Statutory Approvals Committee - minutes

Centre 0035 (Oxford Fertility)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) – application to perform PGT-M for Dilated Cardiomyopathy, in pathogenic RBM20, OMIM #613171

Date:	4 October 2021
Venue:	HFEA, 2nd Floor, 2 Redman Place, London E20 1JQ via Microsoft Teams
Committee Members:	Margaret Gilmore (Chair) Anne Lampe Ruth Wilde Jason Kasraie
Specialist Adviser:	Dr. Alison Male
Legal Adviser:	Gerard Hanratty - Browne Jacobson LLP
Members of the Executive:	Moya Berry - Committee Officer Catherine Burwood - Licensing Manager
Observers:	Jonathan Herring - Authority Member (HFEA)
Apologies:	No apologies were received for the meeting
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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGT-M Application Form
- Redacted Peer Review
- Genetic Alliance (UK) Statement
- 2020-08-27 Statutory Approvals Committee Minutes for Cardiomyopathy, dilated 1P, OMIM #609909
- 2016-05-26 Statutory Approvals Committee Minutes for Cardiomyopathy, dilated and left ventricular non compaction 5, OMIM #613426
- 2015-09-24 Statutory Approvals Committee Minutes for Cardiomyopathy, dilated 1A, OMIM #115200
- 2015-08-27 Statutory Approvals Committee Minutes for Cardiomyopathy, dilated 1Y, OMIM #611878
- 2014-09-25 Statutory Approvals Committee Minutes for Familial Dilated Cardiomyopathy caused by mutations in TROPONIN T2 gene (TNNT2), OMIM #191045 (executive condition known as Cardiomyopathy, dilated 1D, OMIM #601494

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 PGT-M application Dilated cardiomyopathy, in pathogenic RBM20 OMIM #613171, is consistent with the peer review.

1.3. The committee noted that on the OMIM website, ’613171’ is not a phenotype number, but is a genotype number which identifies the RNA-Binding Motif Protein 20; RBM20 gene. The committee noted that the condition in question is identified on the OMIM website as Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172. Therefore, the condition will be known as Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172.

1.4. The committee noted that the condition being applied for is not on the list of approved PGT-M conditions.

1.5. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the condition on patients, their families, and carers.

1.6. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGT-M. The committee was also satisfied that the centre has experience of carrying out PGT-M and that generic patient information about its PGT-M programme and associated consent forms had previously been received by the HFEA.

1.7. 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'.

1.8. The committee noted that Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172, is inherited in an autosomal dominant manner, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

1.9. The committee noted that penetrance of the condition is likely to be relatively high.

1.10. Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172 is a severe form of cardiomyopathy, which is associated with sudden death in up to 50% of those affected. The condition is a heart muscle disease presenting with symptoms of heart failure with breathlessness and fatigue, due to the heart muscle becoming dilated and dysfunctional. The condition is also associated with heart conduction defects which can precipitate sustained ventricular tachycardia/ventricular fibrillation. Symptoms include shortness of breath, reduced exercise tolerance, chest pain, leg oedema, valvular dysfunction, fatigue, heart palpitations and sudden death. The condition can be diagnosed in early childhood but is generally diagnosed in early – mid adulthood. The condition appears to be more severe in males, but in both males and females results in severe disease at an early age (average approximately 40 years).

1.11. There is no cure for the condition. Treatment to address symptoms include implantable defibrillators to reduce the risk of sudden death due to conduction defects, which require invasive procedures to insert and requires lifelong follow-up for monitoring. Cardiac transplantation is also an option in severe disease, though this is a complex surgical procedure with significant risk and requires long term post-operative immunosuppressive therapy.

1.12. The committee noted the executive's request to consider Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172, for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172, is a severe, aggressive, and potentially life limiting condition that can carry the risk of sudden unexpected death from teenage years and early adulthood, usually because of cardiac arrhythmia. Those affected may require cardiac transplant, which itself is not without serious risk and complications. The committee considered the potentially devastating physical and psychological impact on those living with cardiomyopathy and the lifetime uncertainty of sudden death.

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 abnormalities in question and that there is a significant risk that a person with such abnormalities will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

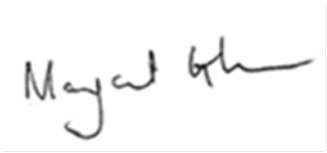
2.3. The committee was therefore satisfied that the following condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Cardiomyopathy, dilated, 1DD (CMD1DD), OMIM #613172

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

27 October 2021