

2007	01	15
2008	03	26
2008	04	17
2009	01	09
2009	09	21
2010	04	01
2012	07	03
2012	08	02
2012	10	23
2012	11	29
2014	05	23
2015	02	09
2015	03	03
2016	06	07
2016	07	05
2017	08	02
2017	10	19
2018	03	06
2018	08	21
2018	09	18
2018	12	06
2019	07	18
2020	08	10

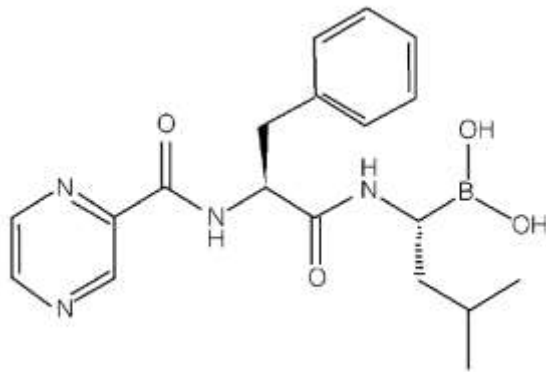
注射用硼替佐米说明书

®

Bortezomib for Injection

Zhusheyong Pengtizuomi

[(1R)-3- 1-[[[(2S)-1- 3- 2-[()]]]]]



$C_{19}H_{25}BN_4O_4$

384.24

2 (1~4)												
	1				2		3	4		5		6
(1.3mg/m ²)	1	--	--	4	8	11		22	25	29	32	
(9mg/m ²)	1	2	3	4	--	--		--	--	--	--	
(60mg/m ²)												
(5~9)												
	1				2	3	4	5	6			
(1.3mg/m ²)	1	--	--	--	8		22	29				
(9mg/m ²)	1	2	3	4	--		--	--				
(60mg/m ²)												

- $\geq 70 \times 10^9/L$ ANC $\geq 1.0 \times 10^9/L$

- 1

2

•	4	25%
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<ul style="list-style-type: none"> • (1) $\leq 30 \times 10^9/L$ $ANC \leq 0.75 \times 10^9/L$ • ≥ 2 ≥ 3 1 2 	$1mg/m^2$ $1mg/m^2$ ($1.3mg/m^2$ $0.7mg/m^2$)
3	$1mg/m^2$ $1mg/m^2$ ($1.3mg/m^2$ $0.7mg/m^2$) / 3

11) 10 ($1.3mg/m^2$ 12 21) 2 2 (1 4 8)

3 1 72

8

1 4 (1 8 15 22) 13

(23 35)

3 4 ()

25%(

$1.3mg/m^2$ $1.0mg/m^2$ $1.0mg/m^2$ $0.7mg/m^2$)

	*	
1 ()		
1 (ADL **)	2 ()	1.0mg/m ² 1.3mg/m ² 1
2 (ADL ***)	3 ()	0.7mg/m ² 1
4 ()		
* NCI CTCAE v 4.0		
** ADL		
*** ADL		

6 6

2

3 1 1 375 mg/m²

750 mg/m² 50 mg/m² 1 2 3 4 5 100

mg/m²

1 ()

- $\geq 100 \times 10^9 / L$ (ANC) $\geq 1.5 \times 10^9 / L$

- $\geq 8g / dL (\geq 4.96 \text{ mmol} / L)$

- 1

3 3 ()

4

<ul style="list-style-type: none"> • ≥ 3 $< 10 \times 10^9/L$ • $< 25 \times 10^9/L$ (1) ANC $< 0.75 \times 10^9/L$ 	<p style="text-align: right;">2</p> <p>ANC $\geq 0.75 \times 10^9/L$ $\geq 25 \times 10^9/L$</p> <ul style="list-style-type: none"> • • ANC $\geq 0.75 \times 10^9/L$ $\geq 25 \times 10^9/L$ (1.3mg/m² 1mg/m² 1mg/m² 0.7mg/m²)
<p>≥ 3</p>	<p style="text-align: right;">2</p> <p>(1.3 mg/m² 1 mg/m² 1 mg/m² 0.7 mg/m²)</p> <p style="text-align: center;">3 /</p>

0.7mg/m²

1.0mg/m² 0.5mg/m²

5

		SGOT (AST)	(1.3mg/m² 2)
	$\leq 1.0x$ ULN	$> ULN$	
	$> 1.0x$ 1.5x ULN		

	> 1.5x 3x ULN		
	> 3x ULN		0.7mg/m ² 0.5mg/m ² 1.0mg/m ²
: SGOT = AST = ULN =			

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
	115 (35%)	97 (43%)
	87 (26%)	74 (32%)
	62 (19%)	55 (24%)
	24 (7%)	15 (7%)
	15 (5%)	11 (5%)
	2 (<1%)	6 (3%)
	1 (<1%)	1 (<1%)
	4 (1%)	2 (<1%)
	9 (3%)	17 (7%)
	6 (2%)	2 (<1%)
	5 (2%)	4 (2%)
	7 (2%)	8 (4%)
	6 (2%)	3 (1%)
b	1 (<1%)	-
	1 (<1%)	-
	1 (<1%)	-
	3 (<1%)	1 (<1%)
	1 (<1%)	1 (<1%)
	9 (3%)	25 (11%)
	14 (4%)	7 (3%)

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
	140 (42%)	97 (43%)
	190 (57%)	116 (51%)
	190 (57%)	145 (64%)
	117 (35%)	82 (36%)
	80 (24%)	48 (21%)
	32 (10%)	30 (13%)
	25 (8%)	19 (8%)
	10 (3%)	1 (<1%)
	2 (<1%)	4 (2%)
	14 (4%)	13 (6%)
	24 (7%)	10 (4%)
	4 (1%)	5 (2%)
b	7 (2%)	3 (1%)
	7 (2%)	3 (1%)
	2 (<1%)	1 (<1%)
	3 (<1%)	2 (<1%)
	1 (<1%)	-
	1 (<1%)	-
	3 (<1%)	-
	1 (<1%)	2 (<1%)
	201 (61%)	149 (65%)
-	40 (12%)	44 (19%)
-	140 (42%)	118 (52%)

