Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Chronic Mucocutaneous Candidiasis also known as Immunodeficiency 31C (IMD31C)

OMIM #614162

Thursday, 28 November 2019

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) 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	Eve Piffaretti	Blake Morgan 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 UK statement
- 2019-02-28 Statutory Approvals Committee Minutes, PGD for Immunodeficiency 21, OMIM 614038.
- 2018-12-13 Statutory Approvals Committee Minutes, PGD for Immunodeficiency 44, OMIM #616636; also, Immunodeficiency 9, OMIM #612782; Immunodeficiency 19, OMIM #615617; Immunodeficiency 24, OMIM #615897; Immunodeficiency 31B, OMIM #613796; and Immunodeficiency 40, OMIM #616433.

- 2008-09-11 Licence Committee Minutes, HLA PGD for Wiscott Aldrich Syndrome, OMIM #301000

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 Chronic Mucocutaneous Candidiasis 7 #614162 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 also noted that Chronic Mucocutaneous Candidiasis 7, OMIM #614162 is referred to as Immunodeficiency 31C, OMIM #614162 on the OMIM website. The committee therefore agreed, at the request of the executive, to refer to the condition for the purposes of this application, as Immunodeficiency 31C (IMD31C) to ensure consistency with the OMIM website.

1.5. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

1.6. 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.

1.7. 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'.

1.8. The committee noted Immunodeficiency 31C (IMD31C), OMIM #614162 is inherited in an autosomal dominant pattern, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

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

1.10. Immunodeficiency 31C (IMD31C), OMIM #614162 causes immune system dysfunction leading to recurrent bacterial, viral, fungal and mycobacterial infections, and autoimmune disorders, such as hypothyroidism or diabetes mellitus. Other features of Immunodeficiency 31C include a risk of delayed puberty, osteopenia, cerebral aneurysms and oral and oesophageal cancer as well as various other cancers which increase the risk of death at a young age.

1.11. There is no cure for this condition and early death may not be avoided despite early interventions such as human stem cell transplantation. Antibiotics and anti-fungal and anti-viral drugs may help to ameliorate the course of some infections but with long term use there is the risk of developing drug resistant infections as well as the drugs themselves having significant side-effects. Other treatments may be tried including regular intravenous immunoglobulin infusions but none can completely prevent infections occurring.

1.12. The committee noted the executive's request to consider Immunodeficiency 31C (IMD31C), OMIM #614162 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 request of the peer reviewer to include a number of other Immunodeficiency condition types for which PGD can be applied. The peer reviewer

considers there to be reasonable evidence that the following condition types have symptoms equivalent in severity to, or worse than, those in Immunodeficiency 31C or other Immunodeficiency condition types already approved for PGD. The conditions for consideration are:

- Lymphoproliferative syndrome, X-linked, 1 (XLR), OMIM #308240
- Combined immunodeficiency, X-linked, moderate (XLR), OMIM #312863
- Immunodeficiency 8 (IMD8), OMIM #615401
- Immunodeficiency 10 (IMD10), OMIM #612783
- Immunodeficiency 11A (IMD11A), OMIM #615206
- Immunodeficiency 12 (IMD12), OMIM #615468
- Immunodeficiency 14 (IMD14), OMIM# 615513
- Immunodeficiency 15B (IMD15B), OMIM #615592
- Immunodeficiency 17, CD3 gamma deficient, OMIM #615607
- Immunodeficiency 18 (IMD18), OMIM #615615
- Immunodeficiency 18, SCID variant, OMIM #615615
- Immunodeficiency 20 (IMD20), OMIM #615707
- Immunodeficiency 22 (IMD22), OMIM #615758
- Immunodeficiency 23 (IMD23), OMIM #615816
- Immunodeficiency 25 (IMD25), OMIM #610163
- Immunodeficiency 26, with or without neurologic abnormalities, OMIM #615966
- Immunodeficiency 27A, mycobacteriosis (IMD27A), OMIM #209950
- Immunodeficiency 28, mycobacteriosis (IMD28), OMIM #614889
- Immunodeficiency 32B (IMD32B), OMIM #226990
- Immunodeficiency 33 (IMD33), OMIM #300636
- Immunodeficiency 34, mycobacteriosis, X-linked, (IMD34), OMIM #300645
- Immunodeficiency 35 (IMD35), OMIM #611521
- Immunodeficiency 36 (IMD36), OMIM #616005
- Immunodeficiency 37 (IMD37), OMIM #616098
- Immunodeficiency 38 (IMD38), OMIM #616126
- Immunodeficiency 41, with lymphoproliferation and autoimmunity (IMD41), OMIM #606367
- Immunodeficiency 42 (IMD42), OMIM #616622
- Immunodeficiency 43 (IMD43), OMIM #241600
- Immunodeficiency 46 (IMD46), OMIM #616740
- Immunodeficiency 47 (IMD47), OMIM #300972
- Immunodeficiency 48 (IMD48), OMIM #269840
- Immunodeficiency 49 (IMD49), OMIM #617237
- Immunodeficiency 50 (IMD50), OMIM #300988
- Immunodeficiency 51 (IMD51), OMIM #613953
- Immunodeficiency 52 (IMD52), OMIM #617514
- Immunodeficiency 53 (IMD53), OMIM #617585
- Immunodeficiency 54 (IMD54), OMIM #609981
- Immunodeficiency 55 (IMD55), OMIM #617827
- Immunodeficiency 56 (IMD56), OMIM #615207
- Immunodeficiency 57 (IMD57), OMIM #618108
- Immunodeficiency 58 (IMD58), OMIM #618131
- Immunodeficiency 59 and hypoglycaemia (IMD59), OMIM #233600
- Immunodeficiency 61 (IMD61), OMIM #300310
- Immunodeficiency 62 (IMD62), OMIM #618459
- Immunodeficiency 63 with lymphoproliferation and autoimmunity (IMD63), OMIM #618495
- Immunodeficiency 64 (IMD64), OMIM #618534

