**Supplementary digital content**

**Supplementary table 1.** Time schedule for the study.

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| --- | --- |
| **Event/procedure** | **Scheduled time** |
| Induction of anesthesia | 07:00 |
| Surgical preparation | 07:30 |
| First trauma (femur fractures, thorax contusion) | 08:15 |
| Hemodilution | 08:25 |
| Second trauma (liver injury) | 09:15 |
| Start of study drug administration | 09:20 |
| Start of observation period | 09:50 |
| End of observation period | 13:20 |

**Supplementary table 2.** Blood loss and survival results. Data are shown as mean ± standard deviation.

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| --- | --- | --- |
| **Study group** | **Total blood loss after the second trauma [mL]** | **Duration of survival after completion of study treatment [min]** |
| Control | 1671 ± 409 | 179 ± 52 |
| PCC | 907 ± 132 | 210 ± 0 |
| PCC+AT50 | 672 ± 63 | 210 ± 0 |
| PCC+AT25 | 535 ± 72 | 210 ± 0 |
| PCC+AT12.5 | 537 ± 50 | 210 ± 0 |
| FCH+PCC | 719 ± 115 | 130 ± 50 |
| FCH+PCC+AT50 | 640 ± 80 | 210 ± 0 |
| TXA+FCH+PCC | 588 ± 98 | 189 ± 23 |
| TXA+FCH+PCC+AT50 | 538 ± 91 | 210 ± 0 |

**Supplementary table 3.** Coagulation parameters. Data are shown as mean ± standard deviation.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Timepoint** | **Study group** | **PT [s]** | **aPTT [s]** | **Fibrinogen [g/L]** | **Anithrombin**  **[%]** | **D-Dimer**  **[mg/L]** | **TAT [μg/L]** |
| Baseline | Control | 10 ± 1 | 10 ± 1 | 1.5 ± 0.2 | 100 ± 12 | 0.5 ± 0.1 | 26 ± 14 |
| PCC | 10 ± 1 | 10 ± 1 | 1.6 ± 0.2 | 101 ± 13 | 0.4 ± 0.2 | 19 ± 12 |
| PCC+AT50 | 9 ± 1 | 10 ± 1 | 1.7 ± 0.2 | 99 ± 15 | 0.6 ± 0.7 | 27 ± 19 |
| PCC+AT25 | 10 ± 2 | 9 ± 0 | 1.4 ± 0.2 | 107 ± 7 | 0.3 ± 0.1 | 55 ± 25 |
| PCC+AT12.5 | 9 ± 1 | 9 ± 1 | 1.8 ± 0.2 | 110 ± 5 | 0.5 ± 0.3 | 35 ± 13 |
| FCH+PCC | 10 ± 1 | 10 ± 1 | 1.6 ± 0.2 | 97 ± 7 | 0.7 ± 0.5 | 22 ± 11 |
| FCH+PCC+AT50 | 10 ± 1 | 10 ± 2 | 1.8 ± 0.2 | 99 ± 10 | 0.4 ± 0.1 | 30 ± 20 |
| TXA+FCH+PCC | 10 ± 0 | 11 ± 1 | 1.6 ± 0.3 | 102 ± 14 | 0.4 ± 0.4 | 38 ± 28 |
| TXA+FCH+PCC+AT50 | 10 ± 1 | 11 ± 1 | 1.6 ± 0.3 | 92 ± 8 | 0.4 ± 0.3 | 31 ± 20 |
| Hemorr-hagic shocka | Control | 12 ± 1 | 11 ± 1 | 0.6 ± 0.1 | 52 ± 12 | 3.0 ± 1.6 | 38 ± 30 |
| PCC | 13 ± 1 | 11 ± 1 | 0.6 ± 0.1 | 46 ± 6 | 2.0 ± 0.6 | 27 ± 8 |
| PCC+AT50 | 13 ± 1 | 11 ± 1 | 0.6 ± 0.1 | 49 ± 8 | 1.7 ± 0.5 | 30 ± 9 |
| PCC+AT25 | 14 ± 2 | 10 ± 1 | 0.5 ± 0.1 | 49 ± 6 | 1.8 ± 0.6 | 28 ± 15 |
| PCC+AT12.5 | 12 ± 1 | 10 ± 1 | 0.7 ± 0.1 | 48 ± 5 | 2.2 ± 0.5 | 80 ± 30 |
