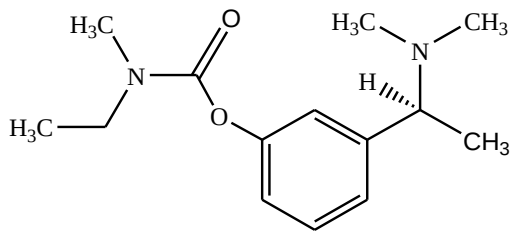




Rivastigmine Transdermal Patch
Lisidiming Toupitieji

S -N- -N- -3-[1-()]-



$C_{14}H_{22}N_2O_2$

250.34

[(2-) ,]
/ /

4.6mg/24

RIV-TDS 4.6mg/24h 9.5mg/24

RIV-TDS 9.5mg/24h

1 4.6mg/24

2 9.5mg/24

4.6mg/24	4.6mg/24	6.9mg	4.6cm ²
9.5mg/24	9.5mg/24	13.8mg	9.2cm ²

4.6mg/24

4

4.6mg/24

9.5mg/24

9.5mg/24

/

3

4.6mg/24

/

•

/

<6mg/

4.6mg/24

•

/

6-12mg/

9.5mg/24

50kg

9.5mg/24

/

17.4mg/24 *

9.5mg/24

2

	1	2			
	(1%~10%	1%)	(0.1%~1%	0.1%)	(0.01%~0.1%
0.01%)	(<0.01%)				
1				2687	
			4.6mg/24		9.5mg/24
13.3mg/24	*	17.4mg/24	*	24-48	

[illegible]

*

13.3mg/24

*

17.4mg/24

**

24

24

/

2

24

2%

)

(

	18 6.2	57 18.8	50 17.0	10 3.3	75 12.6
	18 6.2	31 10.2	16 5.4	10 3.3	49 8.2
	8 2.7	23 7.6	16 5.4	4 1.3	31 5.2
	7 2.4	21 6.9	22 7.5	7 2.3	28 4.7
	2 0.7	15 5.0	12 4.1	3 1.0	17 2.9
	10 3.4	13 4.3	18 6.1	5 1.7	23 3.9
	7 2.4	12 4.0	14 4.8	3 1.0	19 3.2
	11 3.8	12 4.0	13 4.4	4 1.3	23 3.9
	4 1.4	12 4.0	6 2.0	6 2.0	16 2.7
	7 2.4	11 3.6	4 1.4	2 0.7	18 3.0
	5 1.7	9 3.0	17 5.8	3 1.0	14 2.4
	9 3.1	8 2.6	5 1.7	4 1.3	17 2.9
	5 1.7	7 2.3	2 0.7	4 1.3	12 2.0

* 17.4mg/24

3

3%

	<u>9.5mg/24</u> <u>N=247</u> <u>n (%)</u>	<u>12mg/</u> <u>N=251</u> <u>n (%)</u>
	140 (56.7)	157 (62.5)
	27 (10.9)	7 (2.8)
	20 (8.1)	32 (12.7)
	19 (7.7)	31 (12.4)
	16 (6.5)	37 (14.7)
	15 (6.1)	25 (10.0)
	10 (4.0)	7 (2.8)
	10 (4.0)	17 (6.8)
	8 (3.2)	4 (1.6)
	6 (2.4)	11 (4.4)
	5 (2.0)	8 (3.2)

4.9% 8.4%

2.2%

3.7%

-

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3

4.6mg/24

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QT

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48

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®

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/

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50kg

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/

88% 65

55% 75

/

P450



24 48

24

10-20

24

ADAS-Cog -
ADCS-CGIC -
ADCS-ADL -

3 24

4

4	3	24	
ITT-LOCF		®	
	9.5mg/24 N=251	12mg/ N=256	N=282
ADAS-Cog	n=248 27.0±10.3 -0.6±6.4 0.005* ¹	n=253 27.9±9.4 -0.6±6.2 0.003* ¹	n=281 28.6±9.9 1.0±6.8
24	p		
ADCS-CGIC	n=248 3.9±1.20 0.010* ²	n=253 3.9±1.25 0.009* ²	n=278 4.2±1.26
	p		
ADCS-ADL	n=247 50.1±16.3 -0.1±9.1 0.013* ¹	n=254 49.3±15.8 -0.5±9.5 0.039* ¹	n=281 49.2±16.0 -2.3±9.4
24	p		

