Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for Familial Atypical Multiple Mole Melanoma – Pancreatic Carcinoma (FAMM-PC) Syndrome, OMIM #606719

Thursday, 24 September 2020

HFEA, 10 Spring Gardens, London, SW1A 2BU via Teleconference

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Tony Rutherford Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Dr Jenny Carmichael	
Legal Adviser	Dawn Brathwaite	Mills & Reeve - LLP
Observers	Dee Knoyle Matthew Mudford (Induction) Cora Sweet (Induction)	Committee Officer Scientific Policy Officer Policy Officer

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:

- 9th 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
- Supporting Document - Emerging molecular biology of pancreatic cancer, Ralph H.Hruban et al

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 PGD application for Familial Atypical Multiple Mole Melanoma – Pancreatic Carcinoma (FAMM-PC) Syndrome, OMIM #606719, is consistent with the peer review.

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

1.4. The committee noted that Familial Atypical Multiple Mole Melanoma – Pancreatic Carcinoma (FAMM-PC) Syndrome, OMIM #606719 is also known as Melanoma Pancreatic Cancer Syndrome, the primary name for the condition. To ensure consistency with the OMIM website, the condition, for the purposes of this application, will be known as Melanoma Pancreatic Cancer Syndrome, OMIM #606719.

1.5. The committee noted that a Genetic Alliance UK statement had not been provided for this application.

1.6. 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.

1.7. 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 Melanoma Pancreatic Cancer Syndrome, OMIM #606719, 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 the penetrance of the condition varies geographically and could be attributed to different sun exposure patterns. Therefore, penetrance has been estimated at 30-91% in Australia, 50-76% in the USA and 13-58% in Europe.

1.10. Melanoma Pancreatic Cancer Syndrome, OMIM #606719, is characterised by an increased risk of developing cutaneous malignant melanoma and/or pancreatic cancer. The cancers associated with the condition appear at a younger age than normal and can be fatal if not detected early.

1.11. Treatment is not always curative and focuses on early detection and surgical removal of the tumour at the earliest possible stage. Treatment for advanced cancers can include major surgery, chemotherapy, and radiotherapy.

1.12. The committee noted the executive's request to consider Melanoma Pancreatic Cancer Syndrome, OMIM #606719, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.13. The committee noted the recommendation of the peer reviewer to also consider a number of other conditions, for inclusion on the list for which PGD can be applied. The following conditions are all inherited in an autosomal dominant manner, meaning the risk of inheriting them is 50% in each pregnancy if either parent has a relevant mutation. The penetrance of the

conditions is variable, but all conditions have in common an increased risk of developing cutaneous malignant melanoma at a younger age than is usual, which can prove fatal if not detected early. These conditions are:

- Melanoma-Astrocytoma Syndrome, OMIM #155755
- Melanoma, cutaneous malignant, susceptibility to, 2 (CMM2), OMIM #155601
- Melanoma, cutaneous malignant, susceptibility to, 3 (CMM3), OMIM #609048
- Melanoma, cutaneous malignant, susceptibility to, 10 (CMM10), OMIM #615848

2. Decision

2.1. The committee considered that, in the worst-case scenario, Melanoma Pancreatic Cancer Syndrome, OMIM #606719, is a very serious and potentially lethal condition, and given the increased risk of developing malignant melanoma and pancreatic cancer, can result in death if not detected and treated at an early stage. Treatment for the cancers are often aggressive and include chemotherapy and radiotherapy and may not always be successful. The committee considered the potentially devastating physical and psychological impact on the quality of life of those affected with the condition, the lifetime of surveillance they will require, and the associated uncertainty of these cancers developing.

2.2. The committee considered that in the worst-case scenario, the following similarly inherited severe conditions can be fatal if not detected early:

- Melanoma-Astrocytoma Syndrome, OMIM #155755
- Melanoma, cutaneous malignant, susceptibility to, 2 (CMM2), OMIM #155601
- Melanoma, cutaneous malignant, susceptibility to, 3 (CMM3), OMIM #609048
- Melanoma, cutaneous malignant, susceptibility to, 10 (CMM10), OMIM #615848

2.3. 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 that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

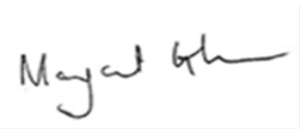
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Melanoma Pancreatic Cancer Syndrome, OMIM #606719
- Melanoma-Astrocytoma Syndrome, OMIM #155755
- Melanoma, cutaneous malignant, susceptibility to, 2 (CMM2), OMIM #155601
- Melanoma, cutaneous malignant, susceptibility to, 3 (CMM3), OMIM #609048
- Melanoma, cutaneous malignant, susceptibility to, 10 (CMM10), OMIM #615848

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
20 October 2020