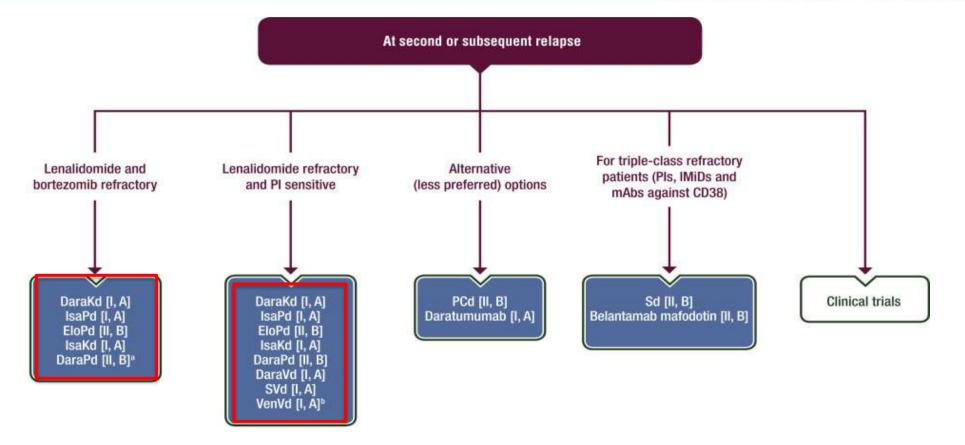
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Previously presented at the European Hematology Association (DHA) Virtual Meeting.

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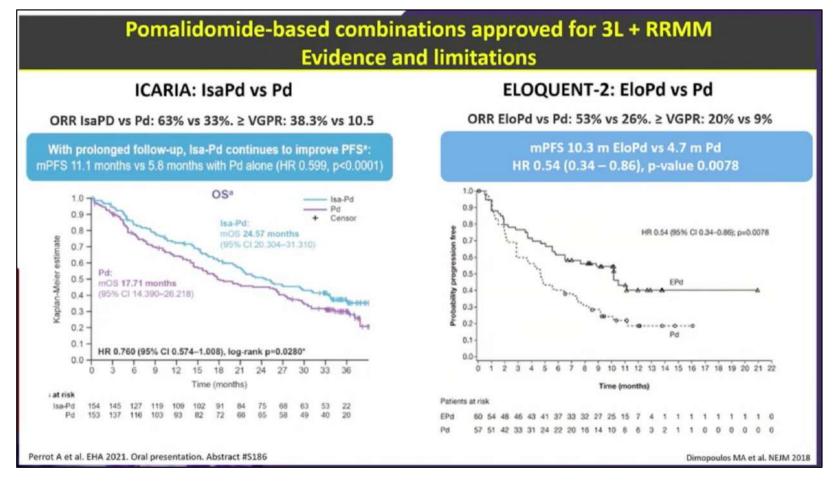




Moreau, Lancet Oncol 2021

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A Multicenter, Phase 1b Study to Assess the Safety, Pharmacokinetics, and Efficacy of Subcutaneous Isatuximab Plus Pomalidomide and Dexamethasone, in Patients With Relapsed/Refractory Multiple Myeloma

INTRODUCTION

National Interaction (1) is a monoclonal antibody that block to a specific opticipation (CDD) and exerts an multiple registrona (MAU) effects through several models of a citizer (lass) exclusions with provide horizontal and discumptioners. (Feld Lagrandia) is optimized in control associates for the treatment of abult patients with preasant in additional discussion (Feld Lagrandia) who have received so prior therapes, including landbalance and additional discussion (Feld Lagrandia) and including landbalance and additional discussion (Feld Lagrandia) and including landbalance and a procession in induces (Feld Lagrandia).

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clary endpoints were overall response rice (OHS), injects neer and CD30 PC

RESULTS

 control of all partners and based the characteristics
 cost of 34 parents were randomized to ise for 10 mg/kg + Polima 121 as SC1000 + Pd (ma 121 or Isa SC1400 + Pd (ma 121 or Isa SC140 An of Nami 51, 2021, 2 patients (St.340) in the IV collect, 4 patients (31.39), in the SC1000 collect, and 3 patients (70.0%) in the SC1400 collect remained on study transmers.