2. Decision

2.1. The committee considered that, in the worst-case scenario Immunodeficiency 31C (IMD31C), OMIM #614162 is a rare, debilitating and severely painful condition which can present in infancy or childhood. Patients affected with infections may require multiple hospital admissions which may be associated with serious complications or possible death. Some affected individuals may also develop malignancies resulting in death at an unusually young age. The committee considered the possible physical and psychological impact on the quality of life for patients living with the condition for which there is no cure.

2.2. The committee considered that in the worst-case scenario the following conditions, were equivalent in severity and similar in presentation to IMD31C.

- Lymphoproliferative syndrome, X-linked, 1 (XLR), OMIM #308240
- Combined immunodeficiency, X-linked, moderate (XLR), OMIM #312863
- Immunodeficiency 8 (IMD8), OMIM #615401
- Immunodeficiency 10 (IMD10), OMIM #612783
- Immunodeficiency 11A (IMD11A), OMIM #615206
- Immunodeficiency 12 (IMD12), OMIM #615468
- Immunodeficiency 14 (IMD14), OMIM# 615513
- Immunodeficiency 15B (IMD15B), OMIM #615592
- Immunodeficiency 17, CD3 gamma deficient, OMIM #615607
- Immunodeficiency 18 (IMD18), OMIM #615615
- Immunodeficiency 18, SCID variant, OMIM #615615
- Immunodeficiency 20 (IMD20), OMIM #615707
- Immunodeficiency 22 (IMD22), OMIM #615758
- Immunodeficiency 23 (IMD23), OMIM #615816
- Immunodeficiency 25 (IMD25), OMIM #610163
- Immunodeficiency 26, with or without neurologic abnormalities, OMIM #615966
- Immunodeficiency 27A, mycobacteriosis (IMD27A), OMIM #209950
- Immunodeficiency 28, mycobacteriosis (IMD28), OMIM #614889
- Immunodeficiency 32B (IMD32B), OMIM #226990
- Immunodeficiency 33 (IMD33), OMIM #300636
- Immunodeficiency 34, mycobacteriosis, X-linked, (IMD34), OMIM #300645
- Immunodeficiency 35 (IMD35), OMIM #611521
- Immunodeficiency 36 (IMD36), OMIM #616005
- Immunodeficiency 37 (IMD37), OMIM #616098
- Immunodeficiency 38 (IMD38), OMIM #616126
- Immunodeficiency 41, with lymphoproliferation and autoimmunity (IMD41), OMIM #606367
- Immunodeficiency 42 (IMD42), OMIM #616622
- Immunodeficiency 43 (IMD43), OMIM #241600
- Immunodeficiency 46 (IMD46), OMIM #616740
- Immunodeficiency 47 (IMD47), OMIM #300972
- Immunodeficiency 48 (IMD48), OMIM #269840
- Immunodeficiency 49 (IMD49), OMIM #617237
- Immunodeficiency 50 (IMD50), OMIM #300988
- Immunodeficiency 51 (IMD51), OMIM #613953
- Immunodeficiency 52 (IMD52), OMIM #617514
- Immunodeficiency 54 (IMD54), OMIM #609981
- Immunodeficiency 55 (IMD55), OMIM #617827
- Immunodeficiency 56 (IMD56), OMIM #615207
- Immunodeficiency 57 (IMD57), OMIM #618108
- Immunodeficiency 58 (IMD58), OMIM #618131
- Immunodeficiency 63 with lymphoproliferation and autoimmunity (IMD63), OMIM #618495
- Immunodeficiency 64 (IMD64), OMIM #618534

