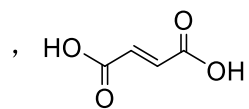
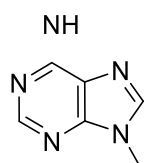


R

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Child-Pugh

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25mg QD 96

670

ALT

11.1%

10.5%

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\_\_\_\_\_

DNA

HBV

6

ALT

HBV

Child-Pugh >9 C HBV

CrCl <50mL/min HBV

3.0% 96 14.4% 4.8% TDF 48 11.4%

HBV

HCV

HDV

HBV

HIV

HBV

HIV

HBV

HIV

-

144

3

18

65

P-

P-gp

P-gp

gp

P-

P-gp

486 246 TDF 34 71%

93.3% 6.4% 28.9%

HBV DNA 7.3log<sub>10</sub> IU/mL ALT 136U/L 60.7% 38.8%

HBV C B

**HBeAg**

270 HBeAg 25mg TDF 300mg

180 90 TDF 42.8

75.2% 93.7% 7.0% 28.5%

HBV DNA 5.8 log<sub>10</sub>IU/mL ALT 121U/L 53.3% 42.6%

HBV B C

48 48 HBV

DNA 20 IU/mL 48

HBeAg HBeAg

25mg QD TDF 3 96

4

|                 | HBeAg       |              | HBeAg  |             |
|-----------------|-------------|--------------|--------|-------------|
|                 | N=486       | TDF<br>N=246 | N=180  | TDF<br>N=90 |
| HBV DNA<20IU/mL | 52.8%       | 55.9%        | 90.2%  | 92.9%       |
| ALT             | 83.6%       | 78.4%        | 89.2%  | 90.8%       |
| HBeAg /         | 17.6%/10.0% | 17.2%/8.9%   | NA     | NA          |
| HBsAg /         | 0/0         | 0/0          | 0.6%/0 | 0/0         |

ALT

ALT

NA=

4

|                 | HBeAg   |                | HBeAg   |               |
|-----------------|---------|----------------|---------|---------------|
|                 | (N=486) | TDF<br>(N=246) | (N=180) | TDF<br>(N=90) |
| HBV DNA<20IU/mL | 71%     | 71.2%          | 93.1%   | 94%           |
| ALT             | 89.4%   | 85.1%          | 91.4%   |               |

0.07% BMD 0.46% TDF BMD  
1.93% BMD 2.06% TDF  
2.06%  
96 BMD

|         |  |   |   |  |                                |                                |
|---------|--|---|---|--|--------------------------------|--------------------------------|
| (q1 q3) | 0.00<br>(-2.10,2.00)<br>(g/cm <sup>2</sup> ) | -2.05<br>(-3.90,0.15)<br>(g/cm <sup>2</sup> ) | -0.50<br>(-2.40,1.40)<br>(g/cm <sup>2</sup> ) | -1.90<br>(-3.90,-0.05)<br>(g/cm <sup>2</sup> ) | 1.00<br>(-4.00,6.00)<br>μmol/L | 2.00<br>(-4.00,6.44)<br>μmol/L |
| ,       | -20.1,59.5<br>(g/cm <sup>2</sup> )           | -18.1,9.1<br>(g/cm <sup>2</sup> )             | -13.9,16.1<br>(g/cm <sup>2</sup> )            | -13.1,35.7<br>(g/cm <sup>2</sup> )             | -56.0,32.8<br>μmol/L           | -20.0,28.0<br>μmol/L           |
| (<br>)* | 0.09(0.181)<br>(g/cm <sup>2</sup> )          | -1.90(0.239)<br>(g/cm <sup>2</sup> )          | -0.50(0.162)<br>(g/cm <sup>2</sup> )          | -2.09(0.213)<br>(g/cm <sup>2</sup> )           | 0.01(0.375)<br>μmol/L          | 1.13(0.492)<br>μmol/L          |
| *       |  | 1.99<br>(1.462,2.523)                         |   | 1.59<br>(1.117,2.062)                          |                                | -1.12<br>(-2.219,-<br>0.027)   |
| P       |  | <0.001  |   | <0.001   |                                | 0.045                          |

- )

HBV

DNA DNA HBV DNA  
( DNA

HBV HepG2.2.15  
EC<sub>50</sub> 1.42nM HepG2 CC<sub>50</sub>>10000 nM

HepG2 ( )  
(rtV173L rtL180M rtM204V/I)  
HBV (EC<sub>50</sub> < 2)  
(rtL180M rtM204V + rtT184G rtS202G rtM250V) HBV  
(rtA181T rtA181V rtN236T) HBV  
rtA181V + rtN236T HBV  
(EC<sub>50</sub> 3.7)

Ames

4

2 7 25 75 225mg/kg ( 25mg/ 10 29 86 ),225mg/kg

NOEAL 75mg/kg

NOAEL 225 mg/kg

NOAEL 75mg/kg

- ( 6~15 )

25 75 225 mg/kg ( AUC 25mg/

18 74 325 ) 225 mg/kg

NOAEL 75mg/kg

6~18

5 25 125mg/kg ( AUC

25mg/

8 31 129 ) 125 mg/kg

5~6

1~12

NOAEL 125 mg/kg

- NOAEL 25mg/kg

6 ( 21 )

10 30 100mg/kg ( 25mg/ 3.9 12 39 )

100 mg/kg (F1 )

NOAEL 100mg/kg

:

300mg

10 ( ) 4 ( )

(25mg/ ) 189 ( )

63 ( )

(25mg/ ) 189



0~528h 85.0%  
12.7% 72.3%

18

HBV TFV

18.07-541U/L

TFV

ALT

HBV TFV

\*

9 A 92 94