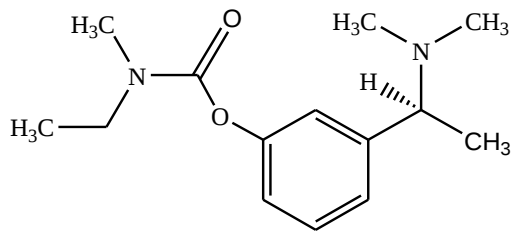




Rivastigmine Transdermal Patch  
Lisidiming Toupitieji

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 <sup>2</sup> |
| 9.5mg/24 | 9.5mg/24 | 13.8mg | 9.2cm <sup>2</sup> |

\_\_\_\_\_

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%) |                  |                 |              |                 |
| <b>1</b>         |          |                  |                 | <b>2687</b>  |                 |
|                  |          |                  | <b>4.6mg/24</b> |              | <b>9.5mg/24</b> |
| <b>13.3mg/24</b> | *        | <b>17.4mg/24</b> | *               | <b>24-48</b> |                 |

[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><br><u>N=247</u><br><u>n (%)</u> | <u>12mg/</u><br><u>N=251</u><br><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%

-

/

\_\_\_\_\_

\_\_\_\_\_

3

4.6mg/24

/

\_\_\_\_\_

/

\_\_\_\_\_

QT

/

\_\_\_\_\_

/

/

/

\_\_\_\_\_

48

/

®

/

/

/

\_\_\_\_\_

50kg

\_\_\_\_\_

/

/

\_\_\_\_\_

\_\_\_\_\_

/

\_\_\_\_\_

/

/

/

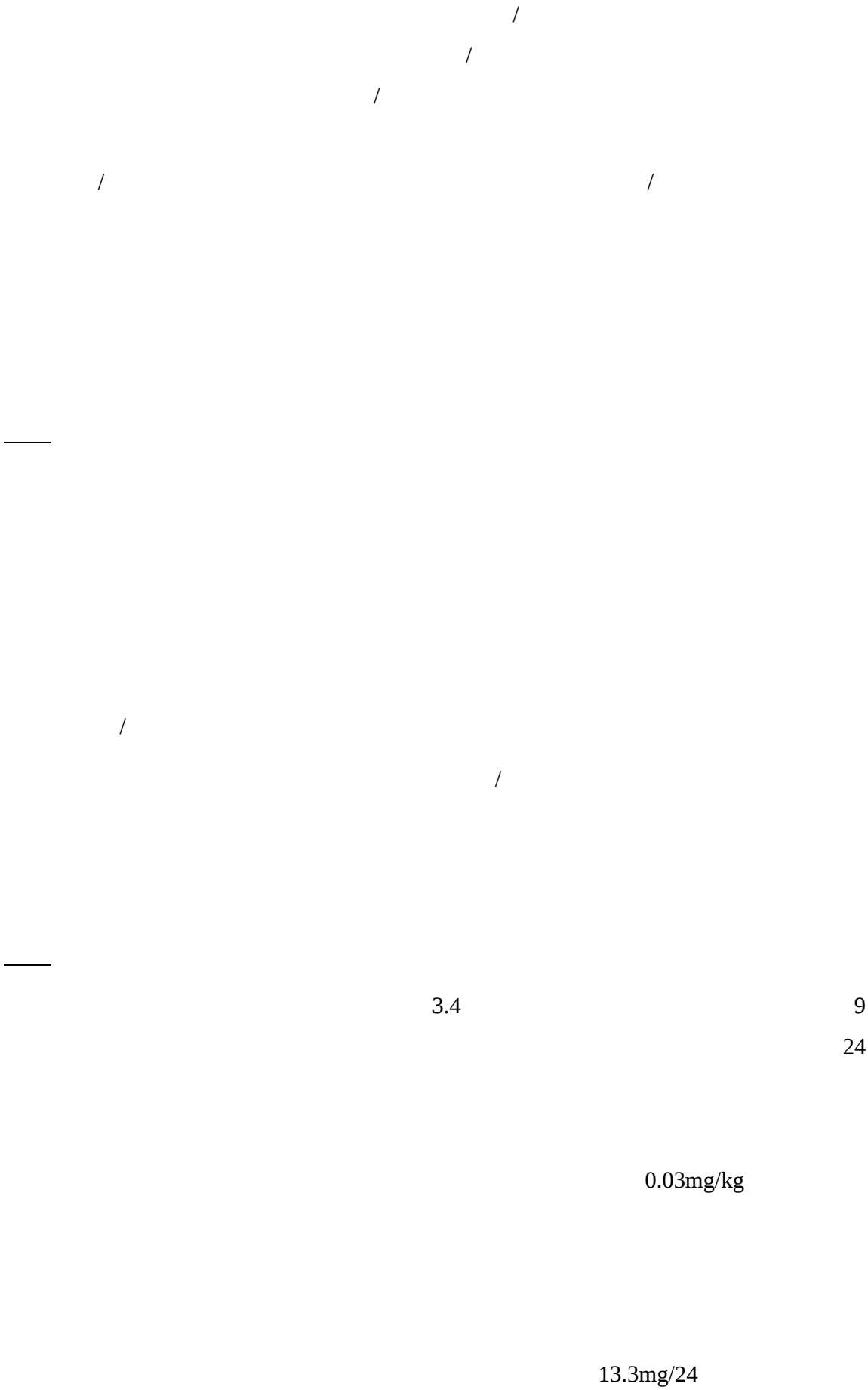
\_\_\_\_\_

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<br>N=251                         | 12mg/<br>N=256                            | N=282                          |
| ADAS-Cog  | n=248<br>27.0±10.3<br>-0.6±6.4<br>0.005*1 | n=253<br>27.9±9.4<br>-0.6±6.2<br>0.003*1  | n=281<br>28.6±9.9<br>1.0±6.8   |
| 24        | p                                         |                                           |                                |
