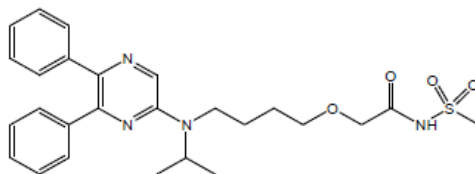


2 0 1 81 2 0 7
 2 0 2 00 3 0 4
 2 0 2 00 6 2 4
 2 0 2 10 4 1 6
 2 0 2 10 9 2 3
 2 0 2 20 2 1 4
 2 032 07 19
 2 032 07 24

® U p t ® a v i
 Se l e x T i a p b a l g e t s
 S i l a i p a g e P i a n

2-{ 4 (5 , 6 -2-) 2-)] }-N-()



C₂₆H₂₈N₄O₄S

4 9 6 . 6 2

0 . 2 m g	“ 2 ”
0 . 4 m g	“ 4 ”
0 . 6 m g	“ 6 ”

/

6

3

PAH

Child-Pugh C

Child-Pugh B

0.2 mg

0.2 mg

Child-Pugh A

e G F R < 30 mL / m² i n / 1 . 7 3 m

C Y P 2 C 8

C Y P 2 C 8

C Y P 2 C 8

11 5 6

P A H

3

7 6 . 4

7 0 . 7

7 1 . 2

6 3 . 7

4 . 2

	$\geq 1/10$	$\geq 1/100$ < 1/10	$\geq 1/1,000$ < 1/100
	*		
	*		
	* * *		
	*		

	* * *		

*

	6 4 %	2 8 %	4 0 %	2 0 %
	3 6 %	1 2 %	3 0 %	1 3 %
	2 9 %	1 3 %	2 0 %	1 0 %
	2 6 %	4 %	2 1 %	4 %
	1 5 %	5 %	9 %	3 %
	1 4 %	5 %	1 3 %	6 %
	1 4 %	4 %	8 %	6 %
	1 1 %	4 %	1 0 %	3 %
	7 %	5 %	9 %	5 %

