Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Best macular dystrophy (Best vitelliform macular dystrophy),

OMIM #153700

Thursday, 25 January 2018

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Tony Rutherford Ruth Wilde	
Members of the Executive	Dee Knoyle Bernice Ash Nana Gyamfi Chereena Harriott	Committee Secretary Committee Secretary (Observing) Licensing Information Officer (Observing) Inspections & Logistics Officer (Observing)
External Adviser	Dr Alison Male	
Legal Adviser	Dawn Brathwaite	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
- Redacted Peer Review
- Genetic Alliance Statement
- Email correspondence from centre confirming change of OMIM number to #153700

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 application for Best Macular Dystrophy (Best Vitelliform Macular Dystrophy), OMIM #153700 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 BVMD affects the retina, the specialised light-sensitive tissue that lines the back of the eye. Specifically, this form of macular dystrophy disrupts cells in the small area near the centre of the retina. This area is needed for detailed tasks such as reading, driving and recognising faces. The condition begins typically in childhood, but the age of onset of symptoms and the severity of vision loss varies. Some patients have an onset of visual failure at 40-50 years of age.

1.9. The committee noted that affected individuals initially have normal vision and then experience blurred vision, or reduced sharpness or clarity of vision. BVMD affects central vision but usually not the peripheral vision and varies in severity, even among members of the same family. Those affected by BVMD develop a mass on the macula that resembles an egg yolk, vitelliform meaning yolk-like. This mass eventually breaks up and spreads throughout the macula, leading to disruption of cells in the retina and a reduction in central vision.

1.10. The committee noted that one complication of BVMD is choroidal neovascularization. This is seen in approximately 20% of those affected by BVMD and can increase the rate and severity of visual impairment.

1.11. The committee noted that there is no curative treatment for this condition.

1.12. The committee noted that the peer reviewer identified that the centre's original application used a gene related OMIM number *607854 to identify BVMD, however this number relates to the gene BEST1, mutations in which cause BVMD and the OMIM website identifies BVMD using the condition related OMIM number #153700. The Person Responsible at the centre agreed that the condition BVMD should be identified in the application by OMIM number #153700.

1.13. The committee noted that the Peer Reviewer also identified that mutations in BEST1 are causally associated with other clinically distinct retinal degenerative diseases, these being:

- Best vitelliform macular dystrophy, OMIM #153700
- Autosomal recessive bestrophinopathy, OMIM #611809
- Adult-onset vitelliform macular dystrophy
- Autosomal dominant vitreoretinochoroidopathy, OMIM #193220

1.14. The committee noted that the Peer Reviewer states that the most common condition is BVMD and that it would be reasonable to consider all four conditions mentioned above as they carry a similar or worse prognosis.

Recommendation:

1.15. The committee noted the inspectorate's request to consider whether BVMD, OMIM #153700 and the mutations in BEST1 identified by the Peer Reviewer, mentioned above, 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 BVMD, OMIM #153700 is serious given that the age of onset can be as early as childhood and affected individuals have progressive visual loss which could lead to blindness. The committee considered that this devastating degenerative disease would severely impact 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 and advice provided by its Specialist Adviser, 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 Best Macular Dystrophy (Best Vitelliform Macular Dystrophy), OMIM #153700 and the mutations in BEST1, which carry a similar or worse prognosis, meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

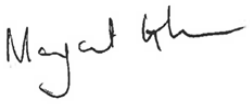
2.3. The committee agreed to authorise testing for the following:

- Best Macular Dystrophy (Best Vitelliform Macular Dystrophy), OMIM #153700
- Autosomal recessive bestrophinopathy, OMIM #611809
- Adult-onset vitelliform macular dystrophy – the Executive state that this is not listed specifically on the OMIM website, however some cases may be late onset cases of BVMD, OMIM #153700
- Autosomal dominant vitreoretinochoroidopathy, OMIM #193220
  (can be associated with microcornea, rod-cone dystrophy, early-onset cataract and posterior staphyloma and retinitis pigmentosa, OMIM #613194 (listed as retinitis pigmentosa-50, OMIM #613194 on the OMIM website)).

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

9 February 2018