

### Online supplementary file S3 OVATION-65 ancillary studies

Study title	Investigators	Primary objective	Secondary objective	Funding
Measuring baseline ascorbic acid levels in the OVATION-65 trial	MC Battista NK Adhikari F Lamontagne	Measure the associations between baseline level of plasma ascorbic acid and peak levels of biomarkers of organ injury* (measured at day 1 [baseline], day 3, and 7) in the permissive hypotension and usual care groups.  Organ injury biomarkers are specified in Table 1 of the manuscript.	Measure the association between baseline ascorbic acid and  1) total dose of vasopressors required to maintain blood pressure;  2) biomarkers of inflammation* (IL-1 $\beta$ , TNF- $\alpha$ , C-reactive protein)  3) biomarkers of endothelial injury* (thrombomodulin, angiopoietin-2)	Lotte and John Hecht Memorial Foundation
Urinary biomarkers of renal injury in the OVATION-65 trial: a Nested analysis of the urinary proteome	FM Boisvert MC Battista NK Adhikari F Lamontagne	Identify and quantify, using a discovery proteomic approach, new peptides and proteins and their pattern of expression between baseline, day 3 and day 7 in the urine of patients in permissive hypotension and usual care groups.	Measure the association between protein clusters and renal function  Validate the predictive value of biomarkers of renal injury*: TIMP2, NGAL, FABPL, CYTC, IGFBP7	Université de Sherbrooke/ Merck Sharp and Dohme
Effects of catecholamine therapy on the immune system: unsuspected consequences of routine medical interventions and opportunities for individualized care	FM Boisvert LH Tai JL Parent X Roucou MC Battista NK Adhikari F Lamontagne	Compare PBMC immune response (Th1/Th2 profiles), adrenergic receptor activity, and proteomic signature between baseline and day 7 in the permissive hypotension and usual care groups		Université de Sherbrooke/ Merck Sharp and Dohme

Abbreviations: CYTC, cytochrome C; FABPL, fatty acid-binding protein, liver-type; IGFBP7, insulin-like growth factor-binding protein 7; IL-1 $\beta$ , interleukin-1 $\beta$ ; NGAL, neutrophil gelatinase-associated lipocalin; PBMC, peripheral blood mononuclear cell; TIMP2, tissue inhibitor of metalloproteinases 2; TNF- $\alpha$ , tumour necrosis factor- $\alpha$

\*All biomarkers are assessed at baseline (day 1) and at days 3 and 7.