| ADCS-CGIC | n=248<br>3.9±1.20<br>0.010*2              | n=253<br>3.9±1.25<br>0.009*2              | n=278<br>4.2±1.26              |
|           | p                                         |                                           |                                |
| ADCS-ADL  | n=247<br>50.1±16.3<br>-0.1±9.1<br>0.013*1 | n=254<br>49.3±15.8<br>-0.5±9.5<br>0.039*1 | n=281<br>49.2±16.0<br>-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/ <sup>®</sup> |       |
| ITT-LOCF                         | N=242    | N=248              | N=276 |
| ADAS-Cog<br>ADCS-CGI<br>ADCS-ADL | 17.4     | 19.0               | 10.5  |
| p                                | 0.037*   | 0.004*             |       |

\* p<0.05

9.5mg/24 12mg/

9.5mg/24

48

MMSE 10-24 24-48

9.5mg/24 13.3mg/24

9.5mg/24 48

MMSE

ADAS-Cog

ADCS-IADL

-

-

2 48 6

6 ADAS-Cog ADCS-IADL

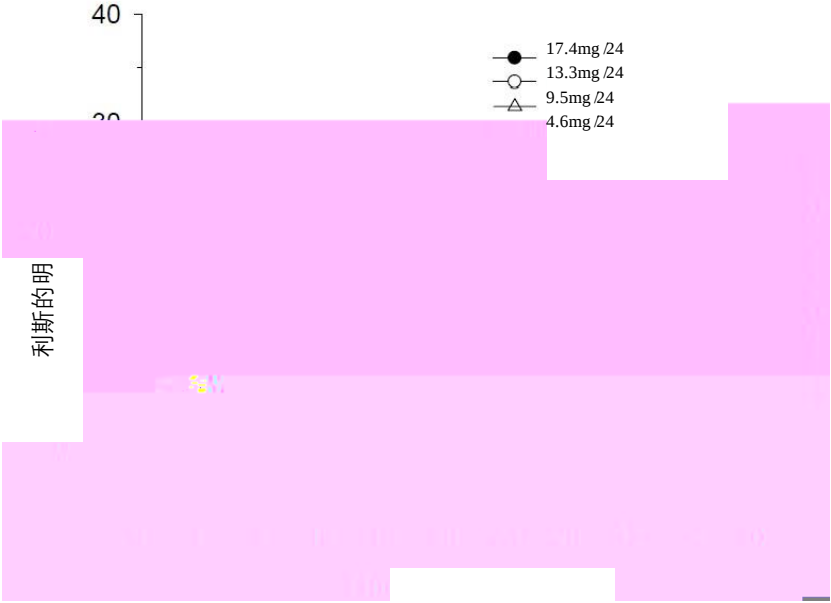
|  |                         |                        |                                  |
|--|-------------------------|------------------------|----------------------------------|
|  | (13.3mg/24h)<br>N = 265 | (9.5mg/24h)<br>N = 271 | (13.3mg/24h)<br>-<br>(9.5mg/24h) |
|  | DLSM 95% CI           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

|  |                         |                        |   |                             |
|--|-------------------------|------------------------|---|-----------------------------|
|  | (13.3mg/24h)<br>N = 265 | (9.5mg/24h)<br>N = 271 | - | (13.3mg/24h)<br>(9.5mg/24h) |
|--|-------------------------|------------------------|---|-----------------------------|