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Skit Lealers	41331.85	2062	1140.43
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e46-06 mL/min/1.72ml	5 (01 2)	6 (50.0)	1 (56)(6)
<00 mL/mm/1.75mV	3 (25 C8	2 (16.7)	4146101
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Lonalitionide	7 (39.3)	11 (91.75	7 (70.4)
11	7 (58.3)	9 (25/0)	9 (56)(0)
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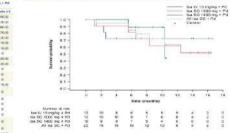
w (%).	10-12)	(a+12)	(n-30)
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Massimprenio	10.85.33	10 (83.3)	8 (25.43	9079-08	37 (76,0)	7 (76.0)
Police la montregenta	1.98.32	1 (8.3)	0		81.06235	2 1381.00
Anemia	3125.0	2 (76,7)	+ 122.79	2 (16.7)	2(30/8	1(10.0)
Thrumbocytopanie	20.67	2(16.7)	1 (0.3)	1 18.30	1 (1 000)	1116.01
Retribution and autrition disorders	8125.0k	9	2 1988.38	311675	813610	0
Physick interior allowed hour	a126.05	1.000	9 (25.4)	3 (25.0)	\$ (56.0)	2 (36.0)
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Nersona system disorders	7358.80		8 995.23		stat.m	0
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higher CRB was advected in the \$2,3400 (80%) versus \$2,1000 ares to refer to \$6.2% in both Atrend scoote and complete response even similar across cohorts the PTS was 73% for the IV and SC1000 cohorts and 80% for the SCI 400 och of (Figure)

	inia the trib integriting in the grant 123	8436 1000 mg + Pd (4-12)	BADC 14991
Restoverall responses of 1981			
Stringent complete requeses (sCFI)		٥	0
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200 + Iso IV 10 wg/kg 250 200 150 79 -188 (7 (89.9) Normal time after first dose thours Table S. Mean (CYN) II. PS.24 and tourth SC or fy administration Citile Greg/reik) CTAW Grates "tet" AUC. 1000 mg (SC pump) 1101282 110 148 101 1442 182001524

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HD was row in th SC1400 (Table 6) Table & CD10 or

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Means IN (SD)	76.0 (6.3)	79.0 (3.4)	46.5 (1.2)
Wether, 'to	73.0	50.2	60.2
Vin-Max 19	68.2-85.1	74.7-042	76.6-83.2

ONCLUSIONS

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The safety of Ira 5C at 1000 mg and 1400 mg + Pd was consistent with the kns profile associated with IV edministration, with no new safety signals identified Influsion-related reactions were infrequent, occurring only at first injection, and local televability of isa SC was very good

Efficacy results were comparable with the Phase & ICARIA registrational tri

Higher $C_{\rm max}$ at 4 weeks DN best predictor of the efficacy) was achieved follow administration compared with N

PX modeling and simulations accounting for imbalances, and CO38 RD sug 1400 mg QW-Q2W for the expansion cohort which is ongoing

Iso SC + Pd appears to be a promising and convenient option for patients with RRMM

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A Multicenter, Phase 1b Study to Assess the Safety, Pharmacokinetics, and Efficacy of Subcutaneous Isatuximab Plus Pomalidomide and Dexamethasone, in Patients With Relapsed/Refractory Multiple Myeloma

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¹Department of Hematology, University Hospital of Nantes, Nantes, France; ²Illawarra Cancer Care Centre, Wollongong, NSW, Australia; ³Immunology and Molecular Oncology, Epworth Healthcare and University of Melbourne, Melbourne, Vic, Australia; ⁴University Hospital Marqués de Valdecilla, University of Cantabria, Santander, Spain; ⁵Department of Hematology/Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, CA, USA; ⁶Banner MD Anderson Cancer Center, Gilbert, AZ, USA; ⁷Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Barcelona, Spain; ⁸Réseau Régional de Cancérologie Onco-Occitanie, Toulouse, France; ⁹Department of Hematology, University Hospitals Leuven, Leuven, Belgium; ¹⁰Gabrail Cancer Center, Canton, OH, USA; ¹¹Sanofi, Cambridge, MA, USA; ¹²Sanofi Research & Development, Vitry-sur-Seine, France; ¹³Clinical Haematology Service, St Vincent's Hospital, University of Melbourne, Melbourne, Vic, Australia

