Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Familial thoracic aortic aneurysm and dissection (TAAD), OMIM #611788,

Thursday, 30 March 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Dee Knoyle Erin Barton	Secretary Governance Manager
External adviser	Dr Alison Male	
Legal Adviser	Sarah Ellson	Fieldfisher
Observers		

Declarations of interest

- Members of the panel 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 Opinion
- Academic paper - Mutations in Smooth Muscle Alpha-Actin (ACTA2) Cause Coronary Artery Disease, Stroke, and Moyamoya Disease, Along with Thoracic Aortic Disease - The American Journal of Human Genetics 84, 617–627, May 15, 2009
- Minutes of the Statutory Approvals Committee meeting on 28 April 2016 which approved Loeys-Dietz syndrome type 1 and 2 as conditions for which PGD can be applied.
- Minutes of the Licence Committee meeting on 9 July 2007 which approved Marfan's Syndrome as a condition for which PGD can be applied

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for Familial thoracic aortic aneurysm and dissection (TAAD), OMIM #611788 is consistent with the Peer Review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient's 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 Familial TAAD is inherited in an autosomal dominant manner which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted that penetrance is difficult to assess and variable, but definitely incomplete. It was understood that approximately 50- 60% mutation carriers develop aortic disease and penetrance may be unreported given the variable age of onset.

1.9. The committee noted that Familial TAAD causes problems with the aorta (the large blood vessel that transports blood from the heart to the rest of the body). The upper part of the aorta can become stretched and weakened (dilatation), progressing to an aortic aneurysm (a bulge in the aortic wall) or dissection (tearing of the layers of the aortic walls). Familial TAAD can be associated with mutations in a number of genes however this application relates to mutations in the ACTA2 gene, which account for 10-14% of familial TAAD cases. Some of the clinical symptoms, particularly thoracic aortic aneurysm and dissection, are also seen in Marfan syndrome, which is already licensed for PGD.

1.10. Familial TAAD is also associated with abdominal aortic aneurysms (AAA). Other arteries may also be affected, leading to cerebral (brain) or peripheral artery aneurysms. ACTA2 mutations can also cause early onset vascular disease, leading to an increased risk of coronary artery disease and myocardial infarction (heart attack) and ischaemic strokes (where there is insufficient blood supply to the brain). Moyamoya disease (MMD) is also possible, in which certain arteries in the brain become narrowed (stenosed) or blocked (occluded) which can result in ischaemic or hemorrhagic strokes (where an artery in the brain leaks or ruptures).

1.11. Thoracic aortic aneurysms tend to be asymptomatic and may not be diagnosed until an acute aortic dissection occurs. Both aortic aneurysms and dissections can cause sudden rupture of the aorta which is frequently fatal. The age of aortic aneurysm development and dissection in Familial TAAD is very variable, but it can occur before 20 years of age. The likelihood of individuals suffering premature coronary artery disease or stroke by age 60 has been estimated to be 80% - this includes TAAD. Very early onset strokes (under the age of 20, and as young as 5 years) have been reported in some families.

1.12. The management of thoracic aortic aneurysm and/or dissection is complex. If diagnosed early, mild to moderate aortic dilatation may be treated with medications such as beta blockers and ACE inhibitors, which reduce the stress on the aorta. Because aortic dilatation may present in childhood, medical therapy may be started at a young age. It is also important to prevent and treat other risk factors such as hypertension. Elective surgical repair of the aorta may be offered once the dilation is above a certain threshold however individuals with ACTA2 mutations have experienced aortic dissection at a lower level of dilatation than would normally be considered for prophylactic surgery, making the timing of surgery a complex decision. Surgical intervention is associated with a significant risk of mortality and morbidity, particularly when performed as an emergency. Patients who have had an aortic repair still require life-long medical attention as they could develop an aneurysm in another vessel.

1.13. The committee noted that there is no curative treatment for the condition.

1.14. The committee noted the inspectorate's recommendation to consider the approval of Familial (TAAD), to be included on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that the condition is serious in its most severe form. The condition affects the large blood vessel that transports blood from the heart to the rest of the body, which can progress to an aortic aneurysm or dissection. The condition is also associated with abdominal aortic aneurysms. The condition may cause early onset vascular disease, leading to an increased risk of coronary artery disease, heart attack and ischaemic strokes due to insufficient blood supply to the brain. Arteries in the brain may also become narrowed or blocked which can result in ischaemic or hemorrhagic strokes and other arteries may be affected.

2.2. The condition can be associated with unpredictable complications which can be catastrophic and fatal for affected individual. The likelihood of affected individuals suffering premature coronary artery disease or stroke, before 60 years of age, has been estimated at up to 80% and early onset strokes, under the age of 20 and as young as 5 years, are possible. Surgical intervention is associated with significant risk, particularly when performed as an emergency and patients still require life-long medical attention as they could develop an aneurysm in another vessel.

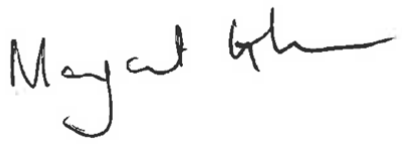
2.3. The committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 to the Act.

2.4. The committee agreed to authorise the testing of embryos for Familial thoracic aortic aneurysm and dissection (TAAD), OMIM #611788.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 March 2017