Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

TPP1/CLN2 - related neuronal ceroid-lipofuscinosis (LINCL), OMIM #204500

Thursday, 25 January 2018

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Ruth Wilde	
Members of the Executive	Bernice Ash Dee Knoyle Nana Gyamfi Chereena Harriott	Committee Secretary Committee Secretary (Observing) Licensing Information Officer (Observing Inspections and Logistics Officer (Observing)
Specialist Adviser	Dr Alison Male	
Legal Adviser	Dawn Braithwaite	Mills & Reeve 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 UK Statement
- One additional paper from centre
- Email from the centre from PR stating that he would like other types of the condition to be considered
- Licence Committee minutes:
  - 30 November 2005; Centre 0070, Application to include embryo testing for Infantile Battens Disease
  - 19 December 2005; Centre 0088, Application to include embryo testing for Batten's Disease

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Alison Male, 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 TPP1 / CLN2-related neuronal ceroid-lipofuscinosis (LINCL), OMIM #204500 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 recessive pattern, which means there is a 25% chance of an embryo being affected with the condition, if both parents have a relevant mutation.

1.8. The committee noted LINCL is a rare and rapidly progressive genetic condition. The condition commonly presents with seizures and / or balance and co-ordination problems (ataxia) between the ages of 2 and 4. This is often combined with language delay, followed by motor and visual deterioration, infantile dementia and early death, usually between 10 to 15 years of age.

1.9. Symptoms include speech and language delay, developmental regression after two years of age, seizures, ataxia, myoclonus, vision loss, retinal degeneration and infantile dementia. There is rapid progression of symptoms and early death. Atypical phenotypes are characterised by later onset and, in some cases, longer life expectancies.

1.10. The committee noted that the condition is 100% penetrant if a child inherits mutations from both parents and it can vary between infantile onset, juvenile-onset and later onset forms.

1.11. The committee noted there is no curative treatment; treatment is only palliative. The symptomatic treatment is sometimes invasive. The condition significantly impacts quality of life and results in early death.

1.12. The committee noted the Peer Reviewer referred to the condition as Neuronal Ceroid-Lipofuscinosis (type CLN2), describing mutations in other genes that can also cause “late-infantile onset NCL”, and suggesting the possibility of extending the application to include the conditions below;

Condition	OMIM	Gene affected
Ceroid Lipofuscinosis, Neuronal, 1; CLN1	#256740	PPT1
Ceroid Lipofuscinosis, Neuronal, 5, CLN5	#256731	CLN5
Ceroid Lipofuscinosis, Neuronal, 6; CLN6	#601780	CLN6
Ceroid Lipofuscinosis, Neuronal, 7; CLN7	#610951	MFSD8
Ceroid Lipofuscinosis, Neuronal, 8; CLN8	#600143	CLN8
Ceroid Lipofuscinosis, Neuronal, 10; CLN10	#610127	CTSD

1.13. The committee noted the PR at the centre had confirmed he we would like the additional types of Ceroid Lipofuscinosis, Neuronal to also be considered as conditions for which PGC can be applied.

1.14. The committee noted, although the abbreviation for this condition is stated in the application as LINCL, the OMIM website lists the condition as Ceroid Lipofuscinosis, Neuronal, Type 2 (CLN2); the Executive suggested that this name and abbreviation should be used forthwith. The committee agreed to consider the application on this basis.

1.15. The committee noted the inspectorate's request to consider whether Ceroid Lipofuscinosis, Neuronal, Type 2 (CLN2), OMIM #204500 should be approved for inclusion on the PGD List. The inspectorate also requested that the committee consider approving the additional types of Ceriod Lipofuscinosis, Neuronal. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Ceroid Lipofuscinosis, Neuronal, Type 2 (CLN2), OMIM #204500, is serious given that it is a rapid, progressive disease, with onset of the condition occurring between the ages of 2 and 4, and the risk of death by the age of 6. The risk of death in infancy, heart and lung disease, alongside bacterial infections, is significant. The condition severely impacts on the family and quality of life.

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 Ceroid Lipofuscinosis, Neuronal, Type 2 (CLN2), OMIM #204500 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

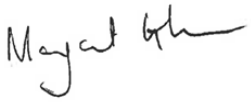
2.3. The committee agreed to authorise testing for Ceroid Lipofuscinosis, Neuronal, Type 2 (CLN2), OMIM #204500. The committee also agreed to authorise testing for the following conditions:

Ceroid Lipofuscinosis, Neuronal, type 1 (CLN1), OMIM #256740
Ceroid Lipofuscinosis, Neuronal, type 5 (CLN5), OMIM #256731
Ceroid Lipofuscinosis, Neuronal, type 6 (CLN6), OMIM #601780
Ceroid Lipofuscinosis, Neuronal, type 7 (CLN7), OMIM #610951
Ceroid Lipofuscinosis, Neuronal, type 8 (CLN8), OMIM #600143
Ceroid Lipofuscinosis, Neuronal, type 10 (CLN10), OMIM #610127

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

9 February 2018