

**Supplementary Table 1 : Baseline demographics and clinical characteristics of study population (N=36).**

| Variables                                    | Infusion dose of remimazolam besylate ( $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) |                   |                   |
|--|--|-------------------|-------------------|
|  | 0.100<br>(n = 12)  | 0.125<br>(n = 12) | 0.150<br>(n = 12) |
|  |  |                   |                   |
| Male   | 7 (58.3)   | 7 (58.3)          | 9 (75.0)          |
| Age, years                                   | 52.6 $\pm$ 13.5  | 58.2 $\pm$ 11.7   | 55.1 $\pm$ 16.0   |
| Weight, kg                                   | 58.9 $\pm$ 8.2   | 62.7 $\pm$ 8.9    | 62.9 $\pm$ 14.1   |
| APACHE II score                              | 7.3 $\pm$ 3.1  | 8.6 $\pm$ 4.2     | 7.8 $\pm$ 3.4     |
| Duration of remimazolam besylate infusion, h | 10.8 $\pm$ 1.7   | 11.4 $\pm$ 2.4    | 11.7 $\pm$ 1.8    |
| Duration of mechanical ventilation, h        | 14.5 [12.3, 19.8]  | 17.5 [13.0, 19.8] | 14.5 [13.0, 15.8] |
| ICU length of stay, h                        | 21.5 [15.3, 34.3]  | 19.5 [14.0, 22.0] | 18.5 [16.3, 23.5] |
| Medical history                              |  |                   |                   |
| Hypertension                                 | 2 (16.7)   | 5 (41.7)          | 3 (25.0)          |
| Coronary artery disease                      | 1 (8.3)  | 2 (16.7)          | 2 (16.7)          |
| Valvular heart disease                       | 1 (8.3)  | 1 (8.3)           | 1 (8.3)           |
| Arrhythmia                                   | 1 (8.3)  | 2 (16.7)          | 1 (8.3)           |
| Diabetes mellitus                            | 0 (0.0)  | 1 (8.3)           | 1 (8.3)           |
| COPD   | 0 (0.0)  | 1 (8.3)           | 2 (16.7)          |
| Cerebrovascular disease                      | 0 (0.0)  | 1 (8.3)           | 1 (8.3)           |
| Cancer                                       | 2 (16.7)   | 1 (8.3)           | 5 (41.7)          |
| Autoimmune disease                           | 2 (16.7)   | 1 (8.3)           | 0 (0.0)           |
| Liver dysfunction                            | 1 (8.3)  | 1 (8.3)           | 0 (0.0)           |
| Surgical site                                |  |                   |                   |
| Upper abdomen                                | 1 (8.3)  | 0 (0.0)           | 1 (8.3)           |
| Lower abdomen                                | 4 (33.3)   | 2 (16.7)          | 3 (25.0)          |
| Spine and extremity                          | 6 (50.0)   | 7 (58.3)          | 7 (58.3)          |
| Urinary system                               | 1 (8.3)  | 1 (8.3)           | 1 (8.3)           |
| Others                                       | 0 (0.0)  | 2 (16.7)          | 0 (0.0)           |

Data are presented as mean  $\pm$  standard deviation, median [interquartile range] or n (%). APACHE II: acute physiology and chronic health evaluation II; COPD: chronic obstructive pulmonary disease.

