Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Denys-Drash Syndrome (DDS), OMIM #194080

Thursday, 30 August 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde	
Members of the Executive	Bernice Ash Paula Robinson Catherine Burwood	Committee Secretary Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
Specialist Adviser	Dr Alan Fryer	
Legal Adviser	Jane Williams	Mills & Reeve LLP
Observers	Stevan Cirkovic	Policy Officer (Induction)

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 UK statement
- Licence Committee minutes, 24 June 2010, Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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 application for PGD for Denys-Drash Syndrome (DDS), OMIM #194080 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion 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 the condition is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted that DDS is caused by a genetic mutation in the WT1 gene which affects the kidneys and genitalia. Kidney disease may present within the first few months of life, sometimes at birth. This progresses to end-stage kidney failure, often in childhood and is fatal without treatment. Children with this condition also have a 74% risk of developing a rare form of kidney cancer known as Wilms tumour. Sometimes Wilms tumours develop in both kidneys. With current treatment, the survival rate for children with Wilms tumour is approximately 85-90%.

1.9. Males with DDS usually have genitalia that do not look clearly male or female or may appear completely female. The testes are undescended and typically men are infertile.

1.10. Symptoms of DDS therefore include the development of an abdominal mass due to a nephroblastoma (Wilms tumour), nephrotic syndrome (foamy urine due to excess protein excretion and severe swelling around the eyes, ankles and feet), symptoms of impaired kidney function (hypertension, fatigue, loss of appetite and weight gain due to fluid retention) and, in males, a disorder of sexual development and infertility as described in 1.9. There can be some clinical variability in expression but in most cases the condition is severe and non-penetrance is rare.

1.11. In terms of treatment, fluid and electrolyte imbalance in end-stage renal failure can be managed using dialysis, although this is disruptive for the DDS patient and their family. Treatment is also available for hypertension. A kidney transplant may be an option although such transplants are not always feasible and, even if possible, not always successful. They may also need to be repeated in DDS patients, because kidney failure typically develops in childhood and a transplanted kidney may last only 8-20 years before failing, necessitating another cycle of dialysis and a further kidney transplant. Chemotherapy is required in those children who develop a Wilms tumour, but again this is a significant treatment, with inconveniences and significant side effects, and is not always successful. DDS has a significant impact on quality of life including having life-long follow up appointments in hospitals.

1.12. The committee noted the penetrance of DDS is close to 100%.

1.13. The executive noted the similarity in the kidney-related symptoms (and their treatment) between DDS and Autosomal Dominant Polycystic Kidney Disease (ADPKD), OMIM# 173900. This latter condition has been approved for PGD since 2010 and the minutes of this approval were acknowledged by the committee.

1.14. The committee noted the inspectorate's request to consider whether Denys-Drash Syndrome (DDS), OMIM #194080 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario Denys-Drash Syndrome (DDS), OMIM #194080 is a serious condition, causing renal failure in childhood, with the risk of cancer developing, requiring multiple treatments. The quality of life for affected individuals is severely impacted.

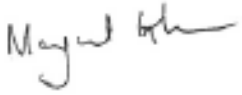
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 condition Denys-Drash Syndrome (DDS), OMIM #194080, meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

2.3. The committee agreed to authorise testing for Denys-Drash Syndrome (DDS), OMIM #194080.

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

26 September 2018