**Supplement Table 1. Experimental Uses of HAE Treatment Agents in Cardiac Surgery**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Study Type** | **Population** | **Age** | **Wt or BMI** | **Treatment** | **Dose** | **CPB time min** | **Main findings** | **Safety Outcomes** |
| Thielman, et al.2006 133 | RCT(open label) | CABG after STEMI | 64 (10) | 77 (11)kg | C1-INH (n=28) | 40 IU/kg | 121 (44) | C1-INH level >80% from preop to 48h postop; lower troponin C at 36h if C1-INH given <6h of | No drug related AE's; No difference in 30-day mortality: 14.3% with C1-INH vs. 13.8% in control (NS) |
|  |  | 65 (9) | 79 (13)kg | Control (n=29) | N.A. | 118 (49) | C1-INH level <70% beween 1-16 h postop; trend for elevated C4 fragment in 24-48 h (NS vs.C1-INH) |  |
| Bokesch, et al. 2012 137 | RCT(double blind) | Mixed Cardiac Surgery (incl. multiple valves,aortic repl., and CABG) | 69.6 (8.2) | 78.3 (13.2)kg | Ecallantide (n=109) | 130 µg/kg i.v.+infusion 140 µg/kg/h | 129 (65.1) | Increased RBC transfusion with ecallantide vs. TXA (median, 900 vs. 300 ml, P<0.001) | Higher 30-day mortality: 12% with ecallantide vs. 4% with TXA (P=0.041); early termination of the RCT |
|  |  | 66.8 (10.8)yr | 81.0 (15.7)kg | TXA (n=109) | Two dosing regimen (\*) | 130 (50.9) | High-dose TXA group received less RBCs than low- dose group (median, zero vs. 400 ml, P=0.008) |  |
| Balaguer, et al. 2013 141 | RCT(double blind) | Mixed Cardiac Surgery (mostly valves and 10%CABG) | 61.0 (2.0)yr | 28.3 (0.9)kg/m2 | Icatibant (n=40) | 22 µg/kg i.v. + infusion at 18µg/kg/h | 115 (5.9) | Elevated tPA during CPB in all groups (NS); no difference in transfusion rate or nadir bloodpressure on CPB | No difference in postoperative atrial fibrillation, pacemaker need, AKI, length of stay, and 30-dayreadmission rate. |
|  |  | 58.5 (2.0)yr | 27.2 (0.8)kg/m2 | EACA(n=37) | 100 mg/kg i.v.+ 30 mg/kg/h | 122 (6.3) | Least D-dimer elevation in EACA group |  |
| 60.1 (1.8)yr | 27.5 (0.8)kg/m2 | Placebo (n=38) | N.A. | 112 (6.0) |  |
| Miyamoto, et al. Observational | Congenital Heart | 9.5 mo | 6.6 (5.5-6.8) | C1-INH | 20 IU/kg | 258 | C1-INH 20 IU/kg i.v. after 60 min on CPB showed | 6 patients excluded due to mortality (whether there was |
| 2019 136 series | Surgery | (6-11) | kg | (n=8) |  | (228-261) | trends for better preservation of C1-INH and C1q, | any association with C1-INH treatment was not |
|  |  |  |  |  |  |  | but no differences in C3, C4, and CH50 after 48h | documented) |
|  |  | 4.5 mo | 5.0 (3.6-7.3) | Control | N.A. | 262 |  |  |
| (3-8.8) | kg | (n=26) |  | (221-289) |

Data are shown as mean (SD) or median (25-75% quartile). Abbreviations: AE=adverse event; AKI=acute kidney insufficiency; C1-INH=C1-esterase inhibitor; C3=complement 3 level; C4=complement 4 level; CABG=coronary artery bypass grafting; CH50=50% hemolytic complement activity test (to test classical complement comsumption); CPB=cardiopulmoary bypass; h=hour(s); EACA=epsilon-aminocaproic acid; h=hour; IU=internatinal unit; min=minute; N.A.=not applicalbe; N.S.=statistically not significant; pd=plasma-derived; preop=preoperative, postop=postoperative; POD=postoperative day; qd=every day; bid=twice a day; rh=recombinant human; TXA=tranexamic acid; RBC=red blood cells; RCT=randomized controlled trial; yr=year-

old