Statutory Approvals Committee - minutes

Centre 0102 (Guys Hospital)

Preimplantation Genetic Diagnosis (PGD) application for Autosomal Recessive ATP1A2, OMIM *182340

Date:	29 April 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Jason Kasraie
Specialist Adviser:	Jenny Carmichael
Legal Adviser:	Darryn Hale – DAC Beachcroft LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Julia Chain - HFEA Chair (Induction) Tim Child - HFEA Authority Member (Induction) Neil Ward - Mills & Reeve LLP (New Legal Adviser) (Induction)
Apologies:	No apologies were received for the meeting
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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGD Application form
- Redacted Peer review
- Supporting Document - Chatron et al, 2019

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 ATP1A2, OMIM *182340, 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 this is a novel condition, and that the application does not reference an OMIM number. The OMIM website lists the gene ATPase, Na+/K+ transporting, alpha-2 polypeptide; ATP1A2 with the OMIM number *182340.

1.5. The committee noted that a Genetic Alliance (UK) statement has not been received for this application.

1.6. The committee had regard to its decision tree. The committee noted that the center is licensed to carry out PGD. The committee was also satisfied that the center 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.

1.7. 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'.

1.8. The committee noted that the condition applied for, caused by mutations in ATP1A2, OMIM *182340, 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.

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

1.10. The condition applied for, caused by mutations in ATP1A2, OMIM *182340, is characterized by widespread problems with brain development, including the area of the brain important in controlling breathing, resulting in severe respiratory failure. It is a lethal condition where affected babies die soon after birth if not given respiratory support. With medical support, those affected can survive for a few months.

1.11. There is no curative treatment for this condition.

1.12. The committee noted the executive's request to consider the condition applied for, caused by mutations in ATP1A2, OMIM *182340, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.13. The committee noted that the peer reviewer has described the condition applied for, caused by mutations in ATP1A2, OMIM *182340 as 'Polymicrogyria in association with homozygous/compound heterozygous ATP1A2 variants (autosomal recessive)' a heterogeneous, microscopic malformation of cortical development, defined by excessive folding of the cortical mantle that results in small gyri with a fused surface. Polymicrogyria is responsible for a wide range of neurological symptoms (e.g. epilepsy, intellectual disability, motor dysfunction). Some cases have a non-genetic cause, but it is recently recognised that homozygous or compound heterozygous mutations in the ATP1A2 gene can cause a lethal syndrome with multiple structural abnormalities of the brain, including polymicrogyria.

1.14. The committee noted the suggestion of the executive that if the application is approved, the committee should consider which of the following two names would be the most appropriate listing for ATP1A2, OMIM *182340, on the HFEA website:

- Homozygous or compound heterozygous ATP1A2 autosomal recessive disorder (AR ATP1A2), OMIM *182340, or
- Polymicrogyria in association with homozygous/compound heterozygous ATP1A2 variants (autosomal recessive), OMIM *182340

2. Decision

2.1. The committee considered that, in the worst-case scenario, the condition applied for, caused by mutations in ATP1A2, OMIM *182340, is a severe, incurable, and lethal condition which is diagnosed in utero and is associated with brain abnormalities, joint contractures and epilepsy. Babies born with the condition usually die in the neonatal period.

2.2. The committee considered the most appropriate listing for the condition applied for, caused by mutations in ATP1A2 and based on the advice and recommendation of its specialist adviser agreed that ATP1A2 should be listed as Polymicrogyria in association with homozygous/compound heterozygous ATP1A2 variants (autosomal recessive), OMIM *182340 on the HFEA website, but noted that once the condition has been given an OMIM number it may be referred to differently on the OMIM website. The committee requested that the HFEA executive requests that the OMIM team issue a number 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 condition's worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

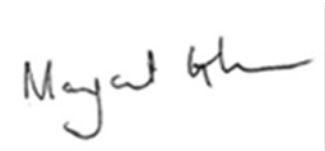
2.4. The committee was therefore satisfied that the following condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Polymicrogyria in association with homozygous/compound heterozygous ATP1A2 variants (autosomal recessive), OMIM *182340

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

1 June 2021