**Supplementary Table 2: Baseline laboratory tests and arterial blood gases of study population (N=36).**

| Variables                            | Normal range | Infusion dose of remimazolam besylate ( $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) |                   |                   |
|--------------------------------------|--------------|--|-------------------|-------------------|
|                                      |              | 0.100<br>(n = 12)  | 0.125<br>(n = 12) | 0.150<br>(n = 12) |
| <b>Laboratory tests</b>              |              |  |                   |                   |
| Hemoglobin, g/L                      | 130 – 175    | 98.1 (22.5)  | 103.3 (29.3)      | 103.6 (22.0)      |
| Leucocytes, $\times 10^9 / \text{L}$ | 3.5 – 9.5    | 10.1 (3.0)   | 9.7 (5.0)         | 10.5 (4.0)        |
| Platelets, $\times 10^9 / \text{L}$  | 125 – 350    | 180.8 (76.4)   | 193.5 (101.1)     | 228.9 (118.3)     |
| Alanine aminotransferase, U/L        | 21 – 72      | 32.5 [21.3, 89.5]  | 29.0 [22.8, 36.5] | 32.0 [24.0, 73.5] |
| Total bilirubin, $\mu\text{mol/L}$   | 3 – 22       | 16.2 [11.9, 20.6]  | 8.4 [6.6, 12.1]   | 16.1 [11.3, 18.8] |
| Serum creatinine, $\mu\text{mol/L}$  | 58 – 110     | 48.5 (18.2)  | 64.2 (14.4)       | 59.2 (17.8)       |
| Prothrombin time, s                  | 11 – 16      | 15.4 (1.3)   | 14.9 (1.3)        | 15.1 (1.0)        |
| APTT, s                              | 28.0 – 43.5  | 39.4 (5.1)   | 38.5 (6.1)        | 38.3 (3.4)        |
| Fibrinogen, g/L                      | 2.0 – 4.0    | 3.5 (1.3)  | 3.2 (1.8)         | 3.1 (1.4)         |
| Creatine kinase MB, ng/mL            | <6.6         | 2.6 [1.4, 9.4]   | 1.7 [1.0, 2.3]    | 5.1 [1.4, 9.2]    |
| Hypersensitive troponin I, ng/L      | <26.2        | 4.6 [2.4, 9.9]   | 2.6 [1.7, 7.5]    | 8.5 [4.0, 13.3]   |
| <b>Arterial blood gases</b>          |              |  |                   |                   |
| pH                                   | 7.35 – 7.45  | 7.40 (0.07)  | 7.39 (0.07)       | 7.35 (0.06)       |
| $\text{PaO}_2/\text{FiO}_2$          | 400 – 500    | 307 [283, 443]   | 353 [203, 513]    | 322 [290, 378]    |
| $\text{PaCO}_2$ , mm Hg              | 35 – 45      | 38.6 (8.2)   | 40.5 (8.6)        | 41.3 (7.0)        |
| Lactate, mmol/L                      | 0.5 – 1.6    | 1.3 [0.8, 1.9]   | 1.2 [0.8, 2.1]    | 1.2 [0.9, 2.4]    |

Data are presented as mean (standard deviation) or median [interquartile range].

APTT: Activated partial thromboplastin time;  $\text{PaO}_2$ : partial pressure of oxygen;  $\text{FiO}_2$ : fraction of inspired oxygen;  $\text{PaCO}_2$ : partial pressure of carbon dioxide.

**Supplementary Table 3: Requirement for propofol during remimazolam besylate infusion.**

| Variables           | Infusion dose of remimazolam besylate ( $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) |                   |                   |
|---------------------|--|-------------------|-------------------|
|                     | 0.100<br>(n = 12)  | 0.125<br>(n = 12) | 0.150<br>(n = 12) |
| Ever                | 6 (50.0)   | 3 (25.0)          | 3 (25.0)          |
| Bolus only          | 2 (16.7)   | 2 (16.7)          | 0 (0.0)           |
| Continuous infusion | 4 (33.3)   | 1 (8.3)           | 3 (25.0)          |

Data are presented as n (%).

**Supplementary Table 4: Incidence of adverse events during remimazolam besylate infusion.**

| Adverse event | Total<br>(n = 36) | Infusion dose of remimazolam besylate ( $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ) |                   |                   |
|---------------|-------------------|--|-------------------|-------------------|
|               |                   | 0.100<br>(n = 12)  | 0.125<br>(n = 12) | 0.150<br>(n = 12) |
| Hypotension   | 9                 | 2  | 4                 | 3                 |
| Bradycardia   | 1                 | 0  | 0                 | 1                 |
| Tachycardia   | 6                 | 4  | 0                 | 2                 |
| Nausea        | 1                 | 1  | 0                 | 0                 |
| Vomiting      | 1                 | 0  | 1                 | 0                 |