Poster ID: P-207

Presented at the18th International Myeloma Workshop (IMW), Vienna, Austria, September 8–11, 2021

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Study design and data

- This multicenter, open-label, Phase 1b study (NCT04045795) evaluated the safety, pharmacokinetics (PK), and efficacy of Isa SC versus Isa IV + Pd in RRMM patients who have received ≥2 prior lines of therapy for MM, including lenalidomide and a PI
- Patients were randomized 2:1 to cohorts 1a (Isa SC 1000 mg dose [SC1000] delivered through a syringe pump) or 1b (Isa IV 10 mg/kg dose)
- Isa SC and Isa IV were administered once weekly for 4 weeks (Cycle 1) and then once every 2 weeks in subsequent cycles (QW–Q2W) in combination with Pd
- After evaluation of Isa SC safety, PK, and CD38 receptor occupancy (RO) data in cohort 1a, new participants were randomized 2:1 to cohorts 2a (Isa SC 1400 mg dose [SC1400]) or 2b (IV 10 mg/kg dose)
- The aim of this study was to select an Isa SC dose
- The primary study endpoints were dose-limiting toxicity (DLT), injection site reactions (ISRs), and PK parameters
- The main secondary endpoints were overall response rate (ORR), progression-free survival (PFS), patient reported outcomes and CD38 RO

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Table 1. Patient baseline characteristics



Patient disposition and baseline characteristics

- A total of 34 patients were randomized to Isa IV 10 mg/kg + Pd (n=12); Isa SC1000 + Pd (n=12); or Isa SC1400 + Pd (n=10) (Table 1)
- As of March 31, 2021, 7 patients (58.3%) in the IV cohort, 4 patients (33.3%) in the SC1000 cohort, and 7 patients (70.0%) in the SC1400 cohort remained on study treatment

Randomized population	lsa IV 10 mg/kg + Pd (n=12)	lsa SC 1000 mg + Pd (n=12)	lsa SC 1400 mg + Pc (n=10)
Median age, years (range)	69.5 (46–83)	67.0 (50-78)	72.5 (63–83)
Age in years by category, n (%)			
<65	5 (41.7)	5 (41.7)	1 (10.0)
≥65 to <75	4 (33.3)	6 (50.0)	6 (60.0)
≥75	3 (25.0)	1 (8.3)	3 (30.0)
Median weight, kg	73.5	70.3	86.9
Median bone marrow plasma cells at baseline, %	7.5	9.0	18.5
Number of bone lesions, n (%)			
No lesion	4 (33.3)	2 (16.7)	1 (10.0)
1-4	4 (33.3)	6 (50.0)	2 (20.0)
5-10	1 (8.3)	2 (16.7)	2 (20.0)
More than 10	3 (25.0)	2 (16.7)	5 (50.0)
Median beta-2 microglobulin, mg/L	3.00	2.65	3.55
ISS stage at study entry, n (%)			
Stage I	4 (33.3)	8 (66.7)	4 (40.0)
Stage II	5 (41.7)	4 (33.3)	6 (60.0)
Stage III	2 (16.7)	0	0
eGFR category, n (%) [MDRD]			
≥90 mL/min/1.73 m²	4 (33.3)	4 (33.3)	1 (10.0)
≤60–90 mL/min/1.73 m²	5 (41.7)	6 (50.0)	5 (50.0)
<60 mL/min/1.73 m ²	3 (25.0)	2 (16.7)	4 (40.0)
Prior lines of therapy, median (range)	3.5 (2-7)	3.0 (2-6)	2.5 (1-4)
Number of prior lines, n (%)			
1	0	0	1 (10.0)
2	4 (33.3)	4 (33.3)	4 (40.0)
≥3	8 (66.7)	8 (66.7)	5 (50.0)
Refractory to, n (%)			
Lenalidomide	7 (58.3)	11 (91.7)	7 (70.0)
PI	7 (58.3)	9 (75.0)	5 (50.0)
IMID and PI	6 (50.0)	8 (66.7)	4 (40.0)

