Statutory Approvals Committee – minutes

Centre 0119 (Birmingham Women's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Susceptibility to breast cancer due to a mutation in the c.7271T>G Ataxia-Telangiectasia Mutated (ATM) Gene, OMIM *607585

Thursday, 30 November 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Bobbie Farsides	
Members of the Executive	Dee Knoyle Bernice Ash Frances Metcalf-Head	Committee Secretary Committee Secretary (Observing) Inspections and Logistics Officer (Observing)
External adviser	Professor Peter Turnpenny	
Legal Adviser	Philip Grey	Mills & Reeve 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
- Peer Review (Redacted)
- Comment from centre on Peer Review
- Genetic Alliance UK Statement
- For reference, committee minutes of the approvals of:
  - Ataxia telangiectasia (25 November 2010)
  - Breast Ovarian Cancer Familial Susceptibility (BRCA2) (24 June 2010)

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 application was specific to breast cancer (familial), OMIM #114480, due to mutation in Ataxia-Telangiectasia Mutated (*ATM*) Gene OMIM *607585. However, the Peer Reviewer stated that there are 23 genes listed under OMIM number 114480 and the risk associated with these genes, and the strength of the evidence available, varies considerably. The Peer Reviewer did not think that OMIM number 114480 should be considered a single condition, or even that ATM heterozygote mutations should be considered as a single entity in themselves, and suggested that the committee considers limiting approval specifically to the c.7271T>G *ATM* mutation.

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. Susceptibility to breast cancer due to the c.7271T>G *ATM* mutation 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. However, according to current knowledge, the life time risk of developing breast cancer of 60-70% applies only to women, which means that at conception there is a 25% chance of having a daughter with an increased risk of developing breast cancer if either parent has a relevant mutation. As the breast cancer risk associated with other variants (mutations) in the *ATM* gene remains to be established, consideration of the application is limited to c.7271T>G.

1.8. The *ATM* c.7271T>G mutation probably carries a life time risk of breast cancer for female heterozygotes roughly equal to that of *BRCA2* mutation carriers (in the region of 60-70% over 80 years).

1.9. Breast cancer can be fatal and requires treatment which includes radiotherapy, chemotherapy and may require a mastectomy, which can be arduous and distressing as well as debilitating. The treatment and prognosis varies according to how advanced the cancer is when diagnosed. There are also breast cancer screening programmes. Breast cancer can have a psychological effect, with the burden of anxiety before cancer develops and then the ongoing treatment and impact on the individual’s quality of life.

1.10. The committee noted the inspectorate's request to consider whether Susceptibility to breast cancer due to a mutation in the Ataxia-Telangiectasia Mutated (*ATM*) Gene, OMIM *607585 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis, specifically for the c.7271T>G *ATM* mutation as advised by the Peer Reviewer.

2. Decision

2.1. The committee considered that Susceptibility to breast cancer due to a mutation in the c.7271T>G Ataxia-Telangiectasia Mutated (ATM) Gene, OMIM *607585 is serious given that individuals have a 60-70% life time risk of developing breast cancer and the condition can be fatal if untreated. Some patients have a poor prognosis depending on how advanced the cancer is when diagnosed, and the treatment can be extremely harsh for female individuals requiring a combination of surgery, chemotherapy and radiotherapy. The treatment for this condition can also be debilitating and stressful and undermine fertility (in child-bearing years), having a severe impact on an individual's quality of life.

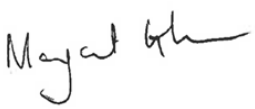
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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, 'Susceptibility to breast cancer due to a mutation in the c.7271T>G Ataxia-Telangiectasia Mutated (*ATM*) Gene, OMIM *607585', 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 Susceptibility to breast cancer due to a mutation in the c.7271T>G Ataxia-Telangiectasia Mutated (*ATM*) Gene, OMIM *607585.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

19 December 2017