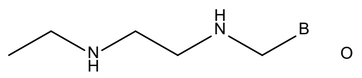
®

2017 11 21
2018 03 09
2018 06 28
2019 05 24
2020 11 19

Bortezomib for Injection
Zhusheyong Pengtizuomi

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



2 3 ADL ***	0.7 mg/m^2 1
4	
* NCI CTCAE v 4.0 ** ADL *** ADL	

6 6

2

3 1 1 375 mg/m^2 750 mg/m^2 50 mg/m^2 1 2 3 4 5 100 mg/m^2

1

- ≥ 100 × 10^9/L ANC ≥ 1.5 × 10^9/L
- ≥ 8 g/dL ≥ 4.96 mmol/L
- 1

3 3

• ≥3 4 7 10 × 10^9/L • 1 25 × 10^9/L ANC 0.75 × 10^9/L	2 ANC ≥ 0.75 × 10^9/L ≥ 25 × 10^9/L • • ANC ≥ 0.75 × 10^9/L ≥ 25 × 10^9/L 1.3 mg/m^2 1 mg/m^2 1 mg/m^2 0.7 mg/m^2
≥3	2 1.3 mg/m^2 1 mg/m^2 1 mg/m^2 0.7 mg/m^2 / 3 /

0.7 mg/m^2 1.0 mg/m^2
0.5 mg/m^2

		SGOT (AST)	1.3 mg/m^2 2
	≤ 1.0x ULN	> ULN	
	> 1.0x 1.5x ULN		
	> 1.5x 3x ULN		0.7 mg/m^2 1.0 mg/m^2 0.5 mg/m^2
	> 3x ULN		
: SGOT = AST = ULN =			

3-5
0.9%

1 mg/mL 2.5mg/mL

1.3 mg/m^2
III M34101-039 669 1~3
II 202 2
M34100-025 - II
1.0 mg/m^2 1.3 mg/m^2 M34100-024

	-	-
	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%)
	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%)
-	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%)
	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%)
	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%)
	21 (6%)	23 (10%)
	70 (21%)	39 (17%)
	65 (20%)	50 (22%)
	21 (6%)	18 (8%)
	4 (1%)	9 (4%)
	4 (1%)	14 (6%)

	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%

>10%

	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%

MedDRA 14.1
MMY-2036 NCI CTCAE

3

MMY-2045
DOXIL-MMY-3001 10%

10%

	n (%)	≥3 n (%)	n (%)	≥3 n (%)	n (%)	≥3 n (%)
	318		318		163	
	301 (95)		314 (99)		154 (94)	
	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)
	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)

	n (%)	≥3 n (%)	n (%)	≥3 n (%)	n (%)	≥3 n (%)
	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 (%)			n (%)	
	n (%)	3	≥4	n (%)	3	≥4
	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
	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

III
MP MP
4% 14% MP 26%
17% 3%
1.3 mg/m^2
MMY-3003 410
411
IFM2005-01 239 239
MMY-3010 130
126 MMY3003
IFM2005-01 MMY3010

≥ 10%

	(N=779)			(N=776)		
		n (%)			n (%)	
	n (%)	2	≥ 3	n (%)	2	≥ 3

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

≥ 5% ≥

	VcR-CAP n=240			R-CHOP 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
	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

	/
	*
	-
	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 2 g/m^2
ARDS

- PRES
PRES PRES
MRI
PRES PRES

-

- /
11

<25000/μL

40%
16 ≥3
5% 4%

		%	**%**
≥75000/μL	309	8 3%	36 (12%)
≥50000/μL <75000/μL	14	2 14%	11 (79%)
≥10000/μL <50000/μL	7	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%

- /
-
-
-
-

mg/m^2 2~3

QT 3.0 mg/m^2

2 1 12~14

2

/

26S 26S

-

26S

1 mg/m^2 1.3 mg/m^2 n=12 20S

5 1 mg/m^2 1.3 mg/m^2 20S

1 mg/m^2 1.3 mg/m^2 70% 84% 73%

83%

2 2

2

12 14 1.2 mg/m^2

Ames

6

≥0.3 mg/m^2 1/4 1.2 mg/m^2

11 1.0 mg/m^2 1.3 mg/m^2 1
57 112 ng/ml 67
106 ng/ml 1.0 mg/m^2 89 120 ng/ml 1.3 mg/m^2
40~193 1.0mg/m^2
1.3mg/m^2 102 112L/h 1.0 mg/m^2 1.3 mg/m^2
15~32 L/h
III PK/PD 1.3mg/m^2
n = 14 n = 17 AUC_{last}
(20.4ng/mL) 223 ng/ml AUC_{last} 0.99 90%
80.18% ~ 122.80%

1.0mg/m^2 1.3mg/m^2
489~1884 L/m^2 100~1000 ng/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/m^2 AUC
AUC 60%

CrCL CrCL
≥60 ml/ /1.73 m^2 n=12 CrCL=40 59 ml/ /1.73 m^2 n=10 CrCL=20 39
ml/ /1.73 m^2 n=9 CrCL < 20 ml/ /1.73 m^2 n=3
8 0.7 1.3 mg/m^2 2
(AUC)

1 /

24

YBH12392020

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