| FCH+PCC | 13 ± 1 | 11 ± 1 | 0.5 ± 0.1 | 39 ± 9 | 2.1 ± 1.0 | 28 ± 5 |
| FCH+PCC+AT50 | 11 ± 2 | 11 ± 2 | 0.7 ± 0.1 | 48 ± 8 | 2.7 ± 0.7 | 30 ± 12 |
| TXA+FCH+PCC | 14 ± 1 | 11 ± 2 | 0.6 ± 0.1 | 52 ± 13 | 2.3 ± 0.7 | 37 ± 13 |
| TXA+FCH+PCC+AT50 | 12 ± 1 | 13 ± 1 | 0.6 ± 0.1 | 45 ± 8 | 2.6 ± 0.5 | 35 ± 19 |
| Comple-tion of study drug administr-ationb | Control | 15 ± 2 | 12 ± 1 | 0.5 ± 0.1 | 46 ± 10 | 2.5 ± 0.9 | 43 ± 16 |
| PCC | 13 ± 2 | 13 ± 2 | 0.5 ± 0.1 | 39 ± 2 | 2.0 ± 0.3 | 505 ± 275 |
| PCC+AT50 | 13 ± 1 | 13 ± 1 | 0.5 ± 0.1 | 145 ± 12 | 1.8 ± 0.4 | 475 ± 145 |
| PCC+AT25 | 13 ± 3 | 12 ± 2 | 0.5 ± 0.1 | 94 ± 10 | 1.6 ± 0.5 | 988 ± 721 |
| PCC+AT12.5 | 11 ± 1 | 12 ± 1 | 0.6 ± 0.0 | 69 ± 4 | 2.4 ± 0.4 | 887 ± 350 |
| FCH+PCC | 8 ± 1 | 11 ± 1 | 2.0 ± 0.2 | 38 ± 8 | 2.4 ± 0.8 | 331 ± 237 |
| FCH+PCC+AT50 | 9 ± 0 | 12 ± 1 | 2.0 ± 0.2 | 136 ± 17 | 2.4 ± 1.0 | 350 ± 171 |
| TXA+FCH+PCC | 9 ± 1 | 12 ± 2 | 2.0 ± 0.2 | 47 ± 14 | 2.1 ± 0.8 | 404 ± 176 |
| TXA+FCH+PCC+AT50 | 9 ± 1 | 13 ± 0 | 1.9 ± 0.3 | 117 ± 15 | 2.8 ± 0.6 | 401 ± 209 |
| 30 min after study drug administr-ation | Control | 15 ± 1 | 12 ± 1 | 0.4 ± 0.1 | 45 ± 10 | 2.3 ± 0.8 | 41 ± 20 |
| PCC | 16 ± 5 | 43 ± 69 | 0.4 ± 0.1 | 41 ± 3 | 13.4 ± 9.7 | 1319 ± 794 |
| PCC+AT50 | 13 ± 1 | 13 ± 1 | 0.5 ± 0.1 | 142 ± 11 | 5.5 ± 6.5 | 737 ± 187 |
| PCC+AT25 | 14 ± 3 | 13 ± 2 | 0.5 ± 0.1 | 94 ± 9 | 2.2 ± 0.7 | 986 ± 409 |
| PCC+AT12.5 | 12 ± 2 | 12 ± 1 | 0.6 ± 0.1 | 71 ± 5 | 4.2 ± 1.1 | 958 ± 382 |
| FCH+PCC | 8 ± 1 | 12 ± 1 | 2.0 ± 0.2 | 37 ± 7 | 2.5 ± 0.8 | 767 ± 258 |
| FCH+PCC+AT50 | 9 ± 1 | 11 ± 1 | 2.0 ± 0.2 | 125 ± 14 | 6.5 ± 6.1 | 693 ± 283 |
| TXA+FCH+PCC | 9 ± 0 | 14 ± 1 | 1.8 ± 0.2 | 44 ± 15 | 2.0 ± 0.9 | 833 ± 367 |
| TXA+FCH+PCC+AT50 | 9 ± 0 | 12 ± 1 | 1.9 ± 0.4 | 117 ± 12 | 2.4 ± 0.5 | 843 ± 426 |
| 90 min after study drug administr-ation | Control | 17 ± 2 | 12 ± 1 | 0.4 ± 0.1 | 44 ± 10 | 2.0 ± 0.5 | 44 ± 14 |
| PCC | 89 ± 70 | 122 ± 98 | 0.2 ± 0.2 | 38 ± 5 | 91 ± 61 | 2060 ± 1280 |
| PCC+AT50 | 13 ± 1 | 14 ± 1 | 0.6 ± 0.1 | 136 ± 11 | 7.6 ± 5.8 | 751 ± 186 |
| PCC+AT25 | 14 ± 3 | 15 ± 3 | 0.5 ± 0.1 | 96 ± 11 | 10.8 ± 10.1 | 1083 ± 644 |
| PCC+AT12.5 | 14 ± 3 | 16 ± 4 | 0.5 ± 0.1 | 73 ± 6 | 26.2 ± 19.1 | 1121 ± 474 |
| FCH+PCC | 8 ± 1 | 13 ± 2 | 1.7 ± 0.2 | 37 ± 8 | 87.7 ± 107.1 | 869 ± 408 |
| FCH+PCC+AT50 | 9 ± 1 | 12 ± 2 | 1.7 ± 0.1 | 121 ± 14 | 7.1 ± 7.7 | 643 ± 228 |
| TXA+FCH+PCC | 9 ± 1 | 14 ± 1 | 1.8 ± 0.2 | 52 ± 15 | 125.6 ± 190.5 | 634 ± 164 |
| TXA+FCH+PCC+AT50 | 9 ± 1 | 12 ± 1 | 1.7 ± 0.2 | 115 ± 9 | 2.2 ± 0.5 | 954 ± 502 |
