

MEETING ABSTRACT

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# Clinical Trial: Heme Arginate in patients planned for Cardiac Surgery (HACS)

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From World Society of Cardiothoracic Surgeons 25th Anniversary Congress, Edinburgh  
Edinburgh, UK. 19-22 September 2015

## Background/Introduction

Acute kidney injury (AKI) is a significant complication of cardiac surgery and is associated with increased morbidity and mortality [1]. Despite much research, there is no specific therapy available. Although AKI can be multifactorial, ischaemia reperfusion injury (IRI) often plays a key role. Thus, cardiac surgery offers an attractive opportunity for translational AKI research given the predictive haemodynamic challenge to renal perfusion.

Hemeoxygenase-1 (HO-1) is a key inducible anti-inflammatory enzyme that catalyses the breakdown of the pro-oxidant protein heme ubiquitously found at inflamed sites. The drug heme arginate has been in use for over 20 years in the treatment of porphyria but also upregulates HO-1 in peripheral blood mononuclear cells (PBMCs) [2] and ameliorates calf muscle ischaemia [3]. In addition, treatment of mice with heme arginate prior to renal IRI strongly upregulates renal HO-1 expression and protects from AKI [4]. We therefore hypothesise that HA may offer a prophylactic therapy for human renal IRI via the upregulation of HO-1.

## Aims/Objectives

The HACS Trial aims to determine whether heme arginate will upregulate HO-1 in PBMCs in patients aged 60 or above who are scheduled for cardiac surgery, and to verify its safety in this patient cohort.

## Method

20 participants, who are scheduled for elective cardiac surgery, will be randomised to receive 1 mg/kg or 3 mg/kg heme arginate. The primary end point will be the difference in PBMC HO-1 protein from baseline at 24 hours.

Secondary end points include HO-1 gene expression, safety and HO-1 genotype.

## Results

Results are expected in July 2015. At the time of abstract submission, 14 of 20 participants have been recruited.

## Discussion/Conclusion

Data from the HACS trial will inform a subsequent multi-centre randomised controlled trial of heme arginate versus placebo in the prevention of AKI in patients deemed to be at higher risk of developing AKI post cardiac surgery

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Published: 16 December 2015

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doi:10.1186/1749-8090-10-S1-A69

Cite this article as: Duthie et al.: Clinical Trial: Heme Arginate in patients planned for Cardiac Surgery (HACS). *Journal of Cardiothoracic Surgery* 2015 **10**(Suppl 1):A69.

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