。

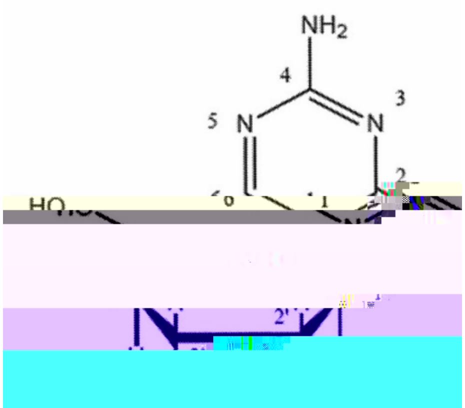
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (1)10mg | 2013 | 06 | 26 | (2) 50mg | 2013 | 06 | 26 |
| | 2015 | 03 | 15 | | 2018 | 01 | 03 |
| | 2018 | 01 | 03 | | 2020 | 12 | 24 |
| | 2020 | 12 | 24 | | 2021 | 04 | 23 |
| | 2021 | 04 | 23 | | | | |

Decitabine for Injection

Zhusheyong Dixitabin

5- -2 ' -

4- -1-(2- - -D- - )-1 3 5- -2(1 )-



$C_8H_{12}N_4O_4$

228.21

IPSS -1 -2

(MDS) MDS FAB

\- -

1 10mg 2 50mg

MDS 3 5

4 4

4

**3**

15mg/m$^2$

3 1000/

μ L

500/ μ L

MDS

25000/ μ L

•3

1 1000/ μ

L 50000/ μ L 6

• 6 8 - 2

11mg/$m^2$ 8 1 33mg/$m^2$/ 99mg/$m^2$/

• 8 10 - 2

11mg/$m^2$ 8 1 33mg/$m^{2/}$ 99mg/$m^2$/

• 10 - 10 7

6

10

1

1 ≥ 2mg/dL 2 ALT ≥ 2

ULN 3

USP 10mg 2ml

50mg 10ml ml 5.0mg

pH 6.7~7.3 0.9% 5%

0.15~1.0mg/ml 15

2 ~8 2 ~8

4

/

(Dacogen™)

3 5

3 N=66 N=98 N=99 1

N=83 N=81

**(D-0007)** **(≥1 )**

| | | |
|---|---|---|
| NOS | 23(28) | 11(14) |
| | 10(12) | 6(7) |
| | 4(5) | 1(1) |
| | | |
| NOS | 5(6) | 0(0) |
| | | |
| | 5(6) | 0(0) |
| | | |
| | 35(42) | 13(16) |
| | 29(35) | 11(14) |
| NOS | 28(34) | 13(16) |
| NOS | 21(25) | 7(9) |
| NOS | 12(14) | 5(6) |
| | 11(13) | 4(5) |
| | 10(12) | 5(6) |
| | 10(12) | 1(1) |
| | 8(10) | 2(2) |
| | 7(8) | 5(6) |
| | 7(8) | 3(4) |
| | 6(7) | 3(4) |
| | 6(7) | 2(2) |
| | 5(6) | 2(2) |
| NOS | 5(6) | 1(1) |
| | 4(5) | 3(4) |
| | 4(5) | 1(1) |
| | 4(5) | 1(1) |
| | 4(5) | 0(0) |
| | 4(5) | 0(0) |
| | | |

| | | |
|---|---|---|
| | 44(53) | 23(28) |
| | 21(25) | 13(16) |
| | 18(22) | 14(17) |
| NOS | 15(18) | 5(6) |
| NOS | 11(13) | 5(6) |
| | 10(12) | 3(4) |
| NOS | 9(11) | 0(0) |
| | 7(8) | 3(4) |
| | 6(7) | 3(4) |
| | 5(6) | 3(4) |
| | 4(5) | 1(1) |
| NOS | 4(5) | 1(1) |
| | 4(5) | 1(1) |
| | 4(5) | 0(0) |
| | 4(5) | 0(0) |
| | | |
| | 12(14) | 4(5) |
| | | |
| NOS* | 18(22) | 11(14) |
| | 10(12) | 6(7) |
| NOS | 8(10) | 1(1) |
| | 7(8) | 0(0) |
| NOS* | 6(7) | 1(1) |
| | 6(7) | 0(0) |
| | 5(6) | 2(2) |
| NOS | 4(5) | 2(2) |
| | 4(5) | 0(0) |
| | | |
| | 6(7) | 3(4) |

