Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Timothy Syndrome (TS), OMIM #601005

Thursday, 27 February 2020

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

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 Alan Fryer	
Legal Adviser	Tom Rider	FieldFisher - LLP
Observer	Emily Tiemann (Induction)	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
- Genetic Alliance UK statement
- 2019-10-31 SAC Minutes, PGD for Anderson Tawil Syndrome
- Gene Review article about Jervell and Lange Nielsen Syndrome

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for Timothy Syndrome (TS) #601005, 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 the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

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 Timothy Syndrome (TS) #601005, is inherited in an autosomal dominant manner which means there is 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted the condition is thought to be fully penetrant with a high mortality rate.

1.9. Timothy Syndrome (TS) #601005, is a rare genetic condition that causes heart abnormalities, (both heart rhythm abnormalities that can lead to sudden unexpected cardiac death and congenital structural heart defects), a weakened immune system leading to recurrent infections which can be fatal, developmental delay, autism, webbing of the fingers and toes that may require surgery and intermittently low levels of blood sugar (which can be fatal).

1.10. There is no cure for this condition and treatment focuses on managing the symptoms. Treatments aimed at stabilising the heart rhythm may not be successful in preventing sudden death.

1.11. The committee noted the executive's request to consider Timothy Syndrome #601005, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee also noted the recommendation of the executive to consider an additional two conditions for approval for which PGD can be applied. As confirmed by the peer reviewer Timothy Syndrome is a syndromic form of LQT (long QT syndrome). The two other syndromic forms of LQT for consideration are Jervell and Lange-Nielsen syndrome 1, (JLNS1), OMIM #220400, and Jervell and Lange-Nielsen syndrome 2, (JLNS2), OMIM #612347. The conditions are both inherited in an autosomal recessive pattern and are characterised by; profound congenital sensorineural hearing loss, prolonged QT interval, fainting, Torsades de pointes (a type of ventricular tachycardia) and sudden cardiac death. Those affected are at risk of early death, with more than half of untreated children with JLNS dying before the age of 15 years.

2. Decision

2.1. The committee considered that, in the worst-case scenario Timothy Syndrome (TS) #601005, is a rare, devastating, multi-system condition which presents soon after birth. There is no cure for the condition, which frequently leads to sudden unexpected death in infancy. The committee noted the serious implications and the impact on the quality of life for those affected with the condition.

2.2. With regard to Jervell and Lange-Nielsen Syndrome 1, (JLNS1), OMIM #220400, and Jervell and Lange-Nielsen Syndrome 2, (JLNS2), OMIM #612347, the committee considered that in the worst-case scenario these are serious early onset conditions resulting in profound deafness and the risk of sudden death in infancy.

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 abnormalities in question and that there is a significant risk that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

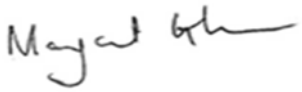
2.4. The committee was therefore satisfied that the following condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Timothy Syndrome (TS), OMIM #601005
- Jervell and Lange-Nielsen Syndrome 1, (JLNS1), OMIM #220400
- Jervell and Lange-Nielsen Syndrome 2, (JLNS2), OMIM #612347

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
17 March 2020