Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)
Pre-implantation Genetic Diagnosis (PGD) application for Capillary Malformation-Arteriovenous Malformation (CM-AVM1), OMIM #608354
Capillary Malformation-Arteriovenous Malformation (CM-AVM2), OMIM #618196

Thursday, 13 December 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford Emma Cave	
Members of the Executive	Dee Knoyle Catherine Burwood Paula Robinson	Committee Secretary Senior Governance Manager (Observer) Head of Planning and Governance (Observer)
Legal Adviser	Eve Piffaretti	Blake Morgan LLP
External adviser	Dr Jenny Carmichael	
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
- 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 PGD for Capillary Malformation-Arteriovenous Malformation (CM-AVM), OMIM #608354 is consistent with the peer review.

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

1.4. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the 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 CM-AVM is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition in each pregnancy, if either parent has a relevant mutation. Penetrance is over 95%.

1.8. The committee noted that Capillary malformations occur in nearly all patients, and arteriovenous malformation in around 30-45% of patients. The condition causes abnormal formation of blood vessels in and under the skin, and in muscle, bones, the spine and brain. This can result in visible red birth marks across the face, neck and limbs, which can be psychologically debilitating. Moreover, abnormal tangled connections of veins and arteries that bypass the capillary system are at increased risk of bleeding and are particularly dangerous if they occur in the brain, because of the risk of cerebral damage from a bleed. In such situations, death may result. Individuals with CM-AVM may also have abnormalities of the lymph system leading to lymphoedema. High blood flow caused by CM-AVM can lead to heart failure.

1.9. The committee noted that CM-AVM is an incurable condition, so treatment is focused on relieving symptoms. Patients may require lifelong monitoring, but this will vary depending upon the symptoms that a patient experiences. Compression stockings can be used to treat lymphoedema. Patients may also have orthopaedic management of limb-length discrepancy. Some will require surgery although this can be a risky procedure and would only be undertaken with the support of an extensive multidisciplinary team of professionals including radiology, neurosurgery, surgery, cardiology, and dermatology. Management can also include cardiology (for the heart), orthopaedic (for leg overgrowth) and dermatology (for cosmetic skin treatment) input, as well as imaging scans to monitor the blood vessels.

1.10. The committee noted the inspectorate's request to consider whether Capillary Malformation-Arteriovenous Malformation (CM-AVM), OMIM #608354 should be approved for inclusion on the list of conditions approved for PGD. The committee further noted that OMIM #608354 relates to Capillary Malformation-Arteriovenous Malformation type 1, resulting from mutation in the RASA1 gene on the OMIM website.

1.11. The committee noted that the inspectorate also request that it considers Capillary Malformation-Arteriovenous Malformation type 2 (CM-AVM2), OMIM #618196 for inclusion on the list of conditions approved for PGD. CM-AVM2 is autosomal dominant resulting from heterozygous mutation in the EPHB4 gene (*600011) on chromosome 7q22. The committee accepted the advice from its Specialist Adviser that CM-AVM2 appears to exhibit the same range of symptoms as CM-AVM1. CM-AVM2 is described on the OMIM website as having variable expressivity.

1.12. The committee had regard to its decision tree and noted that these conditions had the same proposed purpose of testing the embryos in paragraph 1ZA(1)(b) of Schedule 2 of the Act. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario Capillary Malformation-Arteriovenous Malformation (CM-AVM) type 1, OMIM #608354 is a serious condition with severe complications which can affect major organs such as the brain and the heart. Intracerebral aneurysms and intracerebral bleeding can cause severe and permanent neurological impairment, hydrocephalus, seizures and death. The condition can cause overgrowth of a limb and lead to difficulties with mobility and joint pain. Some individuals require surgery and neurosurgery. There is no curative treatment and the quality of life of affected individuals may be severely impacted.

2.2. The committee considered that this is a life-threatening condition which could also have a psychological impact on affected individuals living with aneurysms and not knowing if or when an aneurysm might rupture and cause a brain haemorrhage.

2.3. The committee considered that Capillary Malformation-Arteriovenous Malformation type 2 (CM-AVM2), appears to exhibit the same range of symptoms as CM-AVM1 and therefore carries the same risk of cerebrovascular incidents due to a bleeding AVM, potentially leading to death. The committee also considered the psychological impact of those affected due to visible red birth marks across the face, neck and limbs.

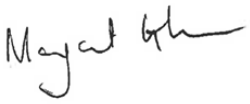
2.4. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing:

- Capillary Malformation-Arteriovenous Malformation Type 1 (CM-AVM1), OMIM #608354
- Capillary Malformation-Arteriovenous Malformation Type 2 (CM-AVM2), OMIM #618196

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

17 January 2019