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Registries and research

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Research priorities in single-ventricle heart conditions: a United Kingdom national study

Original Article

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Abstract

Objective: To bring together stakeholders in the United Kingdom to establish national priorities for research in single-ventricle heart conditions. **Methods:** This study comprised two surveys and a workshop. The initial public online survey asked respondents up to three questions they would like answered for research. Responses were classified as unanswered, already answered, or unable to be answered by scientific research. In the follow-up survey, unanswered questions were divided into categories and respondents were asked to rank categories and questions by priority. A stakeholder workshop attended by patients, parents, healthcare professionals, researchers, and charities was held to determine the final list of research priorities. **Results:** A total of 128 respondents posed 344 research questions, of which 271 were classified as unanswered, and after removing duplicates, 204 questions remained, which were divided into 20 categories. In the second survey, 56 (49.1%) respondents successfully ranked categories and questions. A total of 39 participants attended the workshop, drawing up a list of 30 research priorities across nine priority categories. The nine priority categories are: Associated co-morbidities; Brain & neurodevelopment; Exercise; Fontan failure; Heart function; Living with a single ventricle heart condition; Management of the well-functioning Fontan circulation; Surgery & perioperative care; and Transplantation, mechanical support & novel therapies. **Conclusions:** Through a multi-stage process, we engaged a wide range of interested parties to establish a list of research priorities in single-ventricle heart conditions. This provides a platform for clinicians, researchers, and funders in the United Kingdom and elsewhere to address the most important questions and improve outcomes in these rare but high-impact CHDs.

Priority questions suitable for a registry

Associated co-morbidities

- What are the outcomes in children with multiple co-morbidities?
- What are the common co-morbidities in children with a single ventricle heart condition?

Brain and neurodevelopment

- What factors influence neurodevelopmental outcomes in children with single ventricle heart conditions?
- What is the impact of a single ventricle heart condition on neurodevelopment?

Priority questions suitable for a registry

Fontan failure

- What are the best markers of deterioration in patients with a Fontan circulation?

Living with a single ventricle heart condition

- What are the frequencies of symptoms, limitations, physical and emotional quality of life with a Fontan circulation?
- What are the long-term social, psychosocial and other non-clinical outcomes of children with single ventricle heart conditions?

Priority questions suitable for a registry

Management of the well-functioning Fontan circulation

- What factors best determine a well-functioning Fontan circulation?
- What is the optimal interval for follow-up of patients with a Fontan circulation?
- What is the impact of pregnancy on patients with a Fontan circulation and how can outcomes be improved?

Surgery and perioperative care

- Which modifiable perioperative factors can reduce mortality for the Norwood operation?
- How can perinatal risk stratification be used to identify those in whom the Norwood operation is futile?

Several registries are in existence and others planned

Australia and New Zealand Fontan registry

International Fontan registry

NPC -QIC

Fontan Outcomes Network

Two European Fontan registries

UK Fontan registry



Australia
and New
Zealand
Registry

since 2014

~1500 Fontan patients

~60 publications



Risks of certain outcomes

Balance of good versus bad



Outcomes

Death or transplantation
Hepatocellular carcinoma
Exercise outcomes
Arrhythmia
Brain structural changes
Lymphatic complications
Intellectual and cognition
Quality of life of whole family
Cause of death
Renal and liver outcomes
Growth trajectory
The Super Fontan
Pregnancy and fertility
Male sexual health

Intervention

Warfarin or aspirin
ACE inhibition
Pacing
Outcomes of surgical approaches
Role of Fontan conversion
Effect of forward flow
Age at Fontan
Outcomes of underlying anatomy
Fenestration
Obesity
Health economics

What's lacking in this and other registries



No mechanistic approach to research



We currently do not have any evidence based approach to care and clinical trials have focussed on PVR reduction