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
-	12 (4%)	9 (4%)
-	13 (4%)	22 (10%)
	116 (35%)	82 (36%)
	37 (11%)	27 (12%)
	35 (11%)	27 (12%)
	21 (6%)	5 (2%)
	26 (8%)	16 (7%)
	1 (<1%)	1 (<1%)
	1 (<1%)	1 (<1%)
	1 (<1%)	-
	3 (<1%)	2 (<1%)
	2 (<1%) M34101-040 ^c	-
	1 (<1%)	1 (<1%)
	26 (8%)	41 (18%)
	45 (14%)	17 (7%)
	48 (15%)	29 (13%)
^b	21 (6%)	23 (10%)
()	42 (13%)	26 (11%)
	25 (8%)	13 (6%)

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
	26 (8%)	6 (3%)
	4 (1%)	1 (<1%)
	14 (4%)	15 (7%)
	6 (2%)	2 (<1%)
	6 (2%)	3 (1%)
	13 (4%)	14 (6%)
	10 (3%)	6 (3%)
b	9 (3%)	9 (4%)
	7 (2%)	-
	7 (2%)	8 (4%)
ALT	3 (<1%)	10 (4%)
AST	5 (2%)	12 (5%)
	6 (2%)	8 (4%)
GGT	1 (<1%)	4 (2%)
	112 (34%)	99 (43%)
	24 (7%)	42 (18%)
	5 (2%)	16 (7%)
	7 (2%)	4 (2%)
	8 (2%)	18 (8%)
	50 (15%)	59 (26%)

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
	39 (12%)	32 (14%)
	45 (14%)	60 (26%)
()		
	2 (<1%) M34101-040 c	-
d	120 (36%)	84 (37%)
	91 (27%)	53 (23%)
	45 (14%)	48 (21%)
	85 (26%)	63 (28%)
	17 (5%)	29 (13%)
	9 (3%)	1 (<1%)
	8 (2%)	17 (7%)
	4 (1%)	-
	2 (<1%)	-
	2 (<1%)	-
	31 (9%)	32 (14%)
	21 (6%)	21 (9%)
	2 (1%)	3 (1%)
	5 (2%)	4 (2%)

MedDRA		
	M34100-039 (N=331)	M34100-024/025 (N=228 ^a)
	21 (6%)	23 (10%)
	70 (21%)	39 (17%)
	65 (20%)	50 (22%)
	21 (6%)	18 (8%)
	4 (1%)	9 (4%)
	4 (1%)	14 (6%)
	3 (<1%)	2 (<1%)
	61 (18%)	47 (21%)
	7 (2%)	5 (2%)
	20 (6%)	27 (12%)
/	14 (4%)	8 (4%)
	6 (2%)	7 (3%)
^b	1 (<1%)	-
^a 228	1.3mg/m ²	
^b		
^c	1.3mg/m ²	4
	M34101-039	
^d	MedDRA HLT	()

III

1.3mg/m²

222

7

III

10%

	(N=74)			(N=147)		
MedDRA	, n (%)		, n (%)		, n (%)	
	n (%)	3	≥ 4	n (%)	3	≥ 4
	26(35)	6(8)	0	53(36)	14(10)	4(3)
	16(22)	4(5)	1 (1)	29(20)	9 (6)	0
	20(27)	10(14)	3 (4)	42(29)	22(15)	4(3)
	27(36)	8(11)	6 (8)	52(35)	12(8)	7(5)
	8 (11)	0	0	5 (3)	1 (1)	0
	8 (11)	0	0	3 (2)	0	0
	11 (15)	1 (1)	0	21 (14)	1 (1)	0
	27(36)	3 (4)	1 (1)	35(24)	2 (1)	1(1)
	14(19)	0	0	27(18)	0	0
	12(16)	0	1 (1)	17(12)	3 (2)	0
	14(19)	4 (5)	0	23(16)	3(2)	0

	15(20)	3 (4)	0	17(12)	3(2)	0
	12(16)	0	0	28(19)	0	0
	7(9)	1(1)	0	16(11)	2(1)	0
	7(9)	0	0	14(10)	0	0
	8 (11)	2 (3)	0	8 (5)	1 (1)	0
	8(11)	0	0	5(3)	0	0
	17(23)	7 (9)	0	35(24)	5(3)	0
	36(49)	10 (14)	1 (1)	51(35)	7(5)	0
	8(11)	0	0	18(12)	0	0
	9(12)	2 (3)	0	11(7)	2(1)	0

10%

8

III

>10%

--	--	--

	(N=74)			(N=147)		
MedDRA	n (%)			n (%)		
MedDRA	TEAE	G ≥ 3	Disc	TEAE	G ≥ 3	Disc
TEAE	73(99)	52(70)	20(27)	140(95)	84(57)	33(22)
()	27(36)	4(5)	1(1)	35 (24)	3(2)	1(1)
()	14(19)	0	0	9(6)	1(1)	0
	29(39)	7 (9)	1 (1)	40 (27)	6 (4)	2 (1)
	19(26)	2(3)	0	20(14)	0	0
^a	39(53)	12(16)	10(14)	56 (38)	9(6)	9(6)
^a	TEAE G ≥ 3 ≥ 3 Disc					

3

13%(57% 70%) 5%(22%

27%) (24% 36%) (6%

19%) (27% 39%) (14%

26%) () (38% 53%)

12%~15% 3

10%(6% 16%)

8%

6%

2 (1%)

1

1

6 ()

10%

(MMY-2036)

9 ≥ 10%

(MMY-2036)

