Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health) Pre-implantation Genetic Diagnosis (PGD) application for DICER-1 Related Disorders, specifically: Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome OMIM#601200 and Goiter Multinodular 1, with or without Sertoli- Leydig Cell Tumors, OMIM #138800

Thursday, 30 April 2020

HFEA Teleconference Meeting

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	Graham Miles	Blake Morgan - LLP
Observer	Ermal Kirby	Authority Member

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
- Genetic Alliance UK Statement
- DICER-1 Related Disorders, Gene Reviews 2014

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 descriptions in the PGD application for DICER-1 related disorders, specifically: Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome (PPB), OMIM #601200, and Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors (MNG1), OMIM #138800, are consistent with the peer review.

1.3. The committee noted the advice of its specialist adviser who explained that the term 'DICER-1 related disorders' refers to a group of individual conditions which represent hereditary predisposition to the development of tumours. As a specific condition, Dicer-1 related disorders does not currently exist in the OMIM database but is a catch-all name for all DICER-1 related disorders. Therefore, based on the advice of its specialist adviser, the committee agreed that each DICER-1 related disorder should be individually considered for approval, rather than DICER-1 related disorders being considered as one over-arching condition.

1.4. The committee noted that the conditions being applied for are not on the list of approved PGD conditions.

1.5. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the conditions 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 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 both Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome, OMIM #601200, and Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors, OMIM #138800 are 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.

1.9. The Pleuropulmonary Blastoma in Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome (PPB), OMIM #601200, is a rare lung tumour typically presenting in infants and children as air-filled cysts (type I) causing shortness of breath and is sometimes complicated by pneumothorax. Progression may occur to malignant sarcomatous cystic nodules (type II), solid sarcoma (type III) and to metastatic disease.

1.10. Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors, OMIM #138800, is associated with multiple nodules in the thyroid gland (i.e. multinodular goiter) and, in some of those affected, Sertoli-Leydig cell tumours, usually of the ovary. Symptoms are seen from adolescence onwards. The thyroid gland and ovarian tumours are usually benign but can occasionally become malignant. Those tumours in the ovary may synthesise androgens in excess, with patients presenting in early adulthood with abdominal distention, pain and/or mass, and signs of virilization such as hirsutism, voice changes, and/or acne.

1.11. There is no cure for the underlying predisposition to tumour formation in either of these conditions. Treatments can include chemotherapy, radiotherapy, and surgical resection, but may not always be successful and early death is a possible outcome.

1.12. The committee noted the penetrance of the conditions is unknown.

1.13. The committee noted the executive's request to consider Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome (PPB), OMIM #601200, and Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors (MNG1), OMIM #138800, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the applications on this basis.

1.14. The committee also noted the request of the executive to consider an additional condition for inclusion on the list of conditions approved for PGD following information provided by the peer reviewer. Rhabdomyosarcoma, embryonal, 2, OMIM #180295 is a rare tumour that can arise in the uterine cervix. Tumours often occur in early adulthood and have the potential to become malignant. The risk of inheriting Rhabdomyosarcoma, embryonal 2, OMIM #180295, is 50% in each pregnancy if either parent has a relevant mutation.

2. Decision

2.1. The committee considered that, in the worst-case scenario, the Pleuropulmonary Blastoma in Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome OMIM#601200 typically presents in infants and children younger than the age of six years. Unless detected and resected early, tumours may transform to malignant sarcomas with metastatic potential which can be potentially fatal. Those affected with the condition will require on-going surveillance due to the risk of developing further tumours. The committee noted the serious implications and possible impact on the quality of life for those affected.

2.2. With regard to Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors (MNG1), OMIM #138800, the committee considered in the worst-case scenario, the condition which presents in early adolescence, may result in early death as a result of thyroid or ovarian cancer.

2.3. The committee considered in the worst-case scenario Rhabdomyosarcoma, embryonal 2, OMIM #180295, which presents in adolescence, may result in rare uterine cancer and early death.

2.4. 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 an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

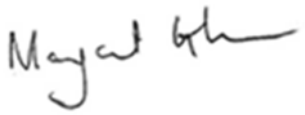
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Pleuropulmonary Blastoma Familial Tumor Predisposition Syndrome, OMIM #601200
- Goiter, multinodular 1, with or without Sertoli-Leydig Cell Tumors (MNG1), OMIM #138800
- Rhabdomyosarcoma, embryonal 2, OMIM #180295

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
20 May 2020