Statutory Approvals Committee – minutes

Centre 0339 (CREATE Fertility, London St Paul's)

Pre-implantation Genetic Diagnosis (PGD) application for

Fontaine Progeroid Syndrome, OMIM #612289

Thursday, 30 January 2020

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

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Dawn Brathwaite	Mills & Reeve LLP

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
- Email Correspondence from the centre

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Fontaine Progeroid Syndrome (FPS), OMIM #612289, 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 Fontaine Progeroid Syndrome (FPS) is also known as Gorlin-Chaudhry-Moss (GCM) Syndrome on the OMIM website. As Fontaine Progeroid Syndrome (FPS), OMIM #612289, is the primary name for this condition, the committee agreed, at the request of the executive, that the use of Gorlin-Chaudhry-Moss (GCM) Syndrome will be discontinued and the condition referred to as Fontaine Progeroid Syndrome (FPS), OMIM #612289, going forward.

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 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 Fontaine Progeroid Syndrome (FPS), OMIM #612289, is inherited in an autosomal dominant pattern, 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 due to the rarity of the condition the penetrance is not known.

1.10. The condition Fontaine Progeroid Syndrome (FPS), OMIM #612289, is associated, in a high proportion of those affected, with death in the postnatal period or within a few months of birth. In those who do survive, multiple anomalies are seen, including intrauterine and post-natal growth retardation, premature aging, complex craniofacial structural anomalies, decreased subcutaneous fat with lax, wrinkled skin, excess hair growth, umbilical hernia and conductive hearing impairment.

1.11. There is no cure for the condition and treatment focuses on the management of specific symptoms.

1.12. The committee noted the executive's request to consider Fontaine Progeroid Syndrome (FPS), OMIM #612289, 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 two other major Progeroid Syndromes for inclusion on the list for which PGD can be applied. The first condition is Hutchinson-Gilford Progeria Syndrome (HGPS), OMIM #176670, a de novo or dominantly inherited disorder due to pathogenic variants in the *LMNA* gene. Affecting the child from the first year of life, this condition can cause premature aging, short stature, low body weight, early loss of hair, lipodystrophy, scleroderma, decreased joint mobility osteolysis and severe hardening of the arteries. Cardiovascular compromise generally leads to early death by 20 years of age.

1.14. The second condition is Werner Syndrome (WRN), OMIM #277700, an autosomal recessive disorder due to pathogenic variants in the *RECQL2* gene. Affected individuals exhibit from their early twenties, premature aging and complications related to aging, such as cataracts,

skin ulcers, type 2 diabetes, diminished fertility, severe hardening of the arteries, and thinning of the bones.

Those affected may also develop multiple rare cancers during their lifetime, any of which can be fatal. Cardiovascular compromise or cancer generally leads to early death in the late forties or early fifties. The committee noted the executive's request for these two conditions to be considered alongside this application.

2. Decision

2.1. The committee considered that in the worst-case scenario, Fontaine Progeroid Syndrome (FPS), OMIM #612289, is a rare, severe and life-limiting condition with symptoms present at birth. There is no cure or mitigating treatment for the condition, and there is a significant risk of death in the post-natal period or within the first few months of birth. Those who do survive may have multiple anomalies that require complex and high-risk surgery. The committee considered the possible adverse physical and psychological impact on the quality of life for patients living with this condition.

2.2. The committee considered that in the worst-case scenario, Hutchinson-Gilford Progeria Syndrome (HGPS), OMIM #176670, is a life-limiting condition which presents in the first year of life. The condition generally leads to severe hardening of the arteries and cardiovascular compromise which results in death by early adulthood.

2.3. With regard to Werner Syndrome (WRN), OMIM #277700, the committee considered that in the worst-case scenario, this is a devastating and potentially life-limiting condition. Those affected may develop multiple, rare cancers and cardiovascular compromise, which can be fatal.

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.

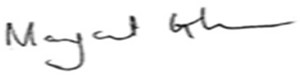
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Fontaine Progeroid Syndrome (FPS), OMIM #612289
- Hutchinson Gilford Progeria Syndrome (HGPS), OMIM #176670
- Werner Syndrome (WRN), OMIM #277700

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
24 February 2020