	(MMY-2036)		
		3	≥4
	130		
n (%)	126 (97)		
MedDRA			
	71 (55)	19 (15)	14 (11)
	48 (37)	5 (4)	1 (1)
	23 (18)	9 (7)	0
	20 (15)	5 (4)	0
	45 (35)	9 (7)	0
	36 (28)	0	0
	14 (11)	0	0
	31 (24)	2 (2)	0
	29 (22)	6 (5)	0
	21 (16)	0	0

	(MMY-2036)		
		3	≥4
	15 (12)	0	0
	17 (13)	3 (2)	1 (1)
	13 (10)	1 (1)	0
	22 (17)	4 (3)	0
	13 (10)	3 (2)	0
	15 (12)	1 (1)	0
	14 (11)	1 (1)	0
<p>MedDRA 14.1</p> <p>MMY-2036</p> <p>NCI CTCAE</p> <p>3</p>			

(MMY-2045)

(DOXIL-MMY-3001)

10%

10 (**10%**)

(DOXIL-MMY-3001 MMY-2045

)

			+		+	
	n (%)	≥ 3 n (%)	n (%)	≥ 3 n (%)	n (%)	≥ 3 n (%)
		318		318		163
	301 (95)		314 (99)		154 (94)	
MedDRA						
	124 (39)	16 (5)	145 (46)	23 (7)	51 (31)	7 (4)
	126 (40)	3 (1)	154 (48)	8 (3)	20 (12)	1 (1)
	98 (31)	2 (1)	99 (31)	3 (1)	50 (31)	9 (6)
	69 (22)	3 (1)	101 (32)	13 (4)	11 (7)	2 (1)
	11 (3)	1 (< 1)	56 (18)	7 (2)	1 (1)	0
	24 (8)	4 (1)	34 (11)	2 (1)	11 (7)	1 (1)
^a	143 (45)	35 (11)	133 (42)	22 (7)	79 (48)	23 (14)
	63 (20)	14 (4)	54 (17)	9 (3)	26 (16)	4 (2)
	56 (18)	0	59 (19)	3 (1)	9 (6)	0
	31 (10)	0	41 (13)	1 (< 1)	22 (13)	2 (1)
	26 (8)	4 (1)	32 (10)	4 (1)	14 (9)	0
	88 (28)	8 (3)	115 (36)	22 (7)	37 (23)	2 (1)
	71 (22)	4 (1)	100 (31)	4 (1)	21 (13)	4 (2)
	56 (18)	12 (4)	71 (22)	19 (6)	33 (20)	2 (1)
	27 (8)	1 (< 1)	32 (10)	1 (< 1)	43 (26)	3 (2)

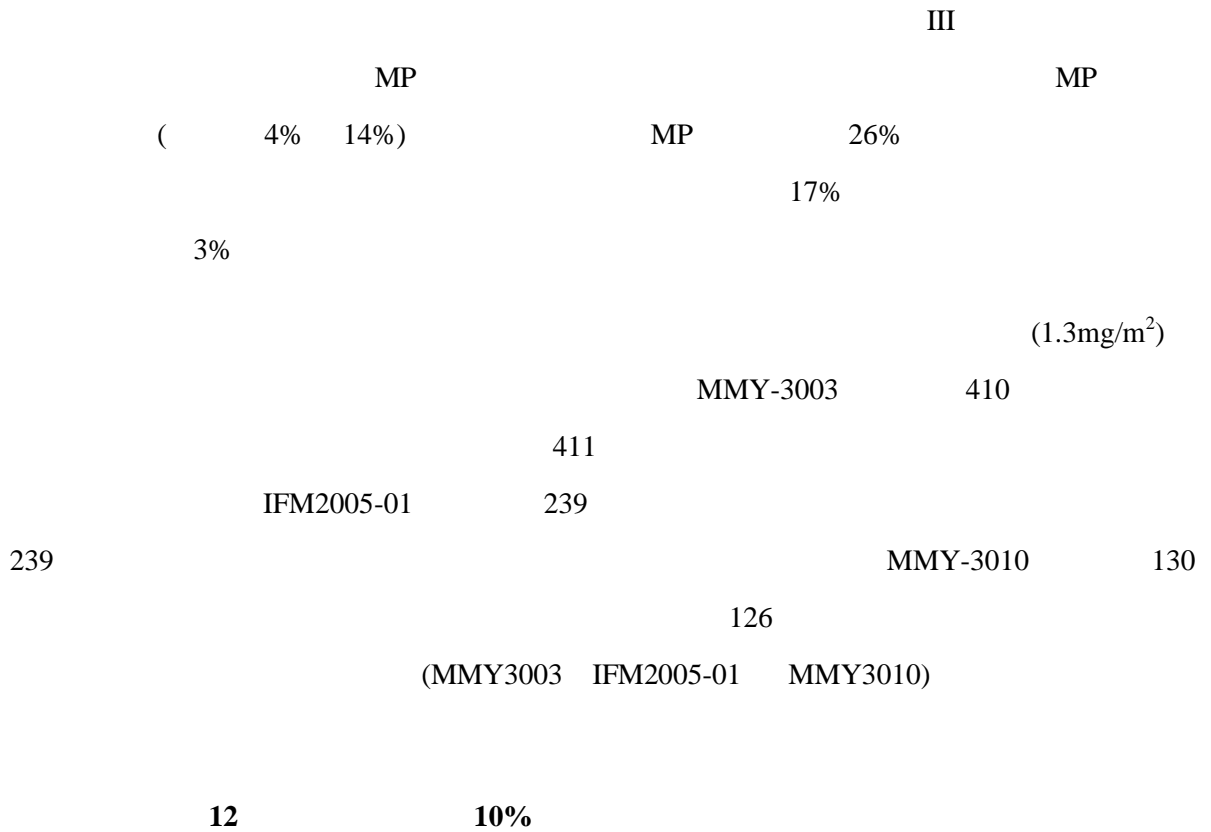
			+		+	
	n (%)	≥ 3	n (%)	≥ 3	n (%)	≥ 3
		n (%)		n (%)		n (%)
	89 (28)	53 (17)	106 (33)	76 (24)	61 (37)	28 (17)
	71 (22)	51 (16)	114 (36)	102 (32)	12 (7)	6 (4)
	68 (21)	30 (9)	80 (25)	29 (9)	35 (21)	16 (10)
	29 (9)	6 (2)	34 (11)	6 (2)	16 (10)	1 (1)
	21 (7)	3 (1)	31 (10)	1 (< 1)	18 (11)	1 (1)
	33 (10)	3 (1)	33 (10)	2 (1)	15 (9)	3 (2)
	39 (12)	6 (2)	39 (12)	4 (1)	25 (15)	2 (1)
	48 (15)	8 (3)	34 (11)	1 (< 1)	16 (10)	2 (1)
	27 (8)	5 (2)	34 (11)	1 (< 1)	14 (9)	1 (1)
	38 (12)	0	58 (18)	0	26 (16)	1 (1)
	28 (9)	10 (3)	34 (11)	3 (1)	13 (8)	3 (2)
	50 (16)	1 (< 1)	83 (26)	8 (3)	9 (6)	0
	29 (9)	3 (1)	48 (15)	2 (1)	8 (5)	0
	12 (4)	0	37 (12)	0	3 (2)	0
	43 (14)	2 (1)	35 (11)	0	18 (11)	1 (1)