| 150 min after study drug administr-ation | Control | 18 ± 3 | 13 ± 1 | 0.4 ± 0.1 | 42 ± 9 | 1.8 ± 0.6 | 51 ± 28 |
| PCC | 107 ± 88 | 149 ± 87 | 0.1 ± 0.1 | 34 ± 6 | 208.4 ± 129.3 | 2010 ± 1370 |
| PCC+AT50 | 14 ± 1 | 15 ± 1 | 0.5 ± 0.1 | 128 ± 10 | 16 ± 10.1 | 755 ± 238 |
| PCC+AT25 | 17 ± 5 | 17 ± 7 | 0.4 ± 0.2 | 96 ± 9 | 27 ± 26 | 991 ± 477 |
| PCC+AT12.5 | 22 ± 12 | 23 ± 10 | 0.3 ± 0.2 | 65 ± 8 | 57.4 ± 43.7 | 952 ± 468 |
| FCH+PCC | 10 ± 1 | 15 ± 4 | 1.2 ± 0.4 | 40 ± 10 | 301.4 ± 226.4 | 631 ± 271 |
| FCH+PCC+AT50 | 10 ± 1 | 12 ± 2 | 1.6 ± 0.1 | 115 ± 13 | 37.1 ± 69.0 | 572 ± 174 |
| TXA+FCH+PCC | 10 ± 1 | 16 ± 2 | 1.4 ± 0.2 | 53 ± 14 | 203.7 ± 158.3 | 613 ± 213 |
| TXA+FCH+PCC+AT50 | 9 ± 1 | 13 ± 1 | 1.5 ± 0.2 | 110 ± 12 | 40.5 ± 100.1 | 901 ± 367 |
| 210 min after study drug administr-ation | Control | 18 ± 5 | 13 ± 1 | 0.4 ± 0.1 | 41 ± 9 | 2.0 ± 0.8 | 89 ± 75 |
| PCC | 149 ± 87 | 152 ± 82 | 0.0 ± 0.1 | 30 ± 10 | 248.6 ± 175.7 | 1604 ± 1000 |
| PCC+AT50 | 14 ± 2 | 16 ± 2 | 0.5 ± 0.1 | 126 ± 11 | 27.1 ± 19.9 | 729 ± 232 |
| PCC+AT25 | 19 ± 7 | 17 ± 5 | 0.3 ± 0.2 | 94 ± 7 | 41.6 ± 38.1 | 903 ± 612 |
| PCC+AT12.5 | 24 ± 14 | 23 ± 11 | 0.3 ± 0.4 | 58 ± 28 | 56.8 ± 58.9 | 1078 ± 551 |
| FCH+PCC | 10 ± 0 | 14 ± 2 | 1.1 ± 0.4 | 46 ± 1 | 193 ± 179.6 | 452 ± 69 |
| FCH+PCC+AT50 | 10 ± 1 | 13.7 ± 2 | 1.5 ± 0.2 | 117 ± 14 | 68.2 ± 79.4 | 580 ± 161 |
| TXA+FCH+PCC | 11 ± 2 | 18 ± 4 | 1.1 ± 0.3 | 48 ± 16 | 210 ± 165.4 | 614 ± 335 |
| TXA+FCH+PCC+AT50 | 10 ± 1 | 13 ± 1 | 1.4 ± 0.2 | 112 ± 17 | 42.2 ± 65.6 | 678 ± 392 |

a 10 minutes after the first trauma; b 30 minutes after the second trauma. aPTT, activated partial thromboplastin time; PT, prothrombin time; TAT, thrombin–antithrombin complex.

**Supplementary table 4.** Hemodynamic variables, lactate and hemoglobin levels, and platelet counts. Data are shown as mean ± standard deviation.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Timepoint** | **Study group** | **Heart rate**  **[bpm]** | **Cardiac output**  **[L/min]** | **MPAP**  **[mmHg]** | **Lactate**  **[mmol/L]** | **Hemoglobin [g/dL]** | **Platelets [x103/µL]** |
| Baseline | Control | 91 ± 7 | 4.2 ± 0.6 | 20 ± 4 | 1.6 ± 0.5 | 9.5 ± 0.8 | 333 ± 34 |
| PCC | 93 ± 4 | 4.3 ± 0.5 | 20 ± 5 | 1.4 ± 0.1 | 8.8 ± 0.4 | 347 ± 41 |
| PCC+AT50 | 94 ± 5 | 4.1 ± 0.4 | 19 ± 2 | 1.5 ± 0.5 | 9.1 ± 0.5 | 319 ± 44 |
| PCC+AT25 | 91 ± 5 | 4.4 ± 0.6 | 16 ± 3 | 1.6 ± 0.2 | 10.1 ± 0.4 | 336 ± 40 |
| PCC+AT12.5 | 90 ± 6 | 4.2 ± 0.5 | 17 ± 3 | 1.3 ± 0.4 | 10.1 ± 0.3 | 313 ± 49 |
