Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health) Pre-implantation Genetic Diagnosis (PGD) application for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560

Thursday, 26 March 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 Alan Fryer	
Legal Adviser	Gerard Hanratty	Browne Jacobson - 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 Statement
- Academic paper provided by the Peer Reviewer

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Alan Fryer, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560, 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 the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

1.5. 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.

1.6. 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'.

1.7. The committee noted for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560 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.

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

1.9. for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560 is a neurodegenerative disorder. In its most severe form, it manifests with neonatal-onset nystagmus (involuntary eye movement), severe spasticity affecting all four limbs with joint contractures and scoliosis, severe developmental language delay with arrested speech development, visual and hearing impairment. It rapidly progresses, resulting in death in early childhood.

1.10. At the milder end of the spectrum (childhood-onset form), motor milestones are achieved normally in the first year of life followed by the development of slowly progressive spasticity (stiff muscles making walking difficult), fine motor in-coordination. Other symptoms include nystagmus, extraocular movement disorder, indistinct speech, abnormal movements, swallowing difficulties, unsteady gait and loss of developmental milestones. This typically leads to wheelchair dependence in the second decade of life.

1.11. There is no cure for this condition. Treatments are available to help manage the symptoms.

1.12. The committee noted the executive's request to consider for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560, 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 executive to consider a number of other similar condition types for inclusion on the list of conditions approved for PGD. The peer reviewer considers them to be of a similar phenotype, with equivalent or more severe symptoms to SPAX8. The main symptoms of these conditions include limb spasticity, ocular movement abnormalities, swallowing and speech problems. Some patients also have myoclonic epilepsy and mild intellectual impairments. The age of onset of symptoms for all the condition types can be before or in early adulthood. All the conditions, with the exception of Spastic Ataxia 1 (SPAX1), OMIM #108600, are inherited in an autosomal recessive manner. The conditions for consideration are:

- Spastic Ataxia 1, Autosomal Dominant (SPAX1) OMIM #108600
- Spastic Ataxia 2, Autosomal Recessive (SPAX2) OMIM #611302
- Spastic Ataxia 3, Autosomal Recessive (SPAX3) OMIM #611390
- Spastic Ataxia 5, Autosomal Recessive (SPAX5) OMIM #614487
- Spastic Ataxia, Charlevoix-Saguenay (SACS) OMIM #270550

1.14. The committee noted the executive's recommendation, not to include the following conditions on the list for which PGD can be applied, as gene assignments are this far based on very small numbers of families affected with the conditions. These conditions are Spastic Ataxia 4. (SPAX4), OMIM #613627, Spastic Ataxia 7 (SPAX7), OMIM #108650, and Spastic Ataxia 9 (SPAX9), OMIM #618438.

2. Decision

2.1. The committee considered that, in the worst-case scenario Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating leukodystrophy (SPAX8), OMIM #617560, is a rare and serious neurodegenerative disorder. The condition can be rapidly progressive and can present in the first year of life resulting in death in early childhood. some of individuals with the condition die before the age of five. There is no cure for the condition and those who do survive into adulthood may live with severe physical disabilities. The committee noted the serious implications and possible impact on the quality of life for those affected with the condition.

2.2. The committee considered in the worst-case scenario the following conditions were of a similar phenotype and presentation to Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560 - Spastic Ataxia 3 has been reported with a neonatal onset and the others more resemble the childhood-onset form of SPAX8:

- Spastic Ataxia 1, Autosomal Dominant (SPAX1) OMIM #108600
- Spastic Ataxia 2, Autosomal Recessive (SPAX2) OMIM #611302
- Spastic Ataxia 3, Autosomal Recessive (SPAX3) OMIM #611390
- Spastic Ataxia 5, Autosomal Recessive (SPAX5) OMIM #614487
- Spastic Ataxia, Charlevoix-Saguenay (SACS) OMIM #270550

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 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.

2.4. With regard to Spastic Ataxia 4. (SPAX4), OMIM #613627, Spastic Ataxia 7 (SPAX7), OMIM #108650, and Spastic Ataxia 9 (SPAX9), OMIM #618438, the committee decided it did not have sufficient information to consider these as part of this specific application, but did not rule out considering them for PGD, should they be raised in future applications.

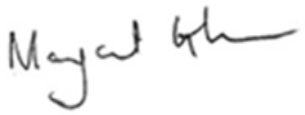
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Spastic Ataxia 1, Autosomal Dominant (SPAX1) OMIM #108600
- Spastic Ataxia 2, Autosomal Recessive (SPAX2) OMIM #611302
- Spastic Ataxia 3, Autosomal Recessive (SPAX3) OMIM #611390
- Spastic Ataxia 5, Autosomal Recessive (SPAX5) OMIM #614487
- Spastic Ataxia 8, for Spastic Ataxia 8, Autosomal Recessive with Hypo-Myelinating Leukodystrophy (SPAX8), OMIM #617560
- Spastic Ataxia, Charlevoix-Saguenay (SACS) OMIM #270550

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
23 April 2020