				+		+
	n (%)	≥3 n (%)	n (%)	≥3 n (%)	n (%)	≥3 n (%)
^a	MedDRA 14.1					
	MMY-2045			NCI CTCAE		

III 340
 (1.3 mg/m²) MP [(9mg/m²) (60mg/m²)]
11 MP 10%

	MP (n=340)			MP (n=337)		
MedDRA	n (%)		n (%)		n (%)	
	n (%)	3	≥4	n (%)	3	≥4
	164 (48)	60 (18)	57 (17)	140 (42)	48 (14)	39 (12)
	160 (47)	101 (30)	33 (10)	143 (42)	77 (23)	42 (12)
	109 (32)	41 (12)	4 (1)	156 (46)	61 (18)	18 (5)
	108 (32)	64 (19)	8 (2)	93 (28)	53 (16)	11 (3)
	78 (23)	46 (14)	17 (5)	51 (15)	26 (8)	7 (2)
	134 (39)	10 (3)	0	70 (21)	1 (<1)	0
	119 (35)	19 (6)	2 (1)	20 (6)	1 (<1)	0
	87 (26)	13 (4)	0	41 (12)	2 (1)	0
	77 (23)	2 (1)	0	14 (4)	0	0
	34 (10)	1 (<1)	0	20 (6)	0	0

MedDRA	MP (n=340)			MP (n=337)		
	n (%)	n (%)		n (%)	n (%)	
	n (%)	3	≥4	n (%)	3	≥4
	156 (46)	42 (12)	2 (1)	4 (1)	0	0
	117 (34)	27 (8)	2 (1)	1 (<1)	0	0
	42 (12)	6 (2)	0	4 (1)	0	0
	85 (25)	19 (6)	2 (1)	48 (14)	4 (1)	0
	54 (16)	18 (5)	0	23 (7)	3 (1)	0
	53 (16)	4 (1)	0	19 (6)	1 (<1)	1 (<1)
	39 (11)	11 (3)	0	9 (3)	4 (1)	0
	64 (19)	6 (2)	0	19 (6)	0	0
	38 (11)	2 (1)	0	7 (2)	0	0
	35 (10)	1 (<1)	0	21 (6)	0	0



	(N=779)			(N=776)		
MedDRA		n (%)			n (%)	
	n (%)	2	≥ 3	n (%)	2	≥ 3
	715 (92)			679 (88)		
	242 (31)	89 (11)	10 (1)	214 (28)	67 (9)	8 (1)
	215 (28)	71 (9)	22 (3)	206 (27)	77 (10)	9 (1)
	133 (17)	29 (4)	23 (3)	110 (14)	26 (3)	6 (1)
	95 (12)	30 (4)	18 (2)	87 (11)	35 (5)	6 (1)
	147 (19)	53 (7)	20 (3)	54 (7)	11 (1)	4 (1)
	101 (13)	24 (3)	11 (1)	80 (10)	15 (2)	2 (<1)
	101 (13)	41 (5)	19 (2)	55 (7)	13 (2)	1 (<1)
	64 (8)	23 (3)	4 (1)	76 (10)	23 (3)	1 (<1)
	158 (20)	50 (6)	21 (3)	161 (21)	68 (9)	21 (3)
	153 (20)	56 (7)	25 (3)	159 (20)	40 (5)	36 (5)
	110 (14)	33 (4)	16 (2)	91 (12)	33 (4)	10 (1)
	239 (31)	54 (7)	63 (8)	171 (22)	27 (3)	27 (3)
	211 (27)	95 (12)	55 (7)	222 (29)	108 (14)	77 (10)
	196 (25)	51 (7)	109 (14)	206 (27)	53 (7)	120 (15)
	86 (11)	50 (6)	24 (3)	18 (2)	9 (1)	5 (1)
	122 (16)	46 (6)	26 (3)	138 (18)	46 (6)	31 (4)
	100 (13)	2 (<1)	29 (4)	82 (11)	6 (1)	12 (2)
	96 (12)	32 (4)	6 (1)	82 (11)	30 (4)	6 (1)
MedDRA 13.1						

MP

21

MP

13

	MP		MP	
MedDRA	n=21	n=337	n=20	n=340
n(%)	21(100)	326(97)	20(100)	338(99)
	18(86)	259(77)	20(100)	279(82)
	3(14)	48(14)	3(15)	59(17)
	0	0	0	1(<1)
	0	18(5)	0	38(11)
	0	2(1)	1(5)	10(3)
	0	28(8)	1(5)	73(21)
	9(43)	185(55)	18(90)	262(77)
	8(38)	199(59)	16(80)	239(70)
	2(10)	27(8)	5(25)	31(9)
	1(5)	6(2)	0	5(1)
	10(48)	182(54)	13(65)	234(69)
	0	40(12)	0	40(12)
	2(10)	21(6)	1(5)	32(9)
	6(29)	124(37)	10(50)	159(47)
	5(24)	151(45)	7(35)	172(51)
()	0	4(1)	0	7(2)
	4(19)	122(36)	13(65)	253(74)