d; dexamethasone; eGFR, estimated glomerular filtration rate; IMiD, immunomodulatory drugs; Isa, isatuximab; ISS, International Staging System; IV, intravenous; MDRD, Modification of Diet in Renal Disease; P, pomalidomide; PI, proteasome inhibitor; SC, subcutaneous

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Table 4. Best overall response



Efficacy

- A trend toward higher ORR was observed in the SC1400 (80%) versus SC1000 and IV cohorts (67% in both cohorts; Table 4)
- Very good partial response and complete response were similar across cohorts

1000 mg + Pd (n=12)	lsa SC 1400 mg + Pd (n=10)
0	0
3 (25.0)	2 (20.0)
2 (16.7)	2 (20.0)
3 (25.0)	4 (40.0)
2 (16.7)	0
8 (66.7)	8 (80.0)
5 (41.7)	4 (40.0)
10 (83.3)	8 (80.0)
1	0 (83.3)

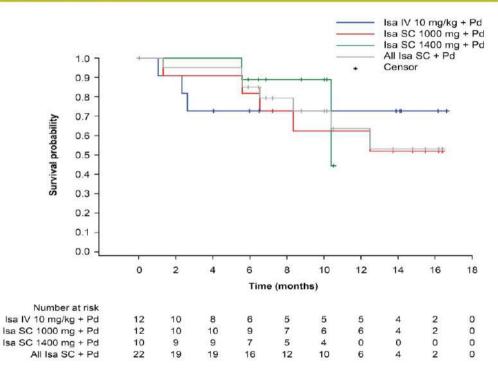
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Figure 1. Progression-free survival

Efficacy (contd.)

 At 8 months, PFS was 73% for the IV and SC1000 cohorts and 89% for the SC1400 cohort (Figure 1)



d, dexamethasone; Isa, isatuximab; IV, intravenous; P, pomalidomide; SC, subcutaneous

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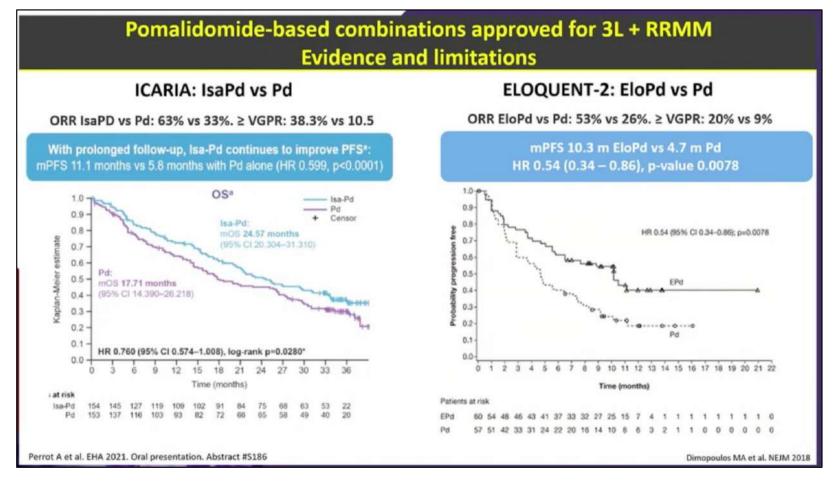


CONCLUSIONS

- The safety of Isa SC at 1000 mg and 1400 mg + Pd was consistent with the known safety profile associated with IV administration, with no new safety signals identified
- Infusion-related reactions were infrequent, occurring only at first injection, and local tolerability of Isa SC was very good
- Efficacy results were comparable with the Phase 3 ICARIA registrational trial
- Higher C_{trough} at 4 weeks (PK best predictor of Isa efficacy) was achieved following SC administration compared with IV
- PK modeling and simulations, accounting for imbalances, and CD38 RO support the dose of 1400 mg QW–Q2W for the expansion cohort which is ongoing
- Isa SC + Pd appears to be a promising and convenient option for patients with RRMM

