Statutory Approvals Committee – minutes

Centre 0017 (Newcastle Fertility Centre at LIFE)

Mitochondrial Donation using Pronuclear Transfer (PNT)

Application Reference: M0006

Mitochondrial Disease, OMIM #590080, (MT-TS1)

Thursday, 22 February 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford Ruth Wilde	
Members of the Executive	Dee Knoyle Paula Robinson Clare Ettinghausen	Committee Secretary Head of Planning & Governance (Observer) Director of Strategy and Corporate Affairs (Observer)
External adviser	Prof Shamima Rahman	
Legal Adviser	Graham Miles	Blake Morgan 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
- Mitochondrial Donation Explanatory Note
- Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015

The following papers were considered by the committee:

- Executive Summary
- Mitochondrial Donation: new case application form
- Clinical Expert Peer Review Form

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Professor Shamima Rahman, who confirmed that the condition was as described in the papers and stated that the OMIM number #590080 refers to the gene and not the specific mutation.

1.2. Professor Rahman agreed that the evidence submitted by the clinic supported the view that PGD was inappropriate or likely to be unsuccessful.

1.3. The committee noted the description in the application for Mitochondrial Disease, OMIM #590080 (MT-TS1) - the details of which have been omitted to protect the identity of the patient.

1.4. The committee had regard to its decision tree.

Administrative requirements

Application

1.5. The committee noted that the application has been submitted as required by General Direction 0008. The centre has submitted an application to perform mitochondrial donation using Pronuclear Transfer (PNT) for Mitochondrial Disease, OMIM #590080 (MT-TS1) for a named patient, on the relevant application form.

Licence - Express provision and variation

1.6. The committee noted that the centre's licence has an 'express provision', granted by the HFEA, to permit mitochondrial donation treatments using PNT and the centre's licence has been varied accordingly.

Embryologist

1.7. The committee noted that the procedure would be carried out by the embryologist named on the centre's licence, who is the only embryologist licensed at the centre to perform mitochondrial donation using PNT.

Patient selection criteria

Pre-implantation Genetic Diagnosis (PGD) considered

1.8. The committee had regard to its Mitochondrial Donation Explanatory Note 2.5 and 7.1 (levels of heteroplasmy/homoplasmy for a particular Mitochondrial DNA (mtDNA) mutation in the germ line) and reminded itself that PNT should only be offered where a patient has undergone an assessment that deems PGD inappropriate or likely to be unsuccessful.

1.9. The committee noted that the application includes a documented rationale as to why PGD may be deemed inappropriate and likely to be unsuccessful in this case. The details of the particular factors underlying this rationale have been omitted to protect the identity of the patient.

1.10. The committee noted that the Peer Reviewer and the Expert Adviser supported the centre's view that PGD would be inappropriate or unlikely to be successful for this patient.

Particular risk

1.11. The committee had regard to its Mitochondrial Donation Explanatory Note and the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015, 8(a)(i) and considered whether there was a particular risk that any embryo which is created by the fertilisation of an egg extracted from the ovaries of a named women may have mitochondrial abnormalities caused by mtDNA.

1.12. The committee noted the evidence that the patient has a clearly identified pathogenic mutation which gives rise to a considerable risk of any children having mitochondrial disease.

1.13. The committee noted that the application sets out relevant information about Mitochondrial Disease, OMIM #590080 (MT-TS1) for a named patient, on the relevant application form, including the patient's family history of affected individuals, their mutation load and clinical manifestations of disease.

Significance and seriousness

1.14. The committee had regard to its decision tree, Mitochondrial Donation Explanatory Note and the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 8(a)(ii). The committee considered whether there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease.

1.15. The committee noted that this patient has not previously been pregnant due to the potential risk of mitochondrial disease in her off-spring.

1.16. The committee noted that the patient has symptoms of the disease affecting her hearing and her offspring are at risk of developing symptoms over their life span. The patient and some of her relatives also have a neurological impairment which impacts on their quality of life, as described in the application.