7. 5 %
2 . 3 % 0 . 5 %
/

P A H 3

-0 . 3 40 . 0 2 g / d L

-0 . 0 50 . 2 5 g / d L 1 0 g / d L
8 . 6 % 5 . 0 %

P A H 3
1 . 6 %

0 . 3 MU / L 2 . 5 MU / L

P A H 3 2-4
3-4 b p m 1 1 . 3 % 8 . 8 %

-
-
- 6
-
-
- 3
-
- C Y P 2 C 8

P A H

≥ 65

7 5

C h i-Pl udg h C

C h i-Pl udg h B

e G F R < 3 0 m Ĺ / m i n / 1 . 7 3 m

I P 2 0 8 0
I P I P

0 1 8

7 5

C Y P 2 C 8 C Y P 3 A 4
U G T A 1 3 U G T 2 B 7
O A T P 1 B 3 O A T P 1 B 3 P-g p
B C R P

C Y P 2 C 8
6 0 0 m g C Y P 2 C 8
2
1 1 C Y P 2 C 8

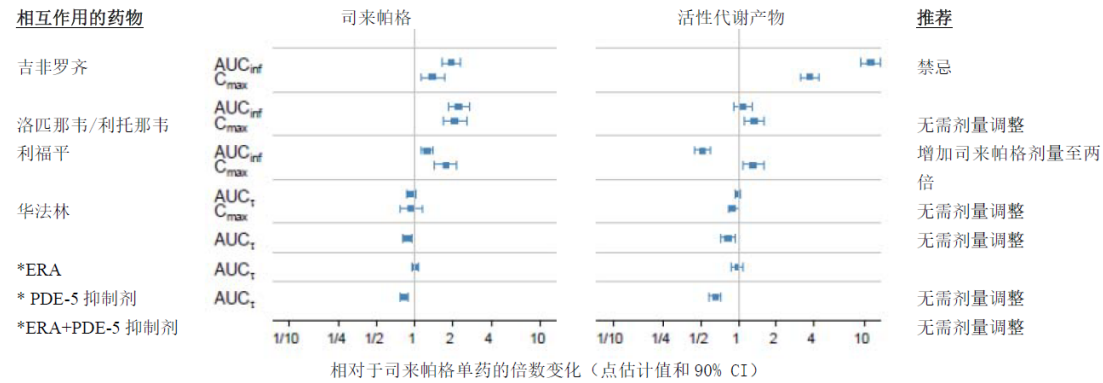
20 mg 0.4g
S- CYP2C9 R- CYP3A4
IN R

1.6g
CYP3A4 1-
CYP3A4

CYP3A4 R- CYP2C9 S-

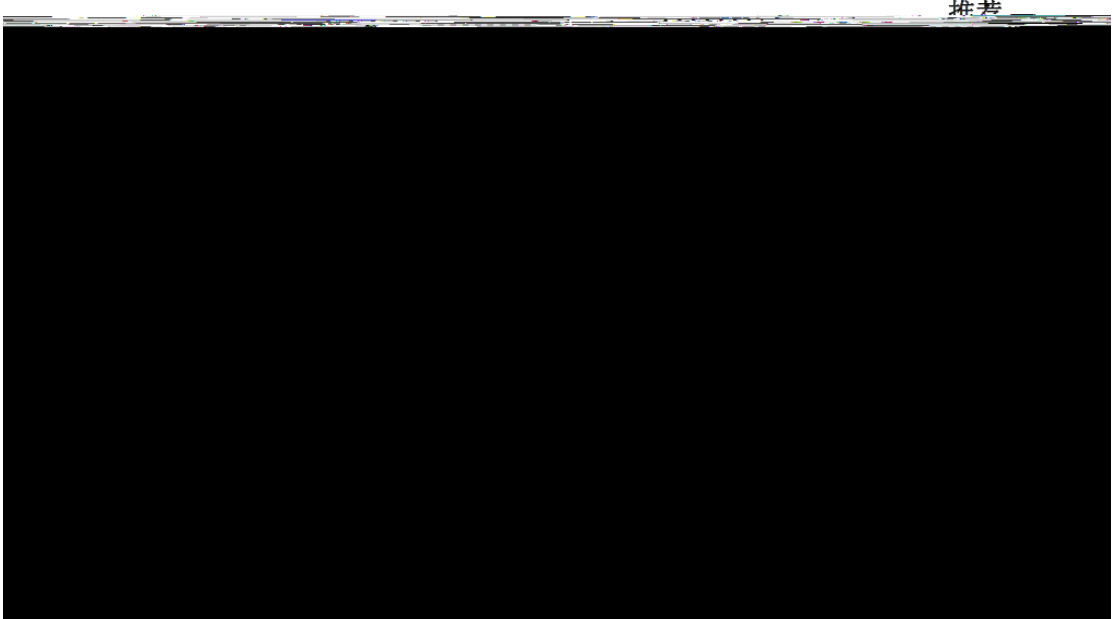
1 2

1.



* G R I P H O N R A P D E

2.



3 . 2 g

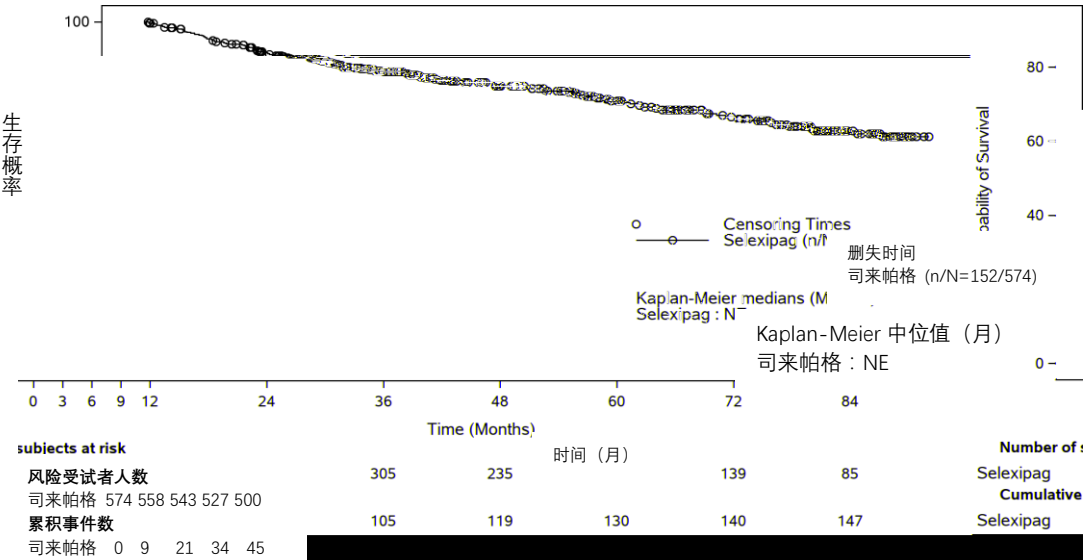
GRIP HON
1 1 5 6 P A H
0 . 8 % 6 % 5 3 % 1 % WHO I I I I I I V
N = 5 8 2 N = 5 7 4 0 . 2 m g
1 . 6 m g
E O T
P A H P A H
6 6 MWD ≥ 1 5 % WHO 6 6 MWD
≥ 1 5 % P A H
4 8 6 5 % 8 0 %
WHO I I I I I
5 8 %
2 9 %
1 0 % 2 % H I V 1 %