-

|           |             |                  |                                                            |                  |           |
|-----------|-------------|------------------|------------------------------------------------------------|------------------|-----------|
|           | 1.1mg/kg/   |                  |                                                            | 1.6mg /kg/       |           |
|           | 0.75mg /kg/ |                  |                                                            |                  |           |
|           |             | AUC              |                                                            | 13.3mg/24        |           |
| —         |             |                  |                                                            |                  |           |
|           |             | /                |                                                            | 0.5-1            |           |
|           |             | /                |                                                            | /                |           |
| 8         |             | C <sub>max</sub> |                                                            | 10-16            |           |
|           | 24          |                  |                                                            |                  |           |
|           |             | 40               |                                                            |                  |           |
|           |             |                  |                                                            | 8                |           |
|           |             | 50%              |                                                            |                  |           |
|           | 0           | 1                | 2                                                          |                  |           |
|           | 4.6mg/24    |                  | 17.4mg/24                                                  |                  |           |
|           |             |                  |                                                            | C <sub>max</sub> | 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 <sub>max</sub> -C <sub>min</sub> )/C <sub>avg</sub> )) |                  | 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/     |

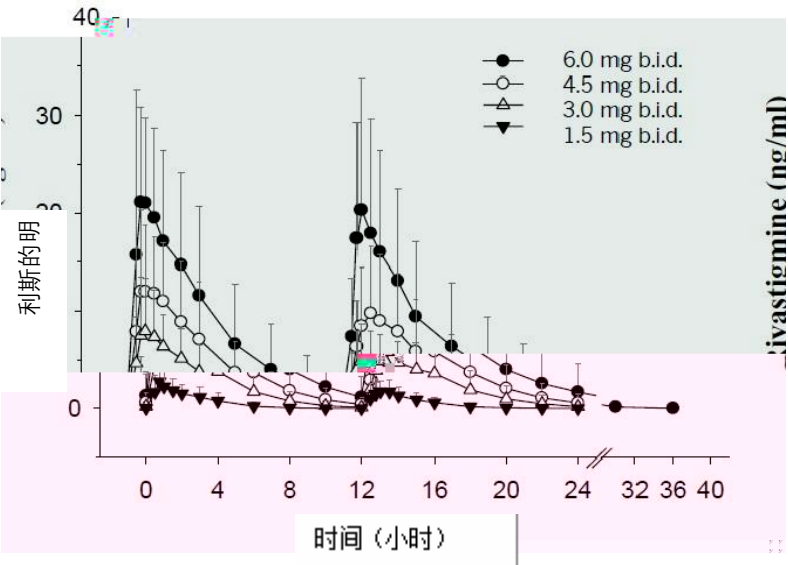
1 24



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%

AUC

2

/

1

40%

/

/

3.5

---

24

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](http://www.luye.cn)

\_\_\_\_\_?

•

•

•

1

•

•

•

•

•

•

24

•

14

•

•

•

2

•

3

•

•

1

1

?

A

- 
- 
- 
- 

A

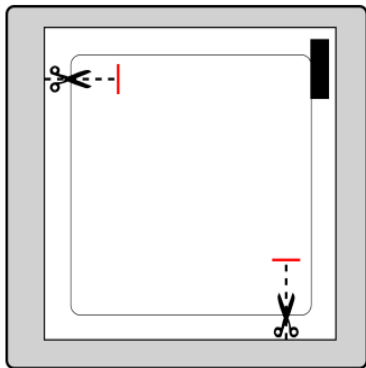


:

1.

B

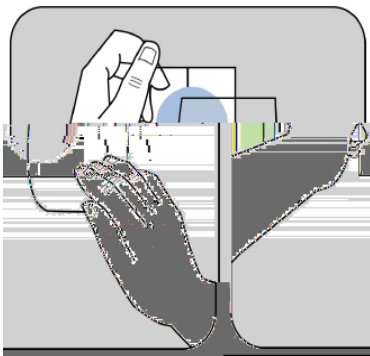
**B**



2.

**C**

**C**

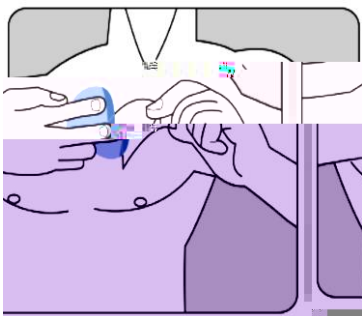


3.

4.

( **D** )

**D**



5.

**E**

**E**