	4(19)	76(23)	0	112(33)
	4(19)	62(18)	2(10)	54(16)
	1(5)	15(4)	1(5)	21(6)
	5(24)	123(36)	8(40)	133(39)
	1(5)	80(24)	8(40)	140(41)
	0	3(1)	0	7(2)
	1(5)	69(20)	6(30)	112(33)

II (M34103-053) 155
1.3mg/m²

14 240
(1.3 mg/m²) (375 mg/m²) (750 mg/m²)
(50 mg/m²) (100 mg/m²)(VcR-CAP)
≥3 (VcR-CAP 4 R-CHOP 3) VcR-CAP
≥3
VcR-CAP 31% R-CHOP 23%
(VcR-CAP 8% R-CHOP
5%)
VcR-CAP R-CHOP 4.6% 0.8%

14 VcR-CAP R-CHOP
(5%) 3 4

(LYM-3002 N=482)

	VcR-CAP			R-CHOP		
	n=240			n=242		
		3	≥4		3	≥4
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	209 (87)	32 (13)	168 (70)	172 (71)	31 (13)	125 (52)
	116 (48)	34 (14)	69 (29)	87 (36)	39 (16)	27 (11)
	106 (44)	27 (11)	4 (2)	71 (29)	23 (10)	4 (2)
	172 (72)	59 (25)	76 (32)	42 (17)	9 (4)	3 (1)
	41 (17)	24 (10)	12 (5)	33 (14)	17 (7)	15 (6)
	68 (28)	25 (10)	36 (15)	28 (12)	15 (6)	2 (1)
	53 (22)	11 (5)	1 (< 1)	45 (19)	6 (3)	0
	18 (8)	4 (2)	0	18 (7)	2 (1)	0
	14 (6)	3 (1)	0	13 (5)	0	0
	14 (6)	2 (1)	0	11 (5)	0	0
	25 (10)	9 (4)	0	1 (< 1)	0	0
	43 (18)	11 (5)	1 (< 1)	38 (16)	5 (2)	0
	48 (20)	7 (3)	0	23 (10)	5 (2)	0
	29 (12)	4 (2)	1 (< 1)	18 (7)	1 (< 1)	0
	16 (7)	1 (< 1)	0	13 (5)	0	0
	54 (23)	1 (< 1)	0	28 (12)	0	0
	42 (18)	1 (< 1)	0	22 (9)	2 (1)	0

	VcR-CAP			R-CHOP		
	n=240			n=242		
		3	≥4		3	≥4
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	20 (8)	2 (1)	0	19 (8)	0	1 (< 1)
	59 (25)	11 (5)	0	11 (5)	3 (1)	1 (< 1)
	24 (10)	1 (< 1)	0	8 (3)	0	0
	13 (5)	0	0	4 (2)	0	0
	20 (8)	8 (3)	5 (2)	11 (5)	5 (2)	3 (1)
	31 (13)	1 (< 1)	1 (< 1)	33 (14)	4 (2)	0
	10 (4)	1 (< 1)	0	17 (7)	10 (4)	0
	36 (15)	2 (1)	0	15 (6)	1 (< 1)	0
	11 (5)	3 (1)	1 (< 1)	6 (2)	1 (< 1)	0
	15 (6)	1 (< 1)	0	3 (1)	0	0
	16 (7)	1 (< 1)	0	8 (3)	0	0
R-CHOP= VcR-CAP=						

$(\geq 1/10)$ $(\geq 1/100)$ $< 1/10$ $(\geq 1/1000)$ $< 1/100$ $(\geq 1/10000)$
 $< 1/1000$ $(< 1/10000)$)

15:

	/
	*
	-
	(Sweet's syndrome)
*	John Cunningham(JC)

(CBC)

•

(PN)

()

(≥ 3)

	III	2	2
24%	41% (p=0.0124)	3	3
6%	16% (p=0.0264)(8)		

III

51%	2	2	
	II	2	3
73%			

•

	II	III	(
)	11%	12%	

/

•

/

III

15%

13%

(

)

5%

4%

QT

•

•

(ARDS)

2

(2g/m²)

ARDS

•

(PRES)

PRES PRES

MRI()

PRES

PRES

•

<25000/μL

40%

16

(≥3)

5% 4%

16

III

* (N=331)**	<10000/μL (%)	10000/μL 25000/μL (%)
≥75000/μL	8(3%)	36 (12%)
≥50000/μL <75000/μL	2(14%)	11 (79%)
≥10000/μL <50000/μL	1(14%)	5 (71%)
* 50000/μL		
**1		

(VcR-CAP)

VcR-CAP ≥4

32%

(R-CHOP)

2% VcR-CAP R-CHOP 3

1.7%(4)

1.2%(3)

VcR-CAP

(CNS)

R-CHOP 1 CNS

VcR-CAP R-CHOP

23% 3%

VcR-CAP R-CHOP ≥4

70% 52% VcR-

CAP R-CHOP ≥4

5% 6%

78% 61%

/

•

•

•

•

0.05mg/kg(0.6mg/m²)

1.3mg/m² ()

0.075mg/kg(0.5mg/m²)

0.05mg/kg(0.6mg/m²)

1.3mg/m² (

)

		669		245(37%)		≥65
125(38%)		120(36%)		≥65		
		(5.5 4.3		8.0
4.9)		≥65		40%(n=46)		(CR+PR)
		18%(n=21)	≤50	51~64 ≥65		3 4
	64%	78%	75%			
			≥65			