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Elotuzumab plus pomalidomide/dexamethasone for relapsed/refractory multiple myeloma: final overall survival from the phase 2 ELOQUENT-3 trial

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Presentation P-193

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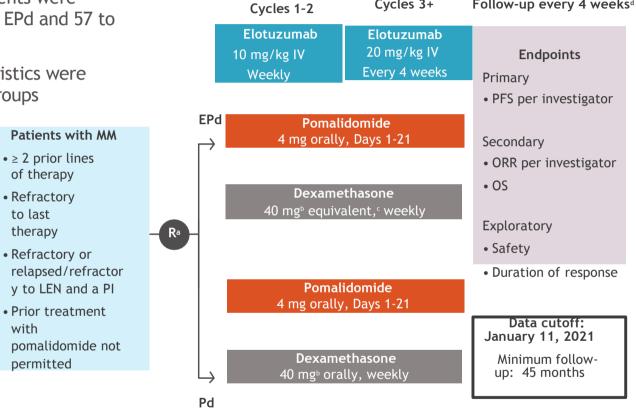
Introduction

- Therapies that extend overall survival (OS) are needed for patients with relapsed/refractory multiple myeloma (RRMM) and prior exposure to lenalidomide (LEN) and a proteasome inhibitor (PI)
- Elotuzumab, an immunostimulatory monoclonal antibody that targets SLAMF7, exerts multiple mechanisms of action to enable selective killing of myeloma cells¹⁻³
- Pomalidomide, like LEN, is an immunomodulatory agent that has tumoricidal and immune- enhancing effects⁴ and activity in LEN-refractory disease^{5,6}
- In the randomized phase 2 ELOQUENT-3 trial, elotuzumab plus pomalidomide/dexamethasone (EPd) significantly improved progression-free survival (PFS) versus Pd in patients with RRMM and \geq 2 prior therapies including LEN and a PI (median 10.3 months vs 4.7 months; HR 0.54 [95% CI, 0.34-0.86]; P = 0.008)⁷
 - Regulatory approval was granted in regions including the USA, EU, and Japan^{8,9}
- Preliminary analysis of OS from ELOQUENT-3 (minimum follow-up of 9.1 months) showed a trend favoring EPd over Pd⁷ which was maintained in a subsequent unplanned interim analysis (minimum follow-up of 18.3 months)¹⁰

Figure 1. ELOQUENT-3 study design (NCT02654132)

Patients and treatment disposition

- A total of 117 patients were • randomized, 60 to EPd and 57 to Pd
- Baseline characteristics were • similar between groups



Cvcles 3+

Follow-up every 4 weeks^d

^aRandomization was stratified by prior lines of therapy (2-3 vs \geq 4) and ISS stage at time of enrollment (I-II vs III); ^b20 mg in patients aged > 75 years; ^cDexamethasone was split between oral (28 or 8 mg in patients aged < 75 or > 75 years) and IV (8 mg) doses on days with elotuzumab; ^dFollow-up continued until disease progression; follow-up for survival occurred at least every 12 weeks.

ISS. International Staging System: ORR. overall response rate.

