Statutory Approvals Committee – minutes

Centre 0301 (London Women's Clinic, Wales)

Pre-implantation Genetic Diagnosis (PGD) application for

Focal Segmental Glomerulosclerosis Type 1 (FSG1), OMIM #603278

Focal Segmental Glomerulosclerosis Type 2 (FSG2), OMIM #603965

Focal Segmental Glomerulosclerosis Type 3 (FSG3), OMIM #607832

Focal Segmental Glomerulosclerosis Type 4 (FSG4), OMIM #612551

Focal Segmental Glomerulosclerosis Type 5 (FSG5), OMIM #613237

Focal Segmental Glomerulosclerosis Type 6 (FSG6), OMIM #614131

Focal Segmental Glomerulosclerosis Type 8 (FSG8), OMIM #615032

Focal Segmental Glomerulosclerosis Type 9 (FSG9), OMIM #616220

Thursday, 26 April 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Dee Knoyle Bernice Ash Paula Robinson Catherine Burwood Clare Ettinghausen	Committee Secretary Committee Secretary (Observer) Head of Planning & Governance (Observer) Senior Governance Manager (Observer) Director of Strategy & Corporate Affairs (Observer)
External adviser	Professor Peter Turnpenny	
Legal Adviser	Gerard Hanratty	Browne Jacobson LLP
Observers		

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:

- 8th 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 opinion
- Comment from centre regarding peer review
- SAC Minutes, 27 April 2017, FSGS7 OMIM #616002
- SAC Minutes, 24 June 2016: Congenital Steroid Resistant Nephrotic Syndrome OMIM #600995
- SAC Minutes, 30 October 2014: Nephrotic Syndrome type 1 OMIM #256300

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 application for Focal Segmental Glomerulosclerosis (FSGS) is consistent with the peer review.

1.3. The committee noted that Genetic Alliance provided a patient perspective and supported the application.

1.4. 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.

1.5. 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 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 that FSGS types 1, 2, 4, 5 and 8 are inherited in an autosomal dominant manner which means there is 50% chance of having an affected child in each pregnancy if either parent has a relevant mutation. FSGS types 3, 6 and 9 are inherited in an autosomal recessive manner which means there is 25% chance of having an affected child in each pregnancy if each parent is a carrier of a relevant mutation.

1.8. The committee noted that FSGS is a progressive condition that impacts on the functioning of the kidneys. Over time, kidney function declines towards end-stage renal disease. FSGS has extremely variable age of onset, typically ranging from adolescence to adulthood.

1.9. The committee noted that generally, the autosomal recessive types (types 3, 6 and 9) have an earlier age of onset, often during childhood. The earliest reported case of FSGS was diagnosed in a 10-month-old infant who required a kidney transplant by age 5 years. The onset of symptoms in the autosomal dominant forms (types 1, 2, 4 and 8) is normally between the second and fourth decades.

1.10. The committee noted that the application states that ‘most forms of FSGS demonstrate incomplete penetrance’ but later that ‘some families demonstrate full penetrance’.

1.11. The committee noted that FSGS impacts the blood filtering parts of the kidney. When these parts of the kidney are damaged or scarred (sclerosis) it allows protein to leak into the urine (proteinuria). This kidney damage can also result in hypertension, oedema (fluid swelling around the body) and nephrotic syndrome. Over time, the damage to the kidney may cause kidney failure and/or end stage renal disease. FSGS does have variable severity among the different types. While most types only impact the functioning of the kidney, some impact the brain leading to ventriculomegaly, cause muscular dystrophy or colobomas of the optic nerve.

1.12. The committee noted that the treatment options available for FSGS depend on the stage of the disease. Often treatment starts with steroid therapy; however, 30-50% of adults with FSGS do not respond to this type of treatment and almost all affected children do not respond to steroid therapy. As the kidney function decreases, patients become dependent on dialysis whilst waiting for a kidney transplant. Additionally, alternative treatments are currently being investigated to prolong kidney function, such as: circulating factors, immune modulation and anti-fibrotic therapy (antibodies). Progression of FSGS varies from one individual to the next, making disease progression difficult to predict. The medications prescribed are an attempt to slow disease progression but typically cause side effects or give rise to complications, such as: diverticulitis, gout, malnutrition, and chronic pain, thus greatly limiting the activity of the affected person.

1.13. The committee noted the inspectorate's request to consider whether the following conditions should be approved for inclusion on the PGD List:

- Focal Segmental Glomerulosclerosis Type 1 (OMIM # 603278)
- Focal Segmental Glomerulosclerosis Type 2 (OMIM # 603965)
- Focal Segmental Glomerulosclerosis Type 3 (OMIM # 607832)
- Focal Segmental Glomerulosclerosis Type 4 (OMIM # 612551)
- Focal Segmental Glomerulosclerosis Type 5 (OMIM # 613237)
- Focal Segmental Glomerulosclerosis Type 6 (OMIM # 614131)
- Focal Segmental Glomerulosclerosis Type 8 (OMIM # 615032)
- Focal Segmental Glomerulosclerosis Type 9 (OMIM # 616220)

The committee noted that both FSGS3 and FSGS4 confer susceptibility to renal disease in the context of particular infectious diseases, and do not appear to constitute highly penetrant monogenic disease entities.

The committee noted that FSGS7 has already been approved for inclusion on the PGD List.

The committee noted that the inspectorate also requests that the following conditions, which belong to a group of conditions that cause Nephrotic syndrome and have a similar phenotype and clinical outcome to FSGS are considered for inclusion on the PGD List:

- Nephrotic syndrome type 3 (NPHS3), OMIM #610725
- Nephrotic syndrome type 4 (NPHS4), OMIM #256370

The committee noted that Nephrotic syndrome, type 1 (NPHS1), OMIM #256300 and Nephrotic syndrome, type 2 (NPHS2), OMIM #600995 have already been approved for inclusion on the PGD List.

1.14. The committee agreed to consider this application for inclusion on the PGD List.

2. Decision

2.1. The committee considered that, in the worst case scenario, FSGS is a serious condition. The age of onset for some types of the condition can be as early as infancy. This is a progressive condition which causes kidney damage that can result in hypertension, oedema and nephrotic syndrome. Some types of FSGS affect the brain. Medication can cause side effects which limit activity and individuals eventually require dialysis and a kidney transplant. This is a life limiting condition.

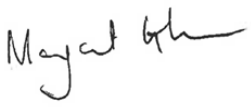
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. 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 and agreed to authorise testing for these conditions:

- Focal Segmental Glomerulosclerosis Type 1 (OMIM # 603278)
- Focal Segmental Glomerulosclerosis Type 2 (OMIM # 603965)
- Focal Segmental Glomerulosclerosis Type 5 (OMIM # 613237)
- Focal Segmental Glomerulosclerosis Type 6 (OMIM # 614131)
- Focal Segmental Glomerulosclerosis Type 8 (OMIM # 615032)
- Focal Segmental Glomerulosclerosis Type 9 (OMIM # 616220)

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

17 May 2018