| | | |
|---|---|---|
| NOS | 4(5) | 1(1) |
| | | |
| NOS | 13(16) | 9(11) |
| NOS | 9(11) | 7(9) |
| AST | 8(10) | 7(9) |
| | 8(10) | 1(1) |
| | 7(8) | 5(6) |
| | 6(7) | 0(0) |
| | 5(6) | 1(1) |
| | 5(6) | 1(1) |
| | 4(5) | 3(4) |
| | 4(5) | 1(1) |
| | 4(5) | 1(1) |
| | | |
| NOS | 27(33) | 16(20) |
| | 20(24) | 14(17) |
| | 20(24) | 6(7) |
| | 18(22) | 10(12) |
| | 16(19) | 13(16) |
| NOS | 13(16) | 12(15) |
| | 13(16) | 8(10) |
| | 11(13) | 3(4) |
| | 5(6) | 4(5) |
| | | |
| | 17(20) | 8(10) |
| | 16(19) | 8(10) |
| | 14(17) | 5(6) |

| | | |
|---|---|---|
| | 6(7) | 1(1) |
| | 5(6) | 0(0) |
| | 4(5) | 1(1) |
| | | |
| | 23(28) | 11(14) |
| | 15(18) | 10(12) |
| | 9(11) | 1(1) |
| | | |
| | 23(28) | 11(14) |
| | 10(12) | 3(4) |
| | 9(11) | 8(10) |
| | | |
| | 5(6) | 3(4) |
| | 4(5) | 1(1) |
| | | |
| | 33(40) | 25(31) |
| | 13(16) | 6(7) |
| | 12(14) | 1(1) |
| | 8(10) | 7(9) |
| | 8(10) | 4(5) |
| | 7(8) | 2(2) |
| | 4(5) | 2(2) |
| | | |
| | 18(22) | 12(15) |
| NOS | 16(19) | 7(9) |
| | 12(14) | 5(6) |
| NOS | 9(11) | 3(4) |
| | 9(11) | 2(2) |
| | 7(8) | 1(1) |

| | | |
|---|---|---|
| NOS | 5(6) | 1(1) |
| | 5(6) | 0(0) |
| | | |
| | 32(39) | 13(16) |
| | 19(23) | 10(12) |
| NOS | 5(6) | 4(5) |
| NOS | 4(5) | 3(4) |
| NOS<br>* | | |

D-0007 3 4

87% 85% 23%

22%

6

83 8

81 1

DACO-020 N=99 20mg/m$^2$ 1

1 5 4 1 2

**2 ≥5%** §

| | **N=99 %** |
|---|---|
| | |
| | 31(31) |
| * | 20(20) |
| | 6(6) |
| * | 38(38) |

| | |
|---|---|
| * | 5(5) |
| | 5(5) |
| * | 27(27) |
| | |
| | 5(5) |
| | 8(8) |
| | |
| | 6(6) |
| | |
| | 14(14) |
| | 6(6) |
| | 30(30) |
| | 28(28) |
| | 10(10) |
| | 5(5) |
| | 5(5) |
| | 40(40) |
| | 5(5) |
| | 11(11) |
| | 6(6) |
| | 16(16) |
| | |
| | 15(15) |
| | [redacted] |