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Efficacy

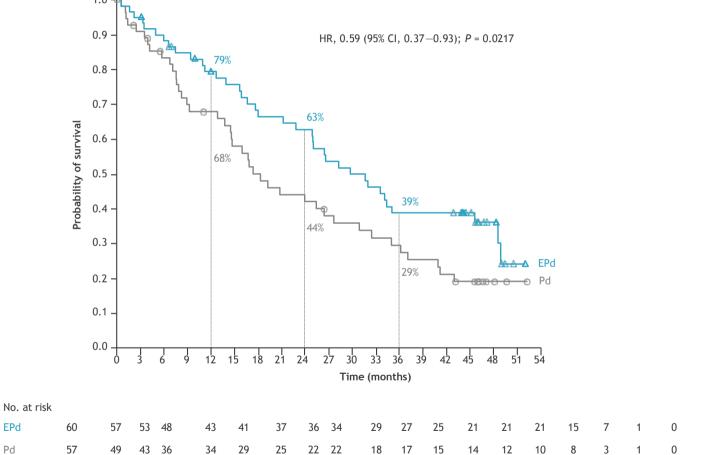
- At final analysis, there were 37 (61.7%) deaths in the EPd group and 41 (74.5%) in the Pd group
 - The most common cause of death in both groups was disease progression (EPd 41.7%, Pd 49.1%)
- OS was significantly improved with EPd versus Pd: median OS was 29.8 months (95% CI, 22.9- 45.7) versus 17.4 months (95% CI, 13.8-27.7), respectively, with a HR of 0.59 (95% CI, 0.37-0.93; 2-sided stratified log-rank P = 0.0217)
- OS rates were consistently higher with EPd than Pd at 1 year (79% vs 68%), 2 years (63% vs 44%), and 3 years (39% vs 29%)
- The OS benefit observed with EPd was maintained across most subgroups, although sample sizes were small
 - These included patients aged \geq 75 years, patients with \geq 4 prior lines of therapy, patients with disease refractory to LEN and a PI, and patients who had received LEN as their most recent prior therapy

EPd

Pd

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Overall survival in all randomized patients



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conclusions

- In this final analysis of OS from ELOQUENT-3, EPd demonstrated a statistically significant and clinically meaningful improvement in OS versus Pd in patients with RRMM and ≥ 2 prior therapies including LEN and a PI
 - 41% reduction in the risk of death
 - 1-year increase in median OS
- Subsequent therapies were balanced between treatment groups, suggesting that the effect on OS was primarily due to EPd
- OS benefit was consistent in key patient subgroups, including patients who had received LEN as their most recent prior therapy
- The safety profile of EPd was consistent with previous reports and no new safety signals were detected^{7,10}
- ELOQUENT-3 is the first randomized controlled study of a triplet regimen incorporating a monoclonal antibody and Pd in RRMM to show both significant PFS and OS benefits

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SELECT Trial in Progress Study Design

- The SELECT study is an open-label phase 2 study ongoing at ~ 40 sites in the EU and US, with expansion to more countries planned
- This study will evaluate the novel primary endpoint of MRD-negative CR to assess the efficacy of KPd in patients with one or two relapses of MM

N ~ 85ª

Key inclusion criteria:

RRMM

- One or two prior lines of therapy
- Refractory to lenalidomide
- ≥ PR to lenalidomide
- · Prior exposure to a PI or anti-CD38 antibody is allowed

Treatment Until Disease Progression

KPd Carfilzomib^b (20/56 mg/m²) + pomalidomide^c + dexamethasone^d

Primary endpoint: MRD-negative CR in the bone marrow at 12 months by NGS (sensitivity of 10⁻⁵) **Secondary endpoints:** ORR, best MRD-negative response at any time, sustained MRD-negative CR, DoR, TTR, PFS, OS, and safety

^aTwenty-six patients are currently enrolled; the target for enrollment completion is January 2022. ^bIV on days 1, 8, and 15 of each 28-day cycle for cycles 1–12 and on days 1 and 15 from cycle 13 until progression or end of study (20 mg/m² on day 1 of cycle 1 and 56 mg/m² thereafter). ^cPO 4 mg on days 1–21 of all cycles. ^dPO or IV 40 mg prior to carfilzomib on days 1, 8, 15, and 22 of cycles 1–12 (20 mg for patients ≥ 75 years old) and 20 mg on days 1 and 15 of cycle 13 onwards (10 mg for patients ≥ 75 years old).

CD33, cluster of differentiation 38; CR, complete response; DoR, duration of response; EU, European Union; IV, intravenous; KPd, carfilzomib, pomalidomide, and dexamethasone; MM, multiple myeloma; MRD, minimum residual disease; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PO, per oral; PR, partial response;

RRMM, relapsed/refractory multiple myeloma; TTR, time to response; US, United States.

Moreau P, et al. Presented at: 18th IMW; September 8-11, 2021; Vienna, Austria. Abstract P-206.