| FCH+PCC | 88 ± 5 | 3.7 ± 0.4 | 18 ± 3 | 1.6 ± 0.9 | 9.2 ± 0.7 | 291 ± 40 |
| FCH+PCC+AT50 | 85 ± 9 | 4.0 ± 0.3 | 20 ± 2 | 1.3 ± 0.2 | 9.3 ± 0.9 | 315 ± 45 |
| TXA+FCH+PCC | 90 ± 6 | 4.3 ± 0.6 | 17 ± 2 | 1.6 ± 0.6 | 9.5 ± 0.5 | 315 ± 27 |
| TXA+FCH+PCC+AT50 | 89 ± 4 | 4.2 ± 0.6 | 18 ± 3 | 1.4 ± 0.3 | 9.7 ± 0.5 | 318 ± 96 |
| Hemorr-hagic shocka | Control | 116 ± 23 | 4.3 ± 1.0 | 16 ± 3 | 4.5 ± 0.9 | 5.3 ± 2.4 | 167 ± 16 |
| PCC | 118 ± 24 | 4.7 ± 1.3 | 17 ± 2 | 3.5 ± 0.7 | 4.4 ± 0.7 | 175 ± 17 |
| PCC+AT50 | 112 ± 12 | 5.0 ± 0.6 | 19 ± 3 | 3.4 ± 0.7 | 4.1 ± 0.3 | 157 ± 20 |
| PCC+AT25 | 101 ± 21 | 4.7 ± 0.9 | 15 ± 4 | 3.2 ± 0.3 | 4.6 ± 0.6 | 178 ± 23 |
| PCC+AT12.5 | 107 ± 13 | 4.9 ± 0.7 | 15 ± 5 | 2.7 ± 0.7 | 4.4 ± 0.3 | 148 ± 42 |
| FCH+PCC | 106 ± 19 | 4.0 ± 0.3 | 16 ± 5 | 3.4 ± 1.5 | 4.0 ± 0.6 | 146 ± 25 |
| FCH+PCC+AT50 | 106 ± 16 | 4.5 ± 0.7 | 19 ± 3 | 3.2 ± 0.8 | 4.5 ± 0.5 | 174 ± 27 |
| TXA+FCH+PCC | 114 ± 15 | 4.3 ± 0.9 | 15 ± 4 | 3.4 ± 1.0 | 4.6 ± 0.1 | 157 ± 21 |
| TXA+FCH+PCC+AT50 | 111 ± 8 | 4.2 ± 0.8 | 16 ± 2 | 3.1 ± 0.9 | 4.8 ± 0.5 | 162 ± 18 |
| Comple-tion of study drug administr-ationb | Control | 136 ± 21 | 3.4 ± 0.9 | 14 ± 2 | 6.2 ± 1.4 | 4.0 ± 0.4 | 145 ± 22 |
| PCC | 115 ± 11 | 4.1 ± 0.6 | 13 ± 2 | 4.6 ± 1.1 | 3.6 ± 0.6 | 142 ± 34 |
| PCC+AT50 | 104 ± 18 | 3.9 ± 0.3 | 16 ± 4 | 3.9 ± 0.9 | 3.7 ± 0.4 | 145 ± 18 |
| PCC+AT25 | 99 ± 12 | 3.9 ± 0.4 | 13 ± 3 | 3.2 ± 0.7 | 4.4 ± 0.6 | 161 ± 23 |
| PCC+AT12.5 | 107 ± 12 | 4.0 ± 0.5 | 11 ± 4 | 3.0 ± 1.3 | 4.1 ± 0.3 | 138 ± 42 |
| FCH+PCC | 100 ± 13 | 3.8 ± 0.6 | 17 ± 8 | 3.8 ± 1.5 | 3.6 ± 0.4 | 136 ± 22 |
| FCH+PCC+AT50 | 101 ± 13 | 4.1 ± 1.1 | 16 ± 2 | 3.7 ± 1.2 | 3.6 ± 0.2 | 154 ± 20 |
| TXA+FCH+PCC | 119 ± 20 | 4.3 ± 0.7 | 14 ± 2 | 4.2 ± 1.5 | 3.6 ± 0.2 | 129 ± 22 |
| TXA+FCH+PCC+AT50 | 110 ± 20 | 3.7 ± 0.5 | 14 ± 3 | 3.5 ± 0.9 | 3.8 ± 0.3 | 146 ± 22 |
| 30 min after study drug administr-ation | Control | 143 ± 26 | 3.7 ± 0.9 | 14 ± 1 | 6.7 ± 1.5 | 3.6 ± 0.6 | 133 ± 18 |
| PCC | 115 ± 13 | 3.7 ± 0.9 | 16 ± 4 | 4.9 ± 2.1 | 3.6 ± 0.3 | 120 ± 30 |
| PCC+AT50 | 96 ± 15 | 4.1 ± 0.3 | 16 ± 3 | 3.7 ± 1.0 | 3.5 ± 0.3 | 140 ± 13 |
| PCC+AT25 | 97 ± 15 | 4.0 ± 0.3 | 13 ± 3 | 3.3 ± 1.0 | 4.1 ± 0.5 | 145 ± 24 |
| PCC+AT12.5 | 104 ± 18 | 4.0 ± 0.5 | 12 ± 4 | 2.8 ± 1.4 | 4.0 ± 0.2 | 143 ± 32 |
| FCH+PCC | 100 ± 13 | 3.5 ± 1.3 | 17 ± 7 | 3.7 ± 0.9 | 3.3 ± 0.2 | 118 ± 28 |
| FCH+PCC+AT50 | 102 ± 10 | 4.2 ± 0.6 | 15 ± 2 | 3.4 ± 1.2 | 3.5 ± 0.2 | 142 ± 20 |
| TXA+FCH+PCC | 106 ± 16 | 4.0 ± 0.6 | 15 ± 2 | 4.3 ± 1.8 | 3.3 ± 0.2 | 110 ± 36 |
