Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for CHST3-related skeletal dysplasia

OMIM #143095

Thursday, 26 September 2019

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Emma Cave Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Dr. Jenny Carmichael	
Legal Adviser	Tom Rider	FieldFisher LLP
Observers	Bernice Ash	Committee 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
- Genetic Alliance UK statement
- Statutory Approvals Committee Minutes, 30 May 2019 – PGD for Spondylometaepiphyseal Dysplasia Short Limb Hand type (SMED-SL), OMIM #271665
- Statutory Approvals Committee Minutes, 27 August 2015 – PGD for Spondylometaepiphyseal Dysplasia Strudwick, OMIM #184250
- Statutory Approvals Committee Minutes, 19 December 2013 - PGD for Desbuquois Dysplasia (DBQD), OMIM #251450

- Licence Committee Minutes, 5 May 2011 – PGD for Spondyloepiphyseal Dysplasia Congenita, OMIM #183900

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 condition is listed on the OMIM website as Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095, resulting from homozygous or compound heterozygous mutations in the CHST3 gene.

1.3. The committee agreed the executive's request to change the name of the condition from CHST3-related skeletal dysplasia #143095 to Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095, to ensure consistency with the OMIM website and the HFEA PGD list.

1.4. The committee noted that the description in the PGD application Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095 is consistent with the peer review.

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 Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

1.7. 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.

1.8. 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'.

1.9. The committee noted that Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095 is inherited in an autosomal recessive pattern, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation.

1.10. The committee noted the penetrance of the condition is 100%.

1.11. The condition is characterised by shortened long bones and limb length, restricted height, abnormal fixed limb posture, club foot, restricted joint mobility, and congenital joint dislocations, most commonly in the knees, but also hips and elbows. Later, arthritis develops, especially in the hips and spine, and the spine degenerates causing abnormal spinal curvature. The condition can be associated with severe long-term chronic pain and long-term physical disability.

1.12. There is no cure or effective treatment for SEDCJD, and there are limited medications suitable for the management of the severe chronic pain that can be associated with the condition. Surgical treatment of dislocations and abnormal joint positions can help but is often only partially successful and multiple procedures may be needed, with associated morbidity. Those affected generally need aids, such as crutches and wheelchairs, for ambulation.

1.13. The committee noted the executive's request to consider Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095 for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.14. The committee also noted the suggestion of the peer reviewer to consider three other conditions associated with congenital joint dislocation for approval as conditions for which PGD can be applied. These conditions are Larsen Syndrome, OMIM #150250, Ehlers-Danlos Syndrome type 1, OMIM #130070 and Spondylo-epimetaphyseal dysplasia with joint laxity, type 1, with or without fractures (SEMDJL1), OMIM #271640.

2. Decision

2.1. The committee considered that, in the worst-case scenario Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095 is a severe, progressive and degenerative condition affecting multiple joints causing limited mobility and resulting in severe chronic pain which is difficult to control. There is no cure for the condition. The committee considered the possible adverse physical and psychological impact on the quality of life for patients living with the condition.

2.2. The committee considered that in the worst-case scenario, Larsen Syndrome, OMIM #150250 is of similar clinical presentation and phenotype to SEDCJD. The condition results in dislocations at birth of the hip, knee and elbow joints with foot deformities and characteristic craniofacial abnormalities and cleft palate. Spinal anomalies include scoliosis and cervical kyphosis resulting in spinal instability, requiring spinal stabilisation close to birth. The condition may also be associated with severe chronic pain which may be very difficult to control. The committee noted the possible effect on the quality of life of those affected with the condition.

2.3. With regard to Ehlers-Danlos Syndrome type 1, OMIM #130070 and Spondylo-epimetaphyseal dysplasia with joint laxity, type 1, with or without fractures (SEMDJL1), OMIM #271640, the committee welcomed the advice of the specialist adviser and agreed that as both these conditions were of a different phenotype to SEDCJD, it was not appropriate to consider them under this application.

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.

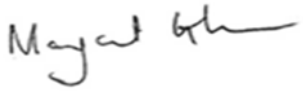
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations (SEDCJD), OMIM #143095
- Larsen Syndrome, OMIM #150250

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
28 October 2019