Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for Harel-Yoon Syndrome (HAYOS), OMIM #617183

Thursday, 27 August 2020

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

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Tony Rutherford	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Jane Williams	Mills & Reeve LLP

Declarations of interest:

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

Apologies:

- Apologies were received from Ruth Wilde.

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.

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Harel-Yoon Syndrome (HAYOS), OMIM #617183, 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 Harel-Yoon Syndrome (HAYOS), OMIM #617183, is generally inherited in an autosomal dominant manner, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation. Harel-Yoon Syndrome can also be inherited in an autosomal recessive manner (depending on the mutation affecting the gene), which means there is a 25% chance of having an affected child in each pregnancy if each parent has a relevant mutation.

1.8. The committee noted that the penetrance of the condition is not known. However, all affected people will have severe physical and mental disability, although the actual symptoms may vary between individuals.

1.9. Harel-Yoon Syndrome (HAYOS), OMIM #617183, is a progressive and life-limiting condition, characterised by serious symptoms which can include severe global developmental delay, hypotonia, intellectual disability, poor or absent speech, optic nerve atrophy leading to blindness, spasticity, seizures, ataxia, scoliosis, hip dysplasia, and hypertrophic cardiomyopathy.

1.10. There is no cure for this condition and treatment focuses on managing the symptoms of patients.

1.11. The committee noted the executive's request to consider Harel-Yoon Syndrome (HAYOS), OMIM #617183, 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 consider Pontocerebellar hypoplasia, hypotonia, and respiratory insufficiency syndrome, neonatal lethal, OMIM #618810, for inclusion on the list for which PGD can be applied. The condition is caused by biallelic deletions in the ATAD3 gene cluster (ATAD3A, ATAD3B and ATAD3C), and is inherited in an autosomal recessive manner, meaning the risk of inheriting the condition is 25% in each pregnancy if each parent has a relevant mutation.

1.13. Onset of Pontocerebellar hypoplasia, hypotonia, and respiratory insufficiency syndrome, neonatal lethal, OMIM #618810, occurs in utero, leading to death in the neonatal period. In rare cases, patients may survive a few months. Affected infants show respiratory insufficiency and almost no spontaneous movement at birth, usually requiring mechanical ventilation and intensive care. Additional features include corneal clouding, seizures, contractures, and progressive pontocerebellar hypoplasia. Some patients may have cardiac anomalies.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Harel-Yoon Syndrome (HAYOS), OMIM #617183, is a rare, progressive, and life-limiting neurodevelopmental disorder that presents in infancy. The condition leads to severe developmental delay, with additional features such as blindness, seizures, and cardiomyopathy. There is no cure for the condition and 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 that in the worst-case scenario, Pontocerebellar hypoplasia, hypotonia, and respiratory insufficiency syndrome, neonatal lethal, OMIM #618810, is a severe, lethal condition which commonly results in death in the neonatal period. There is no cure for this condition.

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 conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

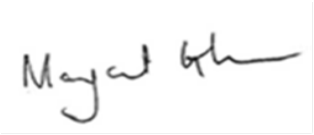
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Harel-Yoon Syndrome (HAYOS), OMIM #617183
- Pontocerebellar hypoplasia, hypotonia, and respiratory insufficiency syndrome, neonatal lethal, OMIM #618810

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
15 September 2020