Supplementary Material

Supplementary Material..............................................................................................................1

†ATTIRE Trial Investigators: Group Authorship
  Trial Steering Committee.........................................................................................................2
  Independent Data Monitoring Committee....................................................................................2
  Data centre at University College Comprehensive Clinical Trials Unit (UCL CCTU)...............2
  Trial Management Group...........................................................................................................3
  University College London Comprehensive Clinical Trials Unit..............................................3
  Research Steering Committee.................................................................................................3
  Microbiology and Adverse Event Review Panel.......................................................................3
  ATTIRE Site Investigators.........................................................................................................3
  ATTIRE Clinical Trial Sites......................................................................................................3
  Trial Funding and Conduct.........................................................................................................4
  Acknowledgements..................................................................................................................4
  ATTIRE Study Protocol............................................................................................................5
ATTIRE Trial Investigators: Group Authorship

**Independent Data Monitoring Group:** Professor Dominique-Charles Valla* (CHAIR), Tim Clayton§ and Dr Vipul Jaraith#. 

**Data centre at University College Comprehensive Clinical Trials Unit (UCL CCTU):**
Kate Bennett^, Scott Bevan#, James Blackstone‡, Kashfia Chowdhury‡, Zainib Shabir‡ and Simon Skene^.

**Trial Steering Committee:** Professor Stephen Brett (CHAIR)§, John Crookenden (Patient Representative), Professor Shahid Khan#, Brennan Kahan†, Professor Graeme Alexander§, Professor Humphrey Hodgson§ and Professor Mike Murphy¥.

**Affiliations (United Kingdom unless stated)**

*Service d'Hépatologie, Hôpital Beaujon, 100 boulevard Général Leclerc, 92118, Clichy, France. dominique.valla@aphp.fr; †The London School of Hygiene and Tropical Medicine, Tim.Clayton@lshtm.ac.uk; #Western University and London Health Sciences Centre, Canada, vjairath@uwo.ca.

^Surrey Clinical Trials Unit, University of Surrey, c.bennetteastley@surrey.ac.uk and s.skene@surrey.ac.uk; Bristol Medical School, Bristol, s.bevan@bristol.ac.uk; and ‡Comprehensive Clinical Trials Unit, University College London, j.blackstone@ucl.ac.uk.

§Imperial College London/Imperial College NHS Trust, United Kingdom stephen.brett@imperial.ac.uk and shahid.khan@imperial.ac.uk; †MRC Clinical Trials Unit at UCL, b.kahan@ucl.ac.uk; §Institute of Liver and Digestive Health, University College London, gja1000@doctors.org.uk and h.hodgson@ucl.ac.uk; and ¥University of Oxford, mike.murphy@nhsbt.nhs.uk.
Trial Management Group

Dr Louise China, Dr Ewan H Forrest, Dr Yiannis Kallis, Jim Portal, Professor Stephen Ryder and Dr Gavin Wright.

UCL CCTU

Dr Ana Arbeloa del Moral, James Blackstone, Kashfia Chowdhury, Dr Ana Carolina Estevao, Rosie Hamilton, Ms Khadra Mohamoud and Dr Nicola Muirhead.

Research Steering Committee

Professor Mauro Bernardi (CHAIR), Paula Milton (Department of Health and Social Care representative) and Nicola Shepherd (Wellcome Trust representative).

Microbiology and Adverse Event Review Panel

Dr Indran Balakrishnan, Dr Mark McPhail, Dr Brian Hogan and Dr Jane Abbott.

ATTIRE Site Investigators

Professor Aftab Ala, Dr Richard Aspinall, Dr Andrew Austin, Dr C Lye Ch'ng, Dr Jeremy Cobbold, Dr Lynsey Corless, Dr Alexandra Daley, Professor Matthew Cramp, Dr Ahmed Elsharkawy, Dr Alex Evans, Prof Graham Foster, Dr Shaun Greer, Dr Mathis Heydtmann, Dr Coral Hollywood, Dr Peter Isaacs, Professor Rajiv Jalan, Dr Richard Keld, Dr Andrew King, Dr Stuart McPherson, Dr Judith Morris, Professor Jane Metcalf, Dr Richard Parker, Dr Janisha Patel, Dr Francisco Porraz-Perez, Dr Praveen Rajasekhar, Dr John Ramage, Dr Paul Richardson, Dr Dariush Sadigh, Dr Deepak Suri, Dr Esther Unit, Professor Sumita Verma and Dr Earl Williams.

ATTIRE Clinical Trial Sites

Trial funding

The work was funded by the Health Innovation Challenge fund (Wellcome Trust and Department of Health and Social Care) HICF reference HICF-R8-439, WT grant number WT102568 awarded to Alastair O'Brien.

This publication presents independent research commissioned by the Health Innovation Challenge Fund, a parallel funding partnership between the Department of Health and Wellcome Trust. The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health and Social Care or Wellcome Trust.

The 20% Human Albumin Solution used was taken from routine hospital stocks throughout the UK and this was funded wholly by the Wellcome Trust and Department of Health and Social Care grant to Professor O'Brien.

Trial Conduct

ATTIRE was conducted and reported according to the protocol, the Medicines for Human Use (Clinical Trials) Regulations 2004, (amended 2006), the European Union Clinical Trials Directive (2001/20/EC) guidelines, the principles of the International Conference on Harmonisation Good Clinical Practice under oversight of the University College London Comprehensive Clinical Trials Unit (UCL CCTU) and provisions of the Declaration of Helsinki.

Acknowledgements

The authors acknowledge funding from the Wellcome Trust and Department of Health and Social Care, the National Institute for Health Research Clinical Research Network for providing research nurse support, the University College London Comprehensive Clinical Trials Unit for trial management activities and University College London for sponsoring the trial.
ATTIRE Study Protocol

Patient admitted to hospital with complication of cirrhosis

- Meets inclusion criteria
  - Albumin <30g/L at enrolment*
  - Expected Admission from enrolment to be >5 days
  - Consent obtained within 72 hours

Patient enrolled & randomised for study

Treatment arm:
- Daily 20% Human Albumin Solution

- Daily 20% HAS infusions with clinicians targeting an ↑ in serum albumin to ≥35g/L throughout intervention period**

Control arm:
- Standard of Care

- Standard treatment as would have been given should the patient not have been involved in the trial***

Daily measurement of new infection, organ dysfunction, serious adverse events and patient location

End of trial intervention period: discharge or 14 days or death

Primary Endpoint:
- Composite of new infection, renal dysfunction or death
  (measured from D3 of intervention period until the day after completion of intervention period D15)

Secondary endpoints:
- Mortality, Liver Transplantation

* Which could be any time point on days 1-3 (72 hours) of admission.

** See table S2 for infusion protocol. The study aim was for treatment arm patients to achieve and sustain a serum albumin ≥30g/L. This was achieved by asking site clinicians to target a serum albumin of ≥35g/L.

*** This can only include albumin as recommended in international evidence based guidance: LVP, SBP & HRS.