				P450(CYP)	1A2	2C9	2C19	2D6
3A4		CYP2D6		(7%)				
CYP2D6				(CYP3A4)			
	12			AUC		35%		
CYP3A4	()						
				(CYP2C19)			
	17							
				(CYP3A4)			
6		AUC		45%				CYP3A4

CYP3A4

CYP3A4

7

21

AUC

17%

(

)

(mg/m²

2~3)

QT

3.0mg/m²

(

2)

1

12~14

2

(

/

)

202

(M34100-025)

6 17

1.3mg/m²

2

2

10 (21 1

)

8

	202
()	59(34 84)
	60% 40%
	81% 10% 8%
≤70	20%
<100g/L	44%
<75×10 ⁹ /L	21%
(%) IgG / IgA /	60% 24% 14%
β ₂ - (mg/L)	3.5
(ml/min)	73.9
	35%
13	15%
()	4.0
VAD	99%
VBMCP	92%
VAD	81%
	83%
	98%
	92%
	66%
	64%
	44%
*	

18

Bladé

			5% M-	100%
(IF)	18		SWOG	SWOG
M	≥75%	M-	≥90%	188
		5		9
98%		1.3mg/m ²	28%	
33%			63%	
		2		6

38 (30~127)

16 (1~18)

18

()N=188	N(%)	(95 CI)
(Bladé)(CR+PR)	52(27.7%)	(21 35)
(CR) ¹	5(2.7%)	(1 6)
(PR) ²	47(25%)	(19 32)
(SWOG) ³	33(17.6%)	(12 24)
Kaplan-Meier (95%CI)	365	(224 NE)
1	5% M- 100%	(IF)
2	6 M ≥50% M- ≥90%	
3 (SWOG)	6 M ≥75% M- ≥90%	

50%

13

54 (M34100-24) 1.0
 mg/m² 1.3 mg/m² 2 2 1
 (CR+PR) 30%(8/27) 38%(10/26)

(1 1) ()
 6 6) β₂-
 (≤2.5mg/L >2.5mg/L)

19

19 III

	N=333	N=336
()	62.0 (33, 84)	61.0 (27, 86)
	56% / 44%	60% / 40%
	90% / 6% / 4%	88% / 7% / 5%
≤70	13%	17%
<100g/L	32%	28%
<75×10 ⁹ /L	6%	4%
(%) IgG / IgA /	60% / 23% / 12%	59% / 24% / 13%
β ₂ - (mg/L)	3.7	3.6
(g/L)	39.0	39.0
≤30ml/min [n (%)]	17 (5%)	11 (3%)
()	3.5	3.1
	2	2
	40%	35%
	60%	65%
	(N=333)	(N=336)
VAD	98%	99%
VAD	77%	76%
VBMCP	91%	92%
	48%	50%
	74%	72%
/	67%	68%
	3%	2%

8 (3) 3 (5)
 3 1.3mg/m² 2 2 (1
 4 8 11) 10 (12 21) 5
 1.3mg/m² 1 4 (1 8 15 22) 13 ()
 23 35)

4 (5) 5 (4)
 5 1 4 9 12 17 20
 40mg/ 15 (21 35) 4 1 4
 40mg/ 24 (5 28)

(n=534) 8.3

8 (3) 34% 1
 11 13% 1
 22 1 44 4 (5) 40% 1
 9 6% 1

III 20
 (EBMT) (CR) 5% M
 100% (IF⁻) (PR) 6
 M ≥50% M- ≥90%
 (nCR) M- 100%
 M- (IF⁺)

20 III

	n=333	n=336	n=132	n=119	n=200	n=217
n (%)	147(44)	196(58)	55(42)	64(54)	92(46)	132(61)
^a (95% CI)	6.2 (4.9, 6.9)	3.5 (2.9, 4.2)	7.0 (6.2, 8.8)	5.6 (3.4, 6.3)	4.9 (4.2, 6.3)	2.9 (2.8, 3.5)
^b	0.55		0.55		0.54	

(95% CI)	(0.44, 0.69)		(0.38, 0.81)		(0.41, 0.72)	
p ^c	< 0.0001		0.0019		<0.0001	
() n (%)	51(15)	84(25)	12(9)	24(20)	39(20)	60(28)
^b	0.57		0.39		0.65	
(95% CI)	(0.40, 0.81)		(0.19, 0.81)		(0.43, 0.97)	
p ^{c,d}	<0.05		<0.05		<0.05	
^e n = 627	n=315	n=312	n=128	n=110	n=187	n=202
CR ^f n (%)	20(6)	2(<1)	8(6)	2(2)	12(6)	0(0)
PR ^f n(%)	101(32)	54(17)	49(38)	27(25)	52(28)	27(13)
nCR ^{f,g} n(%)	21(7)	3(<1)	8(6)	2(2)	13(7)	1(<1)
CR + PR ^f n (%)	121 (38)	56 (18)	57(45)	29(26)	64(34)	27(13)
p ^h	<0.0001		0.0035		<0.0001	
n						
CR ^f	9.9	NE ⁱ	9.9	NE	6.3	NA ^j
nCR ^f	11.5	9.2	NE	NE	11.5	9.2
CR + PR ^f	8.0	5.6	8.1	6.2	7.8	4.1
^a Kaplan-Meier						
^b	COX				1	
^c p	log-rank					
^d	p					
^e						
^f EBMT	nCR	EBMT	CR	IF	EBMT	nCR
	PR					
^g 2	IF					

h	(CR + PR) p	Cochran-Mantel-Haenszel
i		
j		

682 (1:1) III
 [MMY-3002 (VISTA)] MP (1.3mg/m²) MP
 (TTP) 9 (

54)