| TXA+FCH+PCC+AT50 | 113 ± 29 | 3.5 ± 0.6 | 14 ± 3 | 3.4 ± 0.7 | 3.7 ± 0.4 | 137 ± 19 |
| 90 min after study drug administr-ation | Control | 143 ± 28 | 3.6 ± 0.5 | 14 ± 1 | 7.2 ± 1.9 | 3.2 ± 0.3 | 114 ± 25 |
| PCC | 115 ± 10 | 3.6 ± 0.6 | 17 ± 4 | 5.1 ± 3.6 | 3.5 ± 0.4 | 81 ± 38 |
| PCC+AT50 | 90 ± 12 | 4.0 ± 0.3 | 16 ± 3 | 3.3 ± 1.6 | 3.4 ± 0.4 | 133 ± 19 |
| PCC+AT25 | 105 ± 17 | 3.9 ± 0.6 | 14 ± 3 | 3.1 ± 1.4 | 4.2 ± 0.7 | 123 ± 27 |
| PCC+AT12.5 | 104 ± 22 | 3.7 ± 0.4 | 13 ± 4 | 2.1 ± 1.0 | 4.0 ± 0.1 | 120 ± 43 |
| FCH+PCC | 117 ± 18 | 3.2 ± 0.8 | 26 ± 7 | 3.5 ± 1.0 | 3.3 ± 0.3 | 75 ± 35 |
| FCH+PCC+AT50 | 92 ± 13 | 3.9 ± 0.4 | 16 ± 1 | 2.9 ± 1.1 | 3.3 ± 0.2 | 131 ± 13 |
| TXA+FCH+PCC | 106 ± 27 | 3.7 ± 0.8 | 17 ± 4 | 4.0 ± 2.1 | 3.1 ± 0.3 | 102 ± 23 |
| TXA+FCH+PCC+AT50 | 115 ± 30 | 3.6 ± 0.7 | 14 ± 4 | 3.0 ± 0.5 | 3.7 ± 0.3 | 123 ± 20 |
| 150 min after study drug administr-ation | Control | 121 ± 27 | 3.0 ± 1.2 | 16 ± 3 | 8.0 ± 2.8 | 2.7 ± 0.4 | 95 ± 19 |
| PCC | 114 ± 15 | 3.6 ± 0.5 | 20 ± 7 | 4.9 ± 3.8 | 3.5 ± 0.3 | 66 ± 29 |
| PCC+AT50 | 89 ± 17 | 3.9 ± 0.4 | 16 ± 3 | 2.9 ± 1.7 | 3.3 ± 0.3 | 115 ± 18 |
| PCC+AT25 | 107 ± 15 | 3.7 ± 0.4 | 15 ± 4 | 2.3 ± 0.9 | 4.1 ± 0.5 | 108 ± 25 |
| PCC+AT12.5 | 103 ± 20 | 3.8 ± 0.4 | 14 ± 4 | 1.7 ± 0.7 | 3.9 ± 0.2 | 97 ± 36 |
| FCH+PCC | 111 ± 23 | 2.0 ± 1.5 | 29 ± 4 | 3.9 ± 2.5 | 3.3 ± 0.3 | 75 ± 39 |
| FCH+PCC+AT50 | 88 ± 13 | 3.9 ± 0.4 | 17 ± 2 | 2.4 ± 0.9 | 3.3 ± 0.2 | 124 ± 15 |
| TXA+FCH+PCC | 94 ± 21 | 3.3 ± 0.7 | 24 ± 7 | 4.4 ± 2.8 | 3.2 ± 0.2 | 76 ± 22 |
| TXA+FCH+PCC+AT50 | 108 ± 22 | 3.6 ± 0.5 | 14 ± 3 | 2.7 ± 0.7 | 3.5 ± 0.2 | 109 ± 18 |
| 210 min after study drug administr-ation | Control | 122 ± 33 | 3.0 ± 1.1 | 16 ± 4 | 8.1 ± 3.9 | 2.7 ± 0.4 | 91 ± 21 |
| PCC | 108 ± 16 | 3.1 ± 0.9 | 22 ± 7 | 5.0 ± 3.9 | 3.3 ± 0.5 | 56 ± 26 |
| PCC+AT50 | 90 ± 18 | 3.9 ± 0.3 | 17 ± 3 | 2.7 ± 2.1 | 3.4 ± 0.3 | 114 ± 17 |
| PCC+AT25 | 108 ± 22 | 3.6 ± 0.5 | 16 ± 5 | 2.0 ± 0.9 | 4.1 ± 0.7 | 101 ± 27 |
| PCC+AT12.5 | 101 ± 20 | 3.6 ± 0.5 | 16 ± 3 | 1.7 ± 0.7 | 3.7 ± 0.3 | 85 ± 41 |
| FCH+PCC | 103 ± 14 | 3.4 ± 0.7 | 32 ± 5 | 2.6 ± 1.2 | 3.5 ± 0.2 | 75 ± 35 |
| FCH+PCC+AT50 | 93 ± 13 | 3.8 ± 0.5 | 17 ± 2 | 2.3 ± 1.1 | 3.5 ± 0.3 | 115 ± 11 |
| TXA+FCH+PCC | 93 ± 12 | 2.4 ± 1.4 | 29 ± 4 | 4.5 ± 2.4 | 3.3 ± 0.4 | 57 ± 23 |
| TXA+FCH+PCC+AT50 | 106 ± 18 | 3.5 ± 0.6 | 15 ± 3 | 2.9 ± 1.5 | 3.5 ± 0.1 | 99 ± 27 |

a 10 minutes after the first trauma; b 30 minutes after the second trauma. MPAP, mean pulmonary arterial pressure.