		8 0 %	E R A 1 5 % P D E
5	3 2 %	3 3 %	
		0 . 2 0 . 4 m g %	0 . 6 . 0 m g %
1 . 2 . 6 m g	3 %		
			4 0 %

=	" "		3 0 E U =		N U
	H R =	C I =	E P =	N P =	
					9 9 %

8 1 % 7 0 % W H O F I V I I 8 8 % 8 0 % 6 1 % 5 6 %

6. Kaplan-Meier



I P

1

3 7

I P

E R-4 D P F P T P

A m e s C H L

6 0 m g / k g / 1 7 5

7 ~ 1 7

2 6 2 0 m g / k g A / U C

4 7

6 ~ 1 8

3 1 0 3 0 m g / k g A / U C

5 0

7

2 0

2 6 2 0 m g / k g /

2	100 mg / kg /
500 mg / kg AUC	25
0.8 mg	1.8 mg
AUC	43 % 39 %
	24 % 19 %
PAH	PAH
	PAH
34	30 %
	49 %
13	34
C _{max}	30 %
	T _{max}
	AUC
	11.7 L
	99 %
α 1	
CYP2C8	CYP3A4
UGT1A3UGT2B7	
	3 %

P A H
3-4

0 . 82 . 5
6 . 213 . 5 17 . 9 L / h
5 93 %
12 %

P A H

7 5

C_{ma x} A U C

P A H

C h i-P l u d g h A

C h i-P l u d g h B

2 4

1

C h i-P l u d g h B

2

15 mL / mi n / 1 . 73 m < 30
m L / m i n /² 1 . 73 m
- 40 % 70 %

30

/ / / /

0 . 2 m g / 6 0 0 /

0 . 4 m g / 6 0

0 . 6 m g / 6 0

0 . 8 m g / 6 0

1 . 0 m g / 6 0

1 . 2 m g / 6 0

1 . 4 m g / 6 0

1 . 6 m g / 6 0

3 6

J X 2 0 0 0 9 2

0 . 2 m g : HJ2 0 1 8 0 0 7 8

0 . 4 m g : HJ2 0 1 8 0 0 7 9

0 . 6 m g : HJ2 0 1 8 0 0 8 0

0 . 8 m g : HJ2 0 1 8 0 0 8 1

1 . 0 m g : HJ2 0 1 8 0 0 8 2

1 . 2 m g : HJ2 0 1 8 0 0 8 3

1 . 4 m g : HJ2 0 1 8 0 0 8 4

1 . 6 m g : HJ2 0 1 8 0 0 8 5

A c t e l i o n P h a r m a c e u t i c a l s L t d

G e w e r b e s t r a s s e 1 6 , 4 1 2 3 A l l s c h w i l , S

E x c e l l a G m b H & C o . K G

N ü r n b e r g e r , E t z e l t , 9 0 5 7 7

6 5 5 1 7

2 0 0 1 3 1

40 08 6-00 6 7 3

021-80258310

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