Tocilizumab reduces cardiac injury after out-of-hospital cardiac arrest primarily in patients without acute revascularization - Results from a randomized trial, The IMICA trial

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BACKGROUND: Patients remaining comatose after the initial resuscitation from out-of-hospital cardiac arrest (OHCA) have a high risk of morbidity and mortality as part of the ensuing post cardiac arrest syndrome (PCAS). Systemic inflammation and myocardial dysfunction are constituents of PCAS. The cytokine Interleukin-6 (IL-6) is associated with PCAS severity and poor outcome. Also, the extend of cardiac injury is a prognostic marker. We have recently shown that the IL-6 receptor antagonist tocilizumab dampens systemic inflammation and cardiac injury after cardiac arrest.

PURPOSE: To investigate if the reduction in cardiac injury by tocilizumab is differentiated in patients undergoing acute coronary revascularization compared to those who do not.

METHODS: Eighty comatose OHCA patients were randomized 1:1 in a double-blinded placebo-controlled trial to a single infusion of tocilizumab or placebo in addition to standard of care including targeted temperature management. Trial registration: Clinicaltrials.gov NCT03863015. Blood samples were sequentially drawn for biomarker analysis. Endpoints were markers of cardiac injury and inflammation: Troponin T (TnT), N-terminal pro B-type natriuretic peptide (NT-proBNP), and C-reactive protein (CRP). Continuous variables were log2 transformed and analyzed using mixed models; values shown as geometric mean with 95%-confidence limits [95%CL] after back-transformation.

RESULTS: Thirty-nine patients were randomized to treatment with tocilizumab and 41 to placebo. In the tocilizumab group 15 (39%) patients underwent acute revascularization (all PCI), and this was 22 (54%) for placebo. Patients not undergoing acute revascularization had a marked reduction by treatment with tocilizumab in TnT at 6h, as well as NT-proBNP at 48h (Figure). For patients treated with acute revascularization there was no significant group difference in TnT at 6h, whereas there was a marked reduction in NT-proBNP at 48h. There was a substantial reduction in CRP by treatment with tocilizumab irrespective of whether acute revascularization was performed.

CONCLUSION: Treatment with tocilizumab resulted in a significant reduction in myocardial injury as measured by TnT primarily in patients not undergoing acute revascularization, whereas the reduction in NT-proBNP, as well as CRP, was seen irrespective of whether acute revascularization was performed.

Abstract Figure. Acute vs. NO acute revascularization