Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health)

Pre-implantation Genetic Diagnosis (PGD) application for Right Atrial Isomerism (RAI), OMIM #208530

Thursday, 24 September 2020

HFEA, 10 Spring Gardens, London, SW1A 2BU via Teleconference

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Tony Rutherford Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Dr Jenny Carmichael	
Legal Adviser	Dawn Brathwaite	Mills & Reeve – LLP
Observers	Dee Knoyle Matthew Mudford (Induction) Cora Sweet (Induction)	Committee Officer Scientific Policy Officer Policy Officer

Declarations of interest:

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 9th edition of the HFEA Code of Practice.
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive Summary
- PGD Application Form
- Redacted Peer Review
- 2017-07-27 SAC minutes, PGD for X-linked heterotaxy-1 (HTX1) aka ZIC3 associated congenital heart defects and heterotaxy, OMIM #306955

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Jenny Carmichael, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Right Atrial Isomerism (RAI), OMIM #208530, is consistent with the peer review.

1.3. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.4. The committee noted that a Genetic Alliance UK statement had not been provided for this application.

1.5. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGD. The committee was also satisfied that the centre has experience of carrying out PGD and that generic patient information about its PGD programme and associated consent forms had previously been received by the HFEA.

1.6. The committee noted that the proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of Schedule 2 of the Act, i.e. 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

1.7. The committee noted that Right Atrial Isomerism (RAI), OMIM #208530, is inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation.

1.8. The committee noted that the penetrance of the condition is 100%.

1.9. Right Atrial Isomerism (RAI), OMIM #208530, is characterised by a set of complex heart defects which can lead to heart failure from birth, and death in the early months or years of life. The condition is also characterised by lack of/underdevelopment of the spleen, which carries a significant risk of infection.

1.10. There is no cure for this condition and treatment focuses on managing the symptoms. Surgical intervention is sometimes possible but often, is not successful.

1.11. The committee noted the executive's request to consider Right Atrial Isomerism (RAI), OMIM #208530, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee noted the recommendation of the peer reviewer to also include an additional condition for inclusion on the list for which PGD can be applied. The condition Congenital Heart Defects, Multiple Types 6 (CHTD6), OMIM #613854 is inherited in an autosomal recessive manner which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation. Those patients affected with the condition have complex congenital heart disease, which are associated with a high mortality, and additional complications such as neuro-developmental disorders and inguinal hernia.

1.13 The committee also noted the request of the executive to consider the autosomal dominant form of Congenital Heart Defects, Multiple Types 6 (CHTD6), OMIM #613854. The committee noted the advice of its specialist adviser, who indicated the use of an incomplete methodology to identify the condition and therefore agreed not to consider the autosomal dominant presentation of the condition at this time.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Right Atrial Isomerism (RAI), OMIM #208530 is a severe, and potentially fatal condition which presents with very complex heart defects prenatally or at birth. Life expectancy for those born with the condition is heavily

reduced with a significant number of children dying within the first year of life. There is no cure for the condition, and surgery to correct these severe cardiac anomalies is considered to be very high-risk. The committee considered the potentially devastating physical and psychological impact on the quality of life of those affected with the condition.

2.2. The committee considered in the worst-case scenario the condition Congenital Heart Defects, Multiple Types 6, OMIM #613854, is of a similar phenotype and presentation to Right Atrial Isomerism (RAI), OMIM #208530. The condition requires complex high-risk surgeries for survival.

2.3. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk that a person with such an abnormality will, given the condition's worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

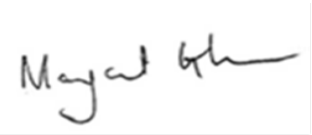
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Right Atrial Isomerism (RAI), OMIM #208530
- Congenital Heart Defects, Multiple Types 6 (CHTD6), OMIM #613854
  (NB This authorisation relates to the autosomal recessive type of the condition only)

3. Chairs signature

3.1. I confirm this is a true and accurate record of the meeting.

Signature



Name
Margaret Gilmore

Date
20 October 2020