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2020 06 02
2021 09 26
2021 11 29
2023 05 12

Afatinib Dimaleate Tablets

Malaisuan Afatini Pian

(2E)-N-[4-(3- -4-)-7-[[3S)- -3-]] -6-]-4-
() -2-

1. EGFR
(NSCLC) EGFR TKI

2.
(NSCLC)

_____ $C_{24}H_{25}ClFN_5O_3$ 1 20mg 2 30mg 3 40mg

d

20mg/

ILD

ILD

[]

1

8

<30mL/min

Child Pugh A

Child Pugh B

Child Pugh C

P-

P-gp

P-

(P-gp)

P-gp

P-gp

6 P-gp 12 P-gp
 P-gp
 10mg P gp

P- P-gp
 P-gp
 10mg P-gp 2-3

100
 15
 100

ADRs

EGFR

(2 3)

40mg

LUX-Lung3(1200.32) 57% LUX-Lung6(1200.34) 33.1% LUX-Lung8
 (1200.125) 25% / 1.3%
 0% (LUX-Lung3) 0% 2.5% LUX-Lung6 3.8% 2.0% LUX-Lung8

4257 LUX- Ä

	LUX-Lung 3	1200.32		229	EGFR TKI	
	40mg	1		111		
	40mg	1		/		
ADR			100%	96%		/
		95%	15%		89%	6%
						57%
			ADR			
				96%	52%	
	1	40mg			/	
ADR			8%	12%		ADR
				1.3%	0%	
	LUX-Lung 6	1200.34		239	EGFR TKI	
	40mg	1		113	/	
	40mg	1		/		
ADR			98.7%	99.1%		/
		90.0%	15.0%	/	81.2%	9.7%
33.1%			ADR			
	1	40mg			/	
ADR			10.0%	39.8%		ADR
				0%	2.5%	
	LUX-Lung8	1200.125		392	NSCLC	40mg
1				395	150mg	1
	28	39	10%			50mg
			ADR		93%	81%
				70%	33%	
67%	67%				27%	
	11%					5%
		40mg	50mg	NSCLC		
	EGFR	EGFR		NSCLC		40 mg

1200.22, 1200.32, 1200.34, 1200.123 497 EGFR TKI
 NSCLC 50 mg 1200.23, 1200.33 1200.41,
 1200.42 1638 EGFR TKI NSCLC
 40mg 50mg 1
 ADR EGFR
 40mg 50mg 1 ADR LUX-Lung 3
 40mg 50mg 58.8% 53.1% CTCAE1 2 ADR 2
 2 ADR CTCAE 1 2
 40mg 50mg 38%
 41% CTCAE 3 4 ADR CTCAE3 ADR
 ADR 7% 11.7%
 EGFR NSCLC
 ADR 2
 2 EGFR NSCLC

	N=497	N=1638
	14.3%	11.8%
	9.9%	17.6%
	1.2%	1.9%
	0.6%	4.5%

40mg 1 0.2% 4 50mg
 1 0.1% 4 3 0.2% 4
 LUX-Lung8 40mg
 ADR EGFR
 LUX-Lung 3 ADR 65% CTCAE 1
 2 CTCAE 3/4 9.9%/0.5% CTCAE 3 5.9%
 11% ADR
 3.8% 2.0%

3	40mg	50mg	NSCLC	ADRs
	ADR		$\geq 1/10$	$\geq 1/100$
<1/10	$\geq 1/1,000$	<1/100	$\geq 1/10,000$	<1/1,000
<1/10,000				

3

ADRs

	1/10	1/100 <1/10	1/1,000 1/100
	1		
	2		
		ALT	
		AST	
	3 4 5 6	8	Stevens-Johnson 7 7
		/	

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8



/Stevens-Johnson

2

3

6

6

12

48

2

3

4257

1.6%

ILD

P-gp

P-gp

2

P- P-gp

P-gp

P-gp

P-gp

P-gp

A

P-gp

C_{max}

50%

$AUC_{0-\infty}$

39%

I

160mg

1

3

100mg

1

2

2

360mg

 EGFR(ErbB1) HER2(ErbB2) HER4(ErbB4)
 ErbB
 EGFR EGFR 19
 21 L858R T790M
 HER2 EGFR HER2 EGFR L858R/7790M
 26
 52
 Ames 1
 Muta™ 4
 4 6 8mg/kg
 6mg/kg 40mg AUC
 8mg/kg
 40mg AUC 0.63
 4
 2
 - 5mg/kg
 40mg AUC 0.2
 10mg/kg 40mg AUC 0.7
 -
 16mg/kg 40mg AUC 2
 1h 6h

80 150

3T3

2-5
 20mg 50mg
 C_{max} $AUC_{0-\infty}$
 50% C_{max} 39% $AUC_{0-\infty}$
 $AUC_{\tau,ss}$ 26%
 92% $AUC_{0-\infty}$
 95%

15mg
 88% 85.4% 4.3%
 8 2.77 AUC 2.11 C_{max}

5%
 ”

50mg Child

PO qd

“

”

Child Pugh C

		927	764	NSCLC		
		28-87				
1	62kg			1	42kg	2.5
		AUC _{τ,ss}	26%	1	95kg	97.5
		22%				
		AUC _{τ,ss}		15%		
		927	6	9		
		CrCL			CrCL	79mL/min
		CrCL	CrCL	60	30mL/min	
		AUC _{τ,ss}	13%	42%	CrCL	90 120mL/min
		6%	20%			

P- (P-gp)

P-

	2		P-gp			
	1		200mg	2	3	40mg
		6				
			119% (AUC _{0-∞})		104% (C _{max})	
	6				111% (AUC _{0-∞})	105%
(C _{max})	2		200mg	2	3	20mg
	1			48% (AUC _{0-∞})	39% (C _{max})	
		P-gp		600mg	7	40mg
				34% (AUC _{0-∞})	22% (C _{max})	

P-gp

P-gp

P-gp

BCRP

BCRP

	OATB1B1	OATP1B3	OATP2B1	OAT1	OAT3	OCT1	OCT2
OCT3							-

P450 CYP

CYP

CYP

-

2%

FMO3

CYP3A4

N-

CYP

CYP

CYP

UDP-

1A1 UGT1A1

UGT1A1

-

30

10 / / / 10 / 3 / /

36

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