21

21 VISTA

	MP N=344	MP N=338
()	71.0 (57, 90)	71.0 (48, 91)
/	51% / 49%	49% / 51%
/ / /	88% / 10% / 1% / 1%	87% / 11% / 2% / 0%
≤70	35%	33%
<100 g/L	37%	36%
<75 × 10 ⁹ /L	<1%	1%
(%) IgG/IgA/	64% / 24% / 8%	62% / 26% / 8%
β ₂ - (mg/L)	4.2	4.3
(g/L)	33.0	33.0
≤30ml/min [n (%)]	20 (6%)	16 (5%)

16.3

MP MP 60.1 MP
 (HR=0.695 p=0.00043) MP 43.1
 MP 56.4 22

22 VISTA

	MP n=344	MP n=338
n (%)	101 (29)	152 (45)
^a (95% CI)	20.7 (17.6, 24.7)	15.0 (14.1, 17.9)
^b (95% CI)	0.54 (0.42, 0.70)	
p ^c	0.000002	
n (%)	135 (39)	190 (56)
^a (95% CI)	18.3 (16.6, 21.7)	14.0 (11.1, 15.0)
^b (95% CI)	0.61 (0.49, 0.76)	
p ^c	0.00001	
^h () n (%)	176 (51.2)	211 (62.4)
^a (95% CI)	56.4 (52.8, 60.9)	43.1 (35.3, 48.3)
^b (95% CI)	0.695 (0.567, 0.852)	
p ^c	0.00043	
^e n = 668	n=337	n=331
CR ^f n (%)	102 (30)	12 (4)
PR ^f n (%)	136 (40)	103 (31)
nCR n (%)	5 (1)	0

CR + PR ^f n (%)	238 (71)	115 (35)
p ^d	<10 ⁻¹⁰	
M g n=667	n=336	n=331
>=90% n (%)	151 (45)	34 (10)
CR PR		
	1.4	4.2
a		
CR ^f	24.0	12.8
CR + PR ^f	19.9	13.1
n (%)	224 (65.1)	260 (76.9)
a (95% CI)	27.0 (24.7, 31.1)	19.2 (17.0, 21.0)
b (95% CI)	0.557 (0.462, 0.671)	
p ^c	(< 0.000001)	

	60.1	16.3	
a	Kaplan-Meier		
b	(β_2 -1)	MP	COX
c	p	(β_2 -)	log-rank
d	(CR + PR) p		Cochran-Mantel-Haenszel
e			
f	EBMT		
g			
h	60.1		
	NE:		

MP 21 MP 23 41 20

23 VISTA

	MP n=21	MP n=20
n (%)	14(67)	9(45)
(95%CI)	11.1 (8.4, 15.7)	14.8 (7.2, NE)
(95%CI)	0.468 (0.183 1.199)	
p	0.10676	

n (%)	19(90)	12(60)
(95%CI)	9.7 (7.3, 12.6)	9.6 (6.2, NE)
(95%CI)	0.604 (0.279 1.309)	
p	0.1975	
n (%)	9(43)	4(20)
(95%CI)	0.385 (0.117 1.259)	
p	0.10135	
CR n (%)	0 (0)	8(40)
PR n (%)	5(24)	5(25)
CR + PR n (%)	5(24)	13(65)
	6.1(1.4 27.2)	
p	0.01112	
NE	16.3	

II

[M34103-053 (PINNACLE)]

155
65 (42~89) 81% 92%
75% 77% IV 91%
37%
1.3mg/m² 2 2 (1 4 8

11 10) 4(
 1~17) 8 24
 (International Workshop Response Criteria, IWRC) CT
 13 1 Kaplan
 Meier 69% 1- Kaplan Meier 94% CR
 CRu 1- Kaplan Meier 100%

24 II

^a (N = 141)	N (%)	95% CI
(IWRC) (CR + CRu + PR)	47 (33)	(26, 42)
(CR + CRu)	11 (8)	(4, 14)
CR	9 (6)	(3, 12)
CRu	2 (1)	(0, 5)

(VcR-CAP) (R-CHOP)

(PFS)

VcR-CAP 1 4 8 11 (1.3 mg/m²) 12-21

21 1 (375 mg/m²) (750 mg/m²) (50

mg/m²) 1-5 (100 mg/m²) 6 2

66 74% 66% 32% 69% /

MCL 54% (IPI) 3() 76%

IV R-CHOP VcR-CAP 6

17% 14% 2 R-CHOP (83%) VcR-CAP (84%)

≥6

(IRC)

(TTP) (TNT) (TFI) (ORR)

(CR/CRu) (OS)

(IWRC)

PFS TTP TNT TFI VcR-CAP

) R-CHOP (14.4) 40 VcR-CAP PFS (24.7

(42.1) R-CHOP (18) 2 59%([HR]=0.63 p<0.001) VcR-CAP

R-CHOP 21.4 40 OS (R-CHOP

56.3 VcR-CAP) VcR-CAP (HR=0.80 p=0.173)

VcR-CAP R-CHOP VcR-CAP 4

53.9% 64.4% 25 40 OS

	VcR-CAP	R-CHOP	
n ITT	243	244	
IRC^a			
n %	133 (54.7)	165 (67.6)	HR ^d (95% CI)=0.63 (0.50;0.79)
^c 95% CI	24.7 (19.8; 31.8)	14.4 (12; 16.9)	p ^e < 0.001
b			
n %	128 (52.7)	179 (73.4)	HR ^d (95% CI)=0.51 (0.41; 0.65)
^c 95% CI	30.7 (25.1; 37.3)	16.1 (14.0; 18.4)	p ^e < 0.001
a			
n %	114 (46.9)	148 (60.7)	HR ^d (95% CI)=0.58 (0.45;0.74)
^c 95% CI	30.5 (22.9; 40.9)	16.1(13.7;18.1)	p ^e < 0.001
n %	94 (38.7)	145 (59.4)	HR ^d (95% CI)=0.50 (0.38;0.65)
^c 95% CI	44.5 (38.8; NE)	24.8 (22.1; 27.5)	p ^e < 0.001
n	240	242	
n %	93 (38.8)	145 (59.9)	HR ^d (95% CI)=0.50 (0.38; 0.65)
^c 95% CI	40.6 (33.6; NE)	20.5 (17.8; 22.8)	p ^e < 0.001
82			
n ITT	243	244	
n %	103 (42.4)	138 (56.6)	HR ^d (95% CI)=0.66 (0.51; 0.85)
^c 95% CI	90.7 (71.4; NE)	55.7 (47.2; 68.9)	p ^e =0.001
n	229	228	
n % CR+CRu ^h	122 (53.3)	95(41.7)	OR ^f (95% CI)=1.688 (1.148; 2.481)
CR+CRu+PR ⁱ n %	211 (92.1)	204 (89.5)	OR ^f (95% CI)=1.428 (0.749; 2.722)
			p ^g =0.275
CR+CRu^j			
n =	122	95	
^c 95% CI	42.1 (30.7; 49.1)	18.0 (14.0; 23.4)	
CR+CRu+PR^k			
n	211	204	
^c 95% CI	36.5 (26.7; 46.7)	15.1 (12.5; 17.0)	