ITT
1
LOCF
ADAS-Cog
ADCS-ADL
2
CMH
van Elteren
ADCS-CGIC
<4

24 5
ADAS-Cog 4 ADCS-CGIC ADCS-ADL

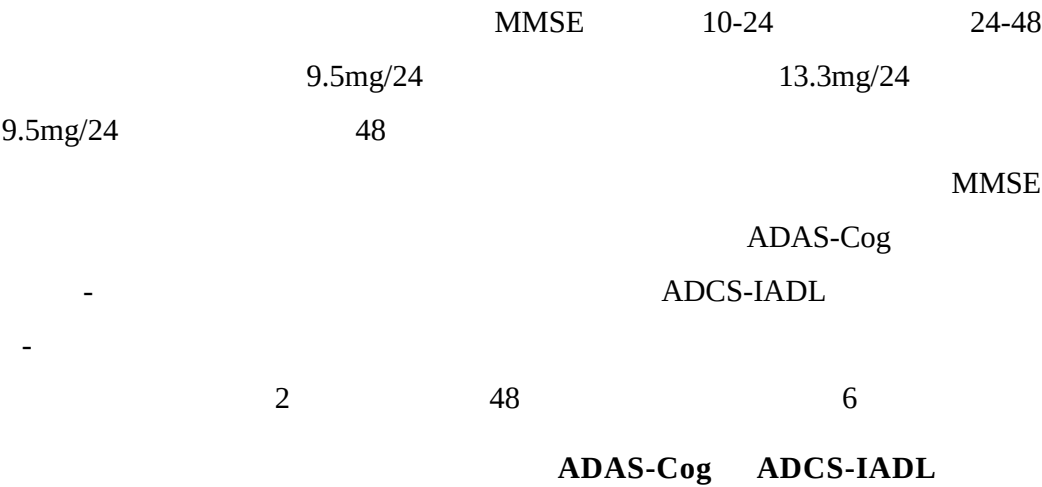
	%		
	9.5mg/24	12mg/ [®]	
ITT-LOCF	N=242	N=248	N=276
ADAS-Cog ADCS-CGI ADCS-ADL	17.4	19.0	10.5
p	0.037*	0.004*	

* p<0.05

9.5mg/24 12mg/

9.5mg/24

48



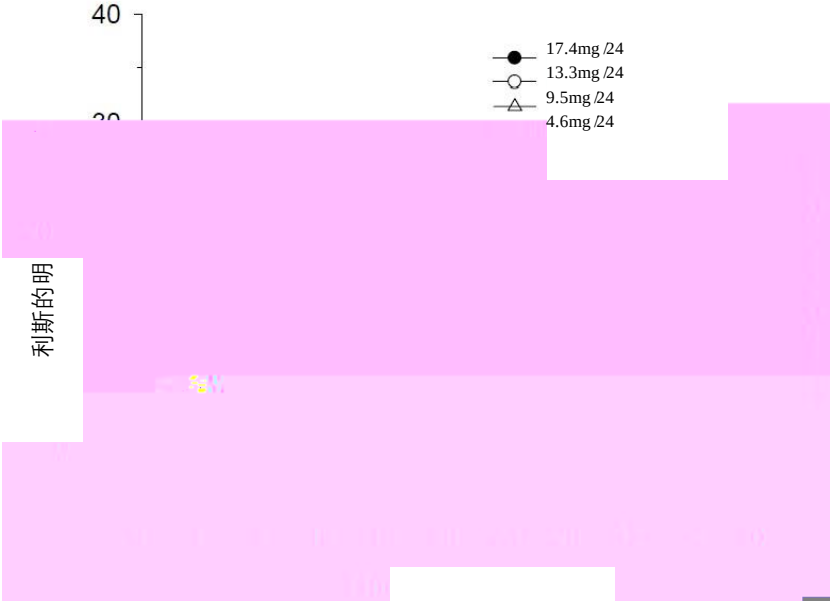
	(13.3mg/24h) N = 265	(9.5mg/24h) N = 271	(13.3mg/24h) (9.5mg/24h)
			-
			DLSM 95% CI P

	(13.3mg/24h) N = 265	(9.5mg/24h) N = 271	-	(13.3mg/24h) (9.5mg/24h)
--	-------------------------	------------------------	---	-----------------------------