1.17. The committee noted that, in severe forms of the disease, patients have profound hearing loss, necessitating the consideration of hearing aids, speech therapy, cochlear implantation, and educational programs and many children require significant support at school. The impact of this on a child/adult's social and emotional life may be considerable.

1.18. The committee noted that hearing impairment is extremely prevalent in patients with mitochondrial disease and can be caused by a number of genetic defects in mitochondrial DNA. Patients who harbour this particular mutation often present with isolated hearing loss (non-syndromic), but it can sometimes be associated with abnormalities of other organ systems as part of a syndrome.

1.19. The Expert Adviser referenced the information provided by the Peer Reviewer outlining a report by Kytovuori in 2017, the case of a Finnish family who had the same gene mutation, in which all affected individuals had hearing impairment and some had additional symptoms such as migraine, epilepsy, mild ataxia.

1.20. The Expert Adviser highlighted the importance of establishing whether this particular patient’s neurological symptoms are resulting from Mitochondrial Disease, OMIM #590080 (MT-TS1) by excluding another identifiable cause.

Recommendation

1.21. The committee noted the inspectorate’s recommendation to consider this application to perform mitochondrial donation using PNT for the patient named in the application.

2. Decision

2.1. The committee had regard to its Decision Tree, Mitochondrial Donation Explanatory Note and the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015, 8(a)(i), 8(a)(ii) and 8(b).

2.2. The committee noted that authorisation for Mitochondrial Donation using Pronuclear Transfer (PNT) for Mitochondrial Disease, OMIM #590080 (MT-TS1) is conditional on the embryo subsequently being created by the fertilisation of an egg extracted from the ovaries of the women so named: regulation 8(b).

2.3. The committee considered the information submitted by the inspectorate which included the centre's application form and the Peer Review. The committee also considered the advice provided by the Expert Adviser.

Patient selection criteria – PGD

2.4. The committee agreed that the evidence presented in this application supports the view that PGD is inappropriate or unlikely to be successful for this patient. The details of the particular factors underlying this rationale have been omitted to protect the identity of the patient.

Particular risk

2.5. The committee was satisfied that there is evidence that the patient has a clearly identified pathogenic mutation which gives rise to a considerable risk of her offspring having mitochondrial disease.

Significance and seriousness

2.6. The committee carefully considered the application and the advice from its Expert Adviser.

2.7. The Expert Adviser stated that in the absence of clinical data on the neurological symptoms of the patient and her relatives and without evidence of testing to establish the cause of this patient's neurological symptoms, she was unable to advise on the severity of the mitochondrial disease in this particular patient who also has relatives with non-syndromic hearing loss.

2.8. The committee agreed that there was insufficient evidence in this application to be satisfied with the severity of the mitochondrial disease in this particular patient.

Futher information required for re-consideration

2.9. The committee was unable to reach a decision after consideration of the available information. The committee suggested that the following information could be of use should the applicant wish the Statutory Approvals Committee to reconsider this application:

- A more complete list of available academic papers to aid robust decision making e.g. Finnish family reported by Kytovuori in 2017;
- Further information about the patient. This might include:

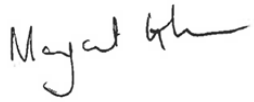
  Information about the relevant positive and negative findings of relevant medical tests/investigations including genetic testing for other causes of ataxia; MRI scans and objective measures of the severity of mitochondrial disease in this patient (such as a score for the Newcastle Mitochondrial Disease Adult Scale).
- An explanation of how a conclusion was reached that the patient's neurological symptoms are related to her mitochondrial disease, to include any relevant papers.

2.10. The committee would welcome any further relevant information to aid the decision making process. The committee agreed the extra information could be supplied either as part of the application form or as an attached letter or statement from the Clinician treating the patient.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

13 March 2018