**Supplementary table 5.** Thromboelastometry variables, measured in whole blood by ROTEM. Data are shown as mean ± standard deviation.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Timepoint** | **Study group** | **EXTEM CT**  **[s]** | **EXTEM CFT  [s]** | **EXTEM MCF**  **[mm]** | **NATEM CT**  **[s]** | **NATEM CFT [s]** | **NATEM MCF [mm]** |
| Baseline | Control | 50 ± 4 | 42 ± 4 | 73 ± 1 | 521 ± 60 | 121 ± 20 | 69 ± 5 |
| PCC | 42 ± 3 | 35 ± 5 | 75 ± 2 | 581 ± 146 | 136± 36 | 71 ± 6 |
| PCC+AT50 | 46 ± 6 | 41 ± 7 | 74 ± 2 | 520 ± 91 | 107 ± 26 | 73 ± 2 |
| PCC+AT25 | 41 ± 5 | 49 ± 4 | 70 ± 2 | 431 ± 103 | 106 ± 25 | 67 ± 4 |
| PCC+AT12.5 | 39 ± 1 | 46 ± 3 | 73 ± 1 | 455 ± 122 | 145 ± 60 | 71 ± 1 |
| FCH+PCC | 50 ± 9 | 37 ± 8 | 74 ± 2 | 546 ± 118 | 132 ± 34 | 72 ± 4 |
| FCH+PCC+AT50 | 49 ± 10 | 41 ± 7 | 75 ± 3 | 512 ± 196 | 134 ± 65 | 73 ± 3 |
| TXA+FCH+PCC | 53 ± 8 | 48 ± 8 | 71 ± 2 | 585 ± 252 | 175 ± 104 | 69 ± 5 |
| TXA+FCH+PCC+AT50 | 49 ± 5 | 43 ± 5 | 73 ± 3 | 551 ± 132 | 156 ± 54 | 70 ± 6 |
| Hemorr-hagic shocka | Control | 55 ± 13 | 72 ± 11 | 61 ± 4 | 379 ± 113 | 117 ± 26 | 61 ± 3 |
| PCC | 46 ± 5 | 71 ± 5 | 62 ± 2 | 349 ± 122 | 91 ± 33 | 62 ± 4 |
| PCC+AT50 | 44 ± 6 | 75 ± 12 | 61 ± 3 | 315 ± 115 | 84 ± 24 | 63 ± 2 |
| PCC+AT25 | 39 ± 7 | 89 ± 11 | 58 ± 4 | 391 ± 216 | 120 ± 39 | 58 ± 4 |
| PCC+AT12.5 | 40 ± 7 | 84 ± 6 | 60 ± 3 | 267 ± 84 | 93 ± 18 | 62 ± 2 |
| FCH+PCC | 53 ± 10 | 74 ± 8 | 61 ± 3 | 434 ± 122 | 122 ± 46 | 58 ± 5 |
| FCH+PCC+AT50 | 53 ± 11 | 72 ± 15 | 62 ± 5 | 368 ± 61 | 89 ± 10 | 62 ± 3 |
| TXA+FCH+PCC | 58 ± 8 | 82 ± 8 | 57 ± 2 | 335 ± 87 | 106 ± 27 | 58 ± 3 |
| TXA+FCH+PCC+AT50 | 59 ± 13 | 68 ± 11 | 60 ± 5 | 394 ± 54 | 102 ± 20 | 59 ± 6 |
| Comple-tion of study drug administr-ationb | Control | 64 ± 13 | 87 ± 9 | 56 ± 3 | 375 ± 98 | 119 ± 31 | 55 ± 2 |
| PCC | 50 ± 6 | 89 ± 6 | 55 ± 2 | 247 ± 74 | 92 ± 7 | 58 ± 3 |
| PCC+AT50 | 45 ± 9 | 84 ± 11 | 58 ± 3 | 317 ± 78 | 97 ± 16 | 61 ± 3 |
| PCC+AT25 | 49 ± 19 | 95 ± 14 | 53 ± 5 | 277 ± 109 | 111 ± 20 | 57 ± 2 |
| PCC+AT12.5 | 40 ± 7 | 96 ± 17 | 55 ± 5 | 197 ± 65 | 91 ± 15 | 59 ± 4 |
| FCH+PCC | 37 ± 4 | 49 ± 5 | 65 ± 2 | 350 ± 52 | 90 ± 13 | 68 ± 2 |
| FCH+PCC+AT50 | 40 ± 7 | 44 ± 10 | 69 ± 4 | 347 ± 60 | 79 ± 11 | 69 ± 2 |
| TXA+FCH+PCC | 37 ± 3 | 58 ± 14 | 61 ± 4 | 283 ± 73 | 84 ± 17 | 64 ± 2 |
| TXA+FCH+PCC+AT50 | 42 ± 4 | 47 ± 5 | 67 ± 3 | 357 ± 79 | 92 ± 26 | 68 ± 3 |
| 30 min after study drug administr-ation | Control | 66 ± 10 | 96 ± 12 | 53 ± 4 | 379 ± 93 | 128 ± 31 | 53 ± 3 |
| PCC | 78 ± 35 | 168 ± 113 | 46 ± 9 | 307 ± 34 | 179 ± 129 | 49 ± 11 |
| PCC+AT50 | 47 ± 5 | 87 ± 11 | 57 ± 3 | 247 ± 39 | 87 ± 12 | 61 ± 3 |
| PCC+AT25 | 50 ± 12 | 102 ± 14 | 52 ± 5 | 251 ± 64 | 110 ± 10 | 57 ± 4 |