| | |
|---|---|
| | 5(5) |
| | 36(36) |
| | |
| | 9(9) |
| | 6(6) |
| * | 20(20) |
| | 6(6) |
| | 8(8) |
| | 5(5) |
| | 10(10) |
| * | 7(7) |
| | |
| | 9(9) |
| | |
| | 6(6) |
| | 5(5) |
| | 9(9) |
| | |
| | 23(23) |
| | 8(8) |
| | 8(8) |
| | 6(6) |
| | 12(12) |
| | 5(5) |
| | |
| | 17(17) |
| | 18(18) |
| | 6(6) |
| | 7(7) |

| | |
|---|---|
| | 5(5) |
| | 5(5) |
| | 9(9) |
| | 18(18) |
| | |
| | 21(21) |
| | 23(23) |
| | |
| | 9(9) |
| | 8(8) |
| | 9(9) |
| | 14(14) |
| | |
| | 27(27) |
| | 29(29) |
| | 13(13) |
| | 8(8) |
| | 5(5) |
| | 5(5) |
| | |
| | 8(8) |
| | 9(9) |
| | 5(5) |
| | 5(5) |
| | 12(12) |
| | 9(9) |
| | 11(11) |
| | 5(5) |
| | |

| | |
|---|---|
| | 6(6) |
| | 11(11) |
| § | |
| * | |

DACO-020 20mg/m$^2$ 1 1

5 3 4 37%

24% 22% 78%

7

8 / 7

99 19

MDS 65

1

2

-

II

- 

- 

- 

1% 2%

- 

/ G-

CSF

MYE-3002 III

D-0007 DACO-020

2011 8

AE

SAE 20% SAE 11% 3%

5 4%

8 6% 3 3 5

**3 MedDRA**

**TEAE ≥5% MYE-3002 -**

| MedDRA | 3 (N=34) | 5 (N=97) | (N=131) |
|---|---|---|---|

| | | | |
|---|---|---|---|
| | 6(17.6) | 9(9.3) | 15(11.5) |
| | 6(17.6) | 8(8.2) | 14(10.7) |
| | 6(17.6) | 8(8.2) | 14(10.7) |
| | 9(26.5) | 5(5.2) | 14(10.7) |
| | 2(5.9) | 5(5.2) | 7(5.3) |
| | 0 | 7(7.2) | 7(5.3) |
| | 3(8.8) | 4(4.1) | 7(5.3) |
| | 3(8.8) | 1(1.0) | 4(3.1) |
| | 2(5.9) | 2(2.1) | 4(3.1) |
| | 2(5.9) | 1(1.0) | 3(2.3) |
| | 3(8.8) | 0 | 3(2.3) |
| | 2(5.9) | 1(1.0) | 3(2.3) |
| | 12(35.3) | 22(22.7) | 34(26.0) |
| | 6(17.6) | 8(8.2) | 14(10.7) |
| | 4(11.8) | 7(7.2) | 11(8.4) |
| | 2(5.9) | 1(1.0) | 3(2.3) |
| | 8(23.5) | 22(22.7) | 30(22.9) |
| | 5(14.7) | 5(5.2) | 10(7.6) |
| | 0 | 9(9.3) | 9(6.9) |
| | 2(5.9) | 3(3.1) | 5(3.8) |
| | 7(20.6) | 20(20.6) | 27(20.6) |
| | 7(20.6) | 14(14.4) | 21(16.0) |
| | 1(2.9) | 8(8.2) | 9(6.9) |
| | 0 | 8(8.2) | 8(6.1) |
| | 2(5.9) | 4(4.1) | 6(4.6) |
| | 7(20.6) | 19(19.6) | 26(19.8) |
| | 3(8.8) | 12(12.4) | 15(11.5) |
| * | 4(11.8) | 3(3.1) | 7(5.3) |
| | 7(20.6) | 9(9.3) | 16(12.2) |