-

	1.1mg/kg/			1.6mg /kg/	
	0.75mg /kg/				
		AUC		13.3mg/24	
—					
	/			0.5-1	
	/		/		
8		C _{max}		10-16	
24					
		40			
				8	
		50%			
0	1	2			
	4.6mg/24	17.4mg/24			
			C _{max}	AUC	
			4.6mg/24		
17.4mg/24		9.5mg/24	13.3mg/24	17.4mg/24	
	4.6mg/24	AUC	2.6	4.9	7.8
(FI)			((C _{max} -C _{min})/C _{avg}))	0.57-0.77	
			FI=3.96	6mg/	-6.24
12mg/				17.4mg/24	
		9-10mg 2	/	18-20mg/	
9.5mg/24			6mg 2	/	12mg/

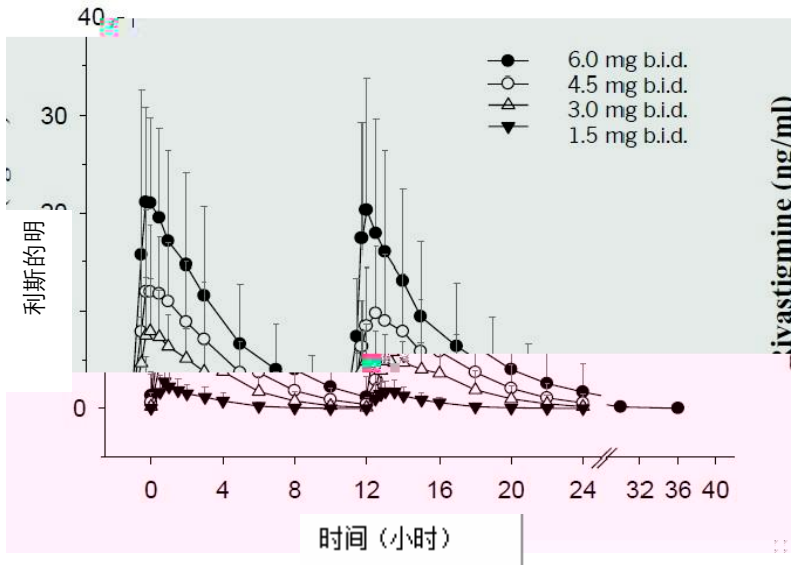
1 24



2

2 /

/



/

/ kg

43% C_{max}

49% AUC_{0-24h}

74% 103%

45% C_{max}

43% AUC_{0-24h}

71% 73%

65kg 35kg 2

100kg

67%

3 2

20-30%

NAP226-90

1

40%

1.8-2.7L/kg

/

<10%

CYP1A2,CYP2D6,CYP3A4/5,CYP2E1,CYP2C9,CYP2C8,CYP2C19, CYP2B6

/

—

AUC

0.7

3.5

NAP226-90

/

 $^{14}\text{C-}$

24

24

>90%

1%

3

2.1

2.8

36

Luye Pharma AG
Am Windfeld 35, 83714 Miesbach, Germany

Luye Pharma AG
Am Windfeld 35, 83714 Miesbach, Germany

15

15

264670

0535-6717618

0535-6717718

www.luye.cn

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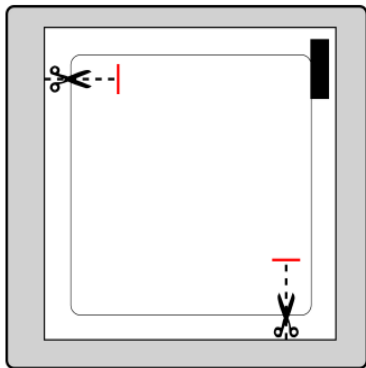


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1.

B

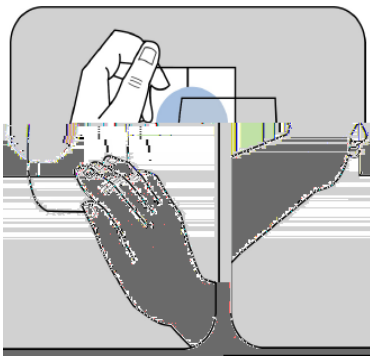
B



2.

C

C

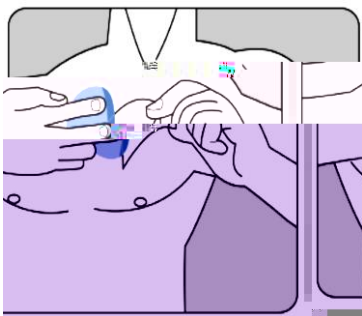


3.

4.

(D)

D



5.

E

E