| PCC+AT12.5 | 40 ± 8 | 102 ± 12 | 54 ± 4 | 230 ± 51 | 103 ± 9 | 58 ± 1 |
| FCH+PCC | 35 ± 5 | 64 ± 28 | 63 ± 7 | 276 ± 70 | 81 ± 9 | 69 ± 1 |
| FCH+PCC+AT50 | 41 ± 5 | 47 ± 12 | 68 ± 4 | 303 ± 79 | 76 ± 15 | 70 ± 2 |
| TXA+FCH+PCC | 39 ± 3 | 70 ± 26 | 58 ± 7 | 302 ± 70 | 103 ± 23 | 63 ± 6 |
| TXA+FCH+PCC+AT50 | 41 ± 4 | 51 ± 8 | 66 ± 2 | 330 ± 79 | 97 ± 24 | 68 ± 2 |
| 90 min after study drug administr-ation | Control | 63 ± 10 | 121 ± 7 | 51 ± 2 | 459 ± 135 | 154 ± 41 | 50 ± 2 |
| PCC | 644 ± 927 | 777 ± 849 | 42 ± 8 | 924 ± 848 | 1073 ± 1016 | 41 ± 18 |
| PCC+AT50 | 51 ± 5 | 95 ± 16 | 57 ± 4 | 283 ± 68 | 93 ± 16 | 60 ± 3 |
| PCC+AT25 | 49 ± 22 | 132 ± 40 | 49 ± 5 | 246 ± 47 | 178 ± 119 | 49 ± 7 |
| PCC+AT12.5 | 65 ± 26 | 137 ± 39 | 49 ± 6 | 253 ± 52 | 133 ± 34 | 52 ± 6 |
| FCH+PCC | 36 ± 6 | 90 ± 30 | 59 ± 5 | 286 ± 62 | 125 ± 34 | 59 ± 8 |
| FCH+PCC+AT50 | 40 ± 7 | 56 ± 12 | 66 ± 3 | 331 ± 67 | 90 ± 21 | 69 ± 2 |
| TXA+FCH+PCC | 43 ± 9 | 81 ± 20 | 58 ± 6 | 336 ± 49 | 114 ± 16 | 63 ± 4 |
| TXA+FCH+PCC+AT50 | 39 ± 3 | 54 ± 9 | 66 ± 1 | 346 ± 101 | 108 ± 31 | 68 ± 1 |
| 150 min after study drug administr-ation | Control | 76 ± 14 | 133 ± 24 | 48 ± 5 | 396 ± 134 | 162 ± 44 | 48 ± 3 |
| PCC | 876 ± 845 | 1280 ± 905 | 25 ± 18 | 1185 ± 945 | 1013 ± 925 | 40 ± 11 |
| PCC+AT50 | 58 ± 13 | 112 ± 19 | 54 ± 4 | 266 ± 74 | 100 ± 19 | 57 ± 3 |
| PCC+AT25 | 71 ± 35 | 192 ± 76 | 45 ± 8 | 327 ± 55 | 204 ± 83 | 46 ± 7 |
| PCC+AT12.5 | 82 ± 74 | 377 ± 516 | 44 ± 12 | 328 ± 103 | 527 ± 601 | 40 ± 14 |
| FCH+PCC | 46 ± 16 | 141 ± 73 | 51 ± 11 | 329 ± 115 | 186 ± 94 | 51 ± 15 |
| FCH+PCC+AT50 | 42 ± 6 | 61 ± 15 | 67 ± 3 | 343 ± 48 | 96 ± 24 | 68 ± 2 |
| TXA+FCH+PCC | 56 ± 22 | 127 ± 44 | 51 ± 9 | 383 ± 132 | 168 ± 62 | 56 ± 8 |
| TXA+FCH+PCC+AT50 | 40 ± 2 | 65 ± 7 | 64 ± 2 | 290 ± 74 | 112 ± 37 | 66 ± 3 |
| 210 min after study drug administr-ation | Control | 74 ± 15 | 134 ± 34 | 47 ± 5 | 469 ± 215 | 238 ± 188 | 48 ± 5 |
| PCC | 1134 ± 913 | 1516 ± 830 | 25 ± 18 | 1044 ± 885 | 1306 ± 909 | 32 ± 12 |
| PCC+AT50 | 60 ± 11 | 118 ± 26 | 54 ± 5 | 292 ± 106 | 116 ± 26 | 54 ± 5 |
| PCC+AT25 | 95 ± 43 | 217 ± 116 | 42 ± 8 | 328 ± 55 | 246 ± 156 | 43 ± 10 |
| PCC+AT12.5 | 130 ± 96 | 627 ± 720 | 37 ± 14 | 421 ± 174 | 703 ± 779 | 37 ± 12 |
| FCH+PCC | 41 ± 3 | 137 ± 77 | 54 ± 11 | 263 ± 0 | 88 ± 0 | 44 ± 16 |
| FCH+PCC+AT50 | 43 ± 6 | 65 ± 17 | 65 ± 3 | 358 ± 112 | 112 ± 48 | 67 ± 2 |
| TXA+FCH+PCC | 60 ± 31 | 209 ± 90 | 44 ± 13 | 373 ± 122 | 236 ± 73 | 47 ± 11 |
| TXA+FCH+PCC+AT50 | 42 ± 3 | 75 ± 14 | 62 ± 3 | 333 ± 81 | 130 ± 33 | 65 ± 3 |

a 10 minutes after the first trauma; b 30 minutes after the second trauma. CFT, clot formation time; CT, clotting time; MCF, maximum clot firmness.