| | | | |
|---|---|---|---|
| | 3(8.8) | 3(3.1) | 6(4.6) |
| | 3(8.8) | 2(2.1) | 5(3.8) |
| | 7(20.6) | 7(7.2) | 14(10.7) |
| | 2(5.9) | 2(2.1) | 4(3.1) |
| | 2(5.9) | 1(1.0) | 3(2.3) |
| | 2(5.9) | 0 | 2(1.5) |
| | 5(14.7) | 7(7.2) | 12(9.2) |
| | 3(8.8) | 6(6.2) | 9(6.9) |
| | 4(11.8) | 6(6.2) | 10(7.6) |
| | 3(8.8) | 3(3.1) | 6(4.6) |
| | 1(2.9) | 8(8.2) | 9(6.9) |
| | 2(5.9) | 3(3.1) | 5(3.8) |
| | 2(5.9) | 3(3.1) | 5(3.8) |
| | 2(5.9) | 1(1.0) | 3(2.3) |
| | 2(5.9) | 0 | 2(1.5) |
| | 2(5.9) | 0 | 2(1.5) |
| | 2(5.9) | 0 | 2(1.5) |
| MedDRA= N= TEAE= <br><br>* | | | |

Sweet

4

≥ 1/10

≥ 1/100 1/10

≥ 1/ 1000 1/100

≥ 1/10000 1/1000

1/10000

**4**

| | | |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

1

/

1 2

MDS

[CrCl] 30ml/min

3

DNA

D

8 9 10 11

0 0.9 3.0mg/m$^2$ 2% 7%

3mg/m$^2$

3mg/m$^2$

9~12 2.4 3.6 6mg/$m^2$

5 8 13%

9 10 3.6mg/$m^2$

6.0mg/$m^2$ 3.6mg/$m^2$

6.0mg/$m^2$

III 83 61 65

21 75

/

CYP450

CYP450

1%

P- P-gp

P-gp

1%

20

Cmax CYP450

CYP

P-gp

P-gp

20

DNA DNA DNA

DNA DNA

DNA DNA

L5178Y lac-I DNA

lac-I

0.15 0.3 0.45mg/$m^2$

0.3%~1% 3 7

≥ 0.3mg/$m^2$

≥ 0.3mg/$m^2$

8 9 10 11 0.9 3mg/m$^2$

2% 7% 3mg/m$^2$

3mg/m$^2$

9~12

2.4 3.6 6.0mg/m$^2$ 5% 8% 13%

9

10 3.6mg/m$^2$

6.0mg/m$^2$

3.6mg/m$^2$

6.0mg/m$^2$

3mg/m RB8rs50D]7#%

70kg 1.73m$^2$ 4

**4** **5** **3**

| | 5 | | 3 | |
|---|---|---|---|---|
| | | 95%CI | | 95%CI |
| $C_{max}$ (ng/mL) | 107 | 88.5~129 | 42.3 | 35.2~50.6 |
| $AUC_{cum}$ (ng.h/mL) | 580 | 480~695 | 1161 | 972~1390 |
| $t_{1/2}$ (min) | 68.2 | 54.2~79.6 | 67.5 | 53.6~78.8 |
| $Vd_{ss}$ (L) | 116 | 84.1~153 | 49.6 | 34.9~65.5 |
| CL (L/h) | 298 | 249~359 | 201 | 168~241 |
| AUC= - CL= $C_{max}$= $t_{1/2}$= $Vd_{ss}$= | | | | |

0.5

<1%

Vdss

DNA

P450

2.4%

4%

P-gp

>200L/h

CV 50%

$^{14}C$-

90% 4%

4

40~87

70

MYE-3002 24 MDS

3 15mg/m$^2$ 8

7 5 20mg/m$^2$ 17 JPN-

MDS-101 8 MDS 15mg/m$^2$

5 3 20mg/m$^2$ 5 5 MYE-3002

JPN-MDS-101

CYP

25

1

24

YBH02322021

(1) 10mg H20153045

(2) 50mg H20130067

5

222069

4008285227 9:00—17:00

http://www.hansoh.cn