2.3. With regard to IDM53, IDM59, IDM61 and IDM62, the committee considered the advice of its specialist adviser and agreed that as these conditions each only related to a single family, it was not possible to confirm whether these conditions were of a similar phenotype to Immunodeficiency 31C. The committee therefore agreed it was not appropriate to consider them under this application at this time.

2.4. 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.

2.5. 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:

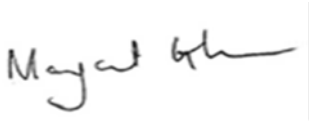
- Immunodeficiency 31C (IMD31C) #614162
- Lymphoproliferative syndrome, X-linked, 1 (XLR), OMIM #308240
- Combined immunodeficiency, X-linked, moderate (XLR), OMIM #312863
- Immunodeficiency 8 (IMD8), OMIM #615401
- Immunodeficiency 10 (IMD10), OMIM #612783
- Immunodeficiency 11A (IMD11A), OMIM #615206
- Immunodeficiency 12 (IMD12), OMIM #615468
- Immunodeficiency 14 (IMD14), OMIM# 615513
- Immunodeficiency 15B (IMD15B), OMIM #615592
- Immunodeficiency 17, CD3 gamma deficient, OMIM #615607
- Immunodeficiency 18 (IMD18), OMIM #615615
- Immunodeficiency 18, SCID variant, OMIM #615615
- Immunodeficiency 20 (IMD20), OMIM #615707
- Immunodeficiency 22 (IMD22), OMIM #615758
- Immunodeficiency 23 (IMD23), OMIM #615816
- Immunodeficiency 25 (IMD25), OMIM #610163
- Immunodeficiency 26, with or without neurologic abnormalities, OMIM #615966
- Immunodeficiency 27A, mycobacteriosis (IMD27A), OMIM #209950
- Immunodeficiency 28, mycobacteriosis (IMD28), OMIM #614889
- Immunodeficiency 32B (IMD32B), OMIM #226990
- Immunodeficiency 33 (IMD33), OMIM #300636
- Immunodeficiency 34, mycobacteriosis, X-linked, (IMD34), OMIM #300645
- Immunodeficiency 35 (IMD35), OMIM #611521
- Immunodeficiency 36 (IMD36), OMIM #616005
- Immunodeficiency 37 (IMD37), OMIM #616098
- Immunodeficiency 38 (IMD38), OMIM #616126
- Immunodeficiency 41, with lymphoproliferation and autoimmunity (IMD41), OMIM #606367
- Immunodeficiency 42 (IMD42), OMIM #616622
- Immunodeficiency 43 (IMD43), OMIM #241600
- Immunodeficiency 46 (IMD46), OMIM #616740
- Immunodeficiency 47 (IMD47), OMIM #300972
- Immunodeficiency 48 (IMD48), OMIM #269840
- Immunodeficiency 49 (IMD49), OMIM #617237
- Immunodeficiency 50 (IMD50), OMIM #300988
- Immunodeficiency 51 (IMD51), OMIM #613953
- Immunodeficiency 52 (IMD52), OMIM #617514
- Immunodeficiency 54 (IMD54), OMIM #609981
- Immunodeficiency 55 (IMD55), OMIM #617827
- Immunodeficiency 56 (IMD56), OMIM #615207

- Immunodeficiency 57 (IMD57), OMIM #618108
- Immunodeficiency 58 (IMD58), OMIM #618131
- Immunodeficiency 63 with lymphoproliferation and autoimmunity (IMD63), OMIM #618495
- Immunodeficiency 64 (IMD64), OMIM #618534

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
24 December 2019