**Supplementary table 6.** Thrombin generation results, as measured using a calibrated automated thrombogram. Data are shown as mean ± standard deviation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Timepoint** | **Study group** | **Lagtime [s]** | **Peak Height [nM]** | **ETP [nM\*min]** |
| Baseline | Control | 3 ± 0.6 | 78 ± 3 | 246 ± 19 |
| PCC | 3 ± 0.8 | 82 ± 19 | 248 ± 65 |
| PCC+AT50 | 4 ± 0.4 | 70 ± 6 | 219 ± 16 |
| PCC+AT25 | 4 ± 0.5 | 72 ± 7 | 222 ± 23 |
| PCC+AT12.5 | 4 ± 0.8 | 78 ± 7 | 229 ± 35 |
| FCH+PCC | 3 ± 0.4 | 82 ± 9 | 246 ± 37 |
| FCH+PCC+AT50 | 3 ± 0.3 | 73 ± 13 | 220 ± 19 |
| TXA+FCH+PCC | 3 ± 0.6 | 76 ± 9 | 222 ± 31 |
| TXA+FCH+PCC+AT50 | 3 ± 0.5 | 81 ± 15 | 241 ± 51 |
| Hemorrhagic shocka | Control | 2 ± 0.3 | 80 ± 11 | 290 ± 19 |
| PCC | 2 ± 0.4 | 83 ± 11 | 288 ± 39 |
| PCC+AT50 | 2 ± 0.1 | 74 ± 8 | 273 ± 37 |
| PCC+AT25 | 2 ± 0.4 | 81 ± 10 | 272 ± 54 |
| PCC+AT12.5 | 2 ± 0.4 | 82 ± 10 | 260 ± 28 |
| FCH+PCC | 2 ± 0.3 | 75 ± 4 | 278 ± 37 |
| FCH+PCC+AT50 | 2 ± 0.2 | 77 ± 7 | 266 ± 15 |
| TXA+FCH+PCC | 2 ± 0.3 | 73 ± 8 | 274 ± 44 |
| TXA+FCH+PCC+AT50 | 2 ± 0.3 | 83 ± 13 | 285 ± 66 |
| Completion of study drug administrationb | Control | 2 ± 0.2 | 71 ± 7 | 275 ± 25 |
| PCC | 2 ± 0.5 | 264 ± 32 | 1484 ± 569 |
| PCC+AT50 | 2 ± 0.2 | 160 ± 15 | 769 ± 84 |
| PCC+AT25 | 2 ± 0.3 | 179 ± 28 | 1080 ± 155 |
| PCC+AT12.5 | 2 ± 0.3 | 220 ± 29 | 1414 ± 235 |
| FCH+PCC | 2 ± 0.6 | 265 ± 29 | 1601 ± 972 |
| FCH+PCC+AT50 | 2 ± 0.3 | 175 ± 11 | 645 ± 286 |
| TXA+FCH+PCC | 2 ± 0.2 | 242 ± 37 | 1701 ± 493 |
| TXA+FCH+PCC+AT50 | 2 ± 0.4 | 195 ± 34 | 902 ± 176 |
| 30 min after study drug administration | Control | 2 ± 0.3 | 65 ± 7 | 271 ± 34 |
| PCC | 2 ± 0.6 | 252 ± 31 | 1640 ± 246 |
| PCC+AT50 | 2 ± 0.2 | 155 ± 9 | 708 ± 71 |
| PCC+AT25 | 2 ± 0.3 | 183 ± 21 | 986 ± 134 |
| PCC+AT12.5 | 2 ± 0.3 | 201 ± 27 | 1206 ± 228 |
| FCH+PCC | 2 ± 0.2 | 254 ± 33 | 1783 ± 308 |
| FCH+PCC+AT50 | 2 ± 0.3 | 169 ± 19 | 699 ± 77 |
| TXA+FCH+PCC | 2 ± 0.2 | 265 ± 45 | 1892 ± 333 |
| TXA+FCH+PCC+AT50 | 2 ± 0.3 | 190 ± 26 | 831 ± 151 |
| 90 min after study drug administration | Control | 2 ± 0.2 | 62 ± 10 | 254 ± 40 |
| PCC | 2 ± 0.5 | 197 ± 45 | 1367 ± 521 |
| PCC+AT50 | 2 ± 0.2 | 140 ± 12 | 627 ± 63 |
| PCC+AT25 | 2 ± 0.4 | 150 ± 18 | 834 ± 123 |
| PCC+AT12.5 | 2 ± 0.3 | 164 ± 25 | 963 ± 112 |
| FCH+PCC | 2 ± 0.2 | 179 ± 28 | 1792 ± 191 |
| FCH+PCC+AT50 | 2 ± 0.3 | 163 ± 18 | 625 ± 66 |
| TXA+FCH+PCC | 2 ± 0.2 | 184 ± 40 | 1843 ± 119 |
| TXA+FCH+PCC+AT50 | 2 ± 0.3 | 171 ± 29 | 701 ± 145 |
| 150 min after study drug administration | Control | 2 ± 0.3 | 56 ± 3 | 232 ± 17 |
| PCC | 2 ± 0.5 | 154 ± 47 | 1104 ± 291 |
| PCC+AT50 | 2 ± 0.1 | 127 ± 19 | 540 ± 79 |
| PCC+AT25 | 2 ± 0.3 | 126 ± 16 | 701 ± 96 |
| PCC+AT12.5 | 2 ± 0.3 | 140 ± 30 | 794 ± 71 |
| FCH+PCC | 2 ± 0.3 | 174 ± 24 | 1650 ± 254 |
| FCH+PCC+AT50 | 2 ± 0.3 | 150 ± 17 | 554 ± 61 |
| TXA+FCH+PCC | 2 ± 0.4 | 158 ± 34 | 1659 ± 378 |
| TXA+FCH+PCC+AT50 | 2 ± 0.3 | 153 ± 26 | 641 ± 122 |
| 210 min after study drug administration | Control | 2 ± 0.6 | 48 ± 9 | 187 ± 29 |
| PCC | 2 ± 0.5 | 128 ± 44 | 839 ± 266 |
| PCC+AT50 | 2 ± 0.2 | 110 ± 16 | 466 ± 65 |
| PCC+AT25 | 2 ± 0.3 | 119 ± 23 | 634 ± 121 |
| PCC+AT12.5 | 2 ± 0.2 | 123 ± 24 | 639 ± 75 |
| FCH+PCC | 2 ± 0.0 | 149 ± 23 | 1276 ± 419 |
| FCH+PCC+AT50 | 2 ± 0.3 | 135 ± 17 | 476 ± 59 |
| TXA+FCH+PCC | 2 ± 0.2 | 149 ± 34 | 1353 ± 355 |
| TXA+FCH+PCC+AT50 | 2 ± 0.2 | 134 ± 32 | 560 ± 113 |

a 10 minutes after the first trauma; b 30 minutes after the second trauma. ETP, endogenous thrombin potential.