40

a. IRC

- b.
c. Kaplan-Meier
d. IPI Cox 1 VcR-
CAP
e. IPI Log-rank test
f. Mantel-Haenszel IPI
OR >1 VcR-CAP
g. p Cochran Mantel-Haenszel IPI
h. IRC CR+CRu LDH
i. IRC CR+CRu+PR LDH
j. IRC CR+CRu LDH PD PD
k. IRC CR+CRu+PR PD PD
IRC= IPI= LDH= CR= CRu =
PR= CI= HR= OR = ITT=
PD=

3 (MMY-3021)
222 2:1
8 1.3 mg/m² 4
(CR) 20 mg
2 <50,000/μL 218
(1 1)
(ISS) (β₂- I II III) 26

26 3 (MMY-3021)

	N=74	N=148
()	64.5 (38,86)	64.5 (42,88)
/	64% / 36%	50% / 50%
/	96% / 4%	97% / 3%
Karnofsky ≤70	16%	22%

(%) IgG/IgA/	72% / 19% / 8%	65% / 26% / 8%
ISS ^a I/II/III(%)	27/41/32	27/41/32
β_2 - (mg/L)	4.25	4.20
(g/L)	3.60	3.55
≤ 30 mL/min[n(%)]	2 (3%)	5 (3%)
()	2.93	2.68
1	65%	62%
1	35%	38%

^a ISS

(CR+PR) 42%
4
(27)

27

(MMY-3021)

^a	n=73	n=145
4		
ORR (CR+PR)	31 (42)	61 (42)
p ^b	0.00201	
CR n (%)	6(8)	9(6)
PR n (%)	25(34)	52(36)
nCR n (%)	4(5)	9(6)
8		
ORR (CR+PR)	38(52)	76(52)
p ^b	0.0001	
CR n (%)	9 (12)	15 (10)
PR n (%)	29(40)	61(42)

nCR n (%)	7(10)	14(10)
^c	n=74	n=148
	9.4	10.4
(95% CI)	(7.6,10.6)	(8.5,11.7)
(95% CI) ^d	0.839 (0.564,1.249)	
p ^e	0.38657	
	8.0	10.2
(95% CI)	(6.7,9.8)	(8.1,10.8)
(95% CI) ^d	0.824 (0.574,1.183)	
p ^e	0.295	
1 (%) ^f	76.7	72.6
(95% CI)	(64.1,85.4)	(63.1,80.0)

a			
b	p		60%
c	222	221	
d		Cox	ISS
e		ISS	
f	11.8		

26S

26S

-

26S

1mg/m² 1.3mg/m² (n=12) 20S
 () 5 1 mg/m² 1.3mg/m² 20S
 1mg/m² 1.3mg/m² 70%
 84% 73% 83%

(2 2)

2
 12 14 1.2mg/m²

Ames ()

1.2mg/m² ≥0.3mg/m²(1/4) 6

11 1.0mg/m² 1.3mg/m² (1)
 57 112ng/mL
 67 106ng/mL (1.0mg/m²) 89 120ng/mL(1.3mg/m²)
 40~193

		1.0mg/m ²	1.3mg/m ²		102	112L/h
1.0mg/m ²	1.3mg/m ²			15~32 L/h		
III	PK/PD				1.3mg/m ²	
(n = 14		n = 17)			(AUC _{last})
		(20.4ng/mL)		(223ng/mL)		AUC _{last}
0.99	90%		80.18% ~ 122.80%			

		1.0mg/m ²	1.3mg/m ²
		489~1884L/m ²	
100~1000ng/mL			83%

		(cDNA)	P450
		P450	3A4 2C19 1A2
2D6	2C9		2
			26S
			8
10	30		

104	(2~16)	2	1.3mg/m ²
	(%CV)	7.79(25%)L/hr/m ²	834(39%)L/m ²
100(44%)			

60

0.5 1.3mg/m²

AUC

AUC

60%

(CrCL)

(CrCL ≥60 mL/ /1.73 m² n=12)

(CrCL=40 59 mL/ /1.73 m² n=10)

(CrCL=20 39 mL/ /1.73 m² n=9)

(CrCL < 20 mL/ /1.73 m² n=3)

8

0.7 1.3

mg/m²

2

(

AUC

)

30 °C

1

24

JX20180195

3.5mg H20171086

3.5mg

J20171067

Janssen-Cilag International N.V.

Turnhoutseweg 30, B-2340 Beerse, Belgium

BSP Pharmaceuticals S.p.A.

Via Appia Km 65, 561, 04013 Latina, Italy

19

710304

400 888 9988

(029) 82576616

<http://www.xian-janssen.com.cn>

25°C

8

8

8

30°C

5%

/

0.9%

	1mg	3.5mg	3.5mg
() (0.9%)	1.0mL	3.5mL	1.4 mL
(mg/mL)	1.0mg/mL	1.0mg/mL	2.5mg/mL