Fundamental problem is systemic venous hypertension but what does that lead to

Role of future registries

Prospective not
retrospective

Consent for
research

Establish patient
relevant outcomes

Interventional
clinical studies



West Midlands Secure Data Environment



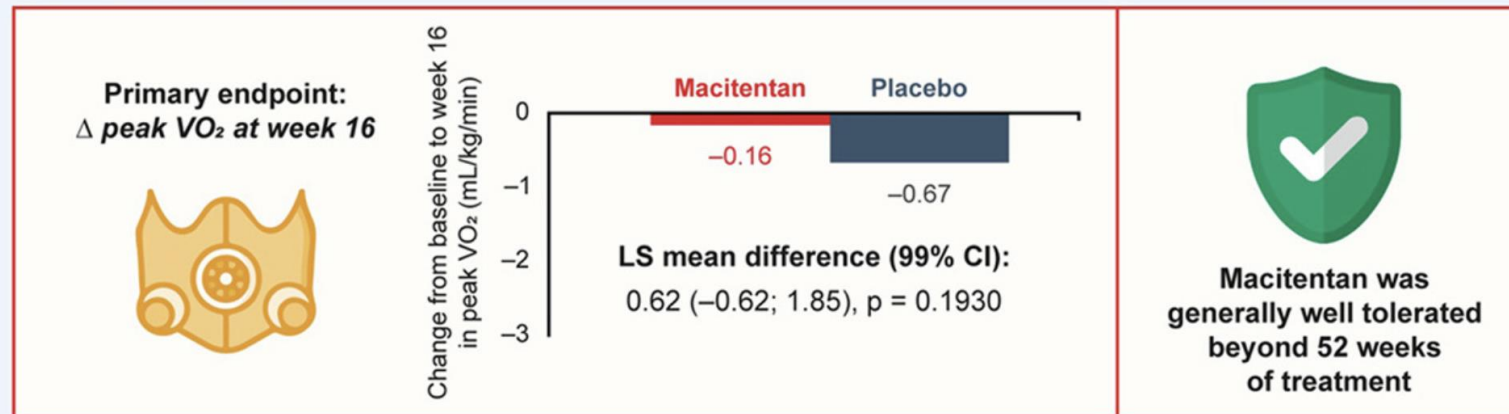
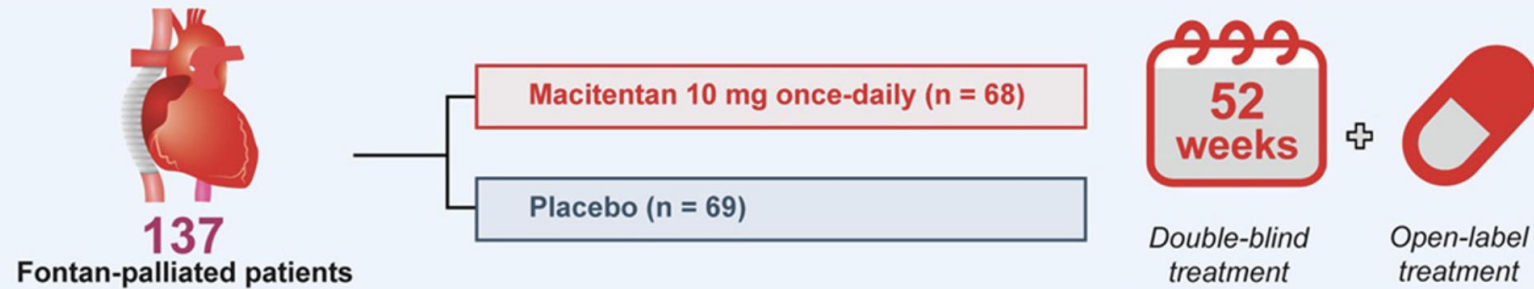
RUBATO

a critical
appraisal

Efficacy and safety of macitentan in Fontan-palliated patients: 52- week randomized, placebo- controlled RUBATO phase 3 trial and open-label extension

Dr. Paul Clift MD¹  , Prof. Felix Berger MD²,
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Efficacy and safety of macitentan in Fontan-palliated patients: 52-week Phase 3 RUBATO-DB trial and open-label extension



The RUBATO trial did not meet its primary endpoint: Macitentan was well tolerated but not efficacious in Fontan-palliated patients

RUBATO

a
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What does future clinical research look like

Collaborative

Multi-centre

Multi-national

Innovative trial design and appropriate endpoints

Interventions based on preliminary mechanistic studies

Involvement of patients and families throughout the process