Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Hereditary Endotheliopathy with Retinopathy, Nephropathy and Stroke (HERNS), OMIM #192315

Thursday, 22 March 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde Anthony Rutherford	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
Specialist Adviser	Dr Jenny Carmichael	
Legal Adviser	Sarah Ellson	FieldFisher LLP
Observers		

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:

- 8th 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
- One additional paper submitted by the peer reviewer for SAC – Stam et al.
- Genetic Alliance UK Statement

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 application for Hereditary Endotheliopathy with Retinopathy, Nephropathy and Stroke (HERNS), OMIM #192315 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

1.4. 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.

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

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 the condition is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition, if either parent has a relevant mutation.

1.8. The committee noted that HERNS is known to be a single condition caused by heterozygous autosomal dominant mutations in TREX1. Homozygous mutations in TREX1 cause Aicardi Goutiere syndrome through different disease mechanisms and the conditions are distinct.

1.9. HERNS is a rare genetic condition that affects the small blood vessels of the brain, retina and kidneys. Symptoms of the condition include central nervous system degeneration, loss of vision, stroke, motor impairment, cognitive decline (dementia with forgetfulness, poor concentration and dysarthria), seizures, migraines, motor impairment (apraxia and hemiparesis), progressive visual loss caused by abnormalities of the microvessels in the retina, psychiatric disturbances and kidney disease. Symptoms of the condition are first seen in adulthood (mean age 42 +/- 8 years).

1.10. The committee noted there is no treatment for the condition. Progressive visual impairment often leads to blindness which has significant adverse effects on quality of life with the inability to perform many ordinary everyday tasks and social isolation. Neurological deficits also make certain tasks difficult or impossible, resulting in a need for assistance from carers. Cognitive impairment affects social interactions and need for assistance. Seizures and migraines can be debilitating. Death usually occurs within 5 - 10 years of the onset of the condition (i.e. on average at age 50 – 60 years.

1.11. The committee noted that penetrance is nearly 100%.

1.12. The committee noted that the condition is described on the OMIM website as Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315 and this name is also used at the start of the peer review. If the condition is approved, the committee was requested to decide whether the condition is added to the PGD condition list as it is named on the OMIM website (Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315), or as it is named in the application, Hereditary Endotheliopathy with Retinopathy, Nephropathy and Stroke (HERNS), OMIM #192315. The committee agreed the condition should be named as Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315.

1.13. The committee noted the inspectorate's request to consider whether Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario, Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315 is serious given it is a progressive, multi-system disorder causing a vast array of symptoms including loss of vision, migraine, strokes and kidney disease, leading to death within 5-10 years of onset of the condition. The committee considered this a devastating condition which can have severe effects on the quality of life of those with the condition and their families.

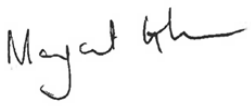
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Vasculopathy, Retinal, with Cerebral Leukodystrophy (RVCL), OMIM #192315.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

9 April 2018