Literature search and clinical opinion on alternate keratoprosthesis (excluding Boston KPro).

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This literature review provides supplementary information to the following documents:

National Institute for Health and Care Excellence (NICE) (2017) Medtech Innovation Briefing. Boston Keratoprosthesis Type I for corneal blindness. MIB 91
https://www.nice.org.uk/advice/mib91

National Institute for Health and Care Excellence (NICE) (2015) Interventional Procedure Guidance "Implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes" IPG534
https://www.nice.org.uk/guidance/ipg534

Introduction

Keratoprosthesis is a surgical procedure where a diseased cornea is replaced with an artificial cornea. Traditionally, keratoprosthesis is recommended after a person has had a failure of one or more donor corneal transplants (Akpek et al 2014). More recently, a less invasive, non-penetrating artificial cornea has been developed which can be used in more routine cases of corneal blindness. While conventional cornea transplant uses donor tissue for transplant, an artificial cornea is used in the Keratoprosthesis procedure. The surgery is performed to restore vision in patients suffering from severely damaged cornea due to congenital birth defects, infections, injuries and burns.

Keratoprotheses are made of clear plastic with excellent tissue tolerance and optical properties. They vary in design, size and even the implantation techniques may differ across different treatment centers. The procedure is done by ophthalmologists.

Although many keratoprostheses have been developed, only four models are currently have a CE mark. These include Boston keratoprosthesis, AlphaCor KPro ,the KeraKlear Artificial Cornea and Legeais. According to Salvador et al (2016), AlphaCor has recently been discontinued after patients due to patients developing severe mid- and long-term complications. It is also believed that Legeais is no longer available as only one study have been published to date. The clinical community in England is unaware of implanted with Legeais.

This document presents literature search results and clinical opinion on the AlphaCor the KeraKlear Artificial Cornea and Legeais.

Literature search results

A literature search was undertaken for AlphaCor KPro, KeraKlear and Legeais in the PubMed database. The search dates applied to the search were from 1st May 2005 to 10th May 2017. All study designs reporting primary research published in English were included.

Eight studies were identified for AlphaCor KPro, three studies KeraKlear Artificial Cornea and one study for Legeais. References for each of the three keratoprosthesis are listed below.

AlphaCor KPro (Argus Biomedical)

1. Hoffart L, Carles G, Matonti FLamellar corneal lenticule graft to treat keratolysis after AlphaCor keratoprosthesis implantation. Eur J Ophthalmol. 2015 Jan-Feb;25(1):1-7.
2. Jirásková N, Rozsival P, Burova M, Kalfertova M. AlphaCor artificial cornea: clinical outcome. Eye (Lond). 2011 Sep;25(9):1138-46.
3. Holak SA, Holak HM, Bleckmann H. AlphaCor keratoprosthesis: postoperative development of six patients. Graefes Arch Clin Exp Ophthalmol. 2009 Apr;247(4):535-9.
4. Ngakeng V, Hauck MJ, Price MO, Price FW Jr. AlphaCor keratoprosthesis: a novel approach to minimize the risks of long-term postoperative complications. Cornea. 2008 Sep;27(8):905-10.
5. Chalam KV, Chokshi A, Agarwal S, Edward DP. Complications of AlphaCor keratoprosthesis: a clinicopathologic report. Cornea. 2007 Dec;26(10):1258-60.
6. Hicks CR, Crawford GJ, Dart JK, Grabner G, Holland EJ, Stulting RD, Tan DT, Bulsara M. AlphaCor: Clinical outcomes. Cornea. 2006 Oct;25(9):1034-42.
7. Bleckmann H, Holak S. Preliminary results after implantation of four AlphaCor artificial corneas. Graefes Arch Clin Exp Ophthalmol. 2006 Apr;244(4):502-6.
8. Crawford GJ, Eguchi H, Hicks CR. Two cases of AlphaCor surgery performed using a small incision technique. Clin Exp Ophthalmol. 2005 Feb;33(1):10-5.

KeraKlear Artificial Cornea KPro (KeraMed)

1. Studeny P, Krizova D, Kuchynka P. Use of PocketMaker Microkeratome for Creation of Corneal Pocket for Foldable Keratoprosthesis KeraKlear Implantation - Case Series. Open Ophthalmol J. 2015 Jun 26;9:126-30.
2. Alio JL, Abdelghany AA, Abu-Mustafa SK, Zein G. A new epidescemetic keratoprosthesis: pilot investigation and proof of concept of a new alternative solution for corneal blindness. Br J Ophthalmol. 2015 Nov;99(11):1483-7.

3. Alio JL, Abbouda A, Vega-Estrada A. An innovative intrastromal keratoprosthesis surgery assisted by femtosecond laser. Eur J Ophthalmol. 2014 24(4):490-3.

Legeais BioKPro-III (FCI Ophthalmics)

1. Hollick EJ, Watson SL, Dart JK, Luthert PJ, Allan BD. Legeais BioKpro III keratoprosthesis implantation: long term results in seven patients. Br J Ophthalmol. 2006 Sep;90(9):1146-51. Eur J Ophthalmol. 2014 Jul-Aug;24(4):490-3.

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Clinical Opinion:

Policy Working Group Clinical Opinion:

The above papers were reviewed and summarised in the following table:

AlphaCor					
No.	**Name**	**Type**	**Patients**	**Follow-up**	**Comment**
1	Hoffart	Case series	12	2-38 mths	Post-op VA range 6/19 to light perception 7 melt, 4 extrusions
2	Jiraskova	Case series	15	12-67 mths	1 patient achieved 6/60 by end of f/u Stromal melt in 9 cases, 6 explanted
3	Holak	Case series	6	13-36 mths	3 patients achieved 6/60 at end of f/u Stromal melt in 3 cases
4	Ngakeng	Case series	6	14-38 mths	Altered technique Fewer complications, but none got 6/60
5	Chalam	Case report	1	10 mths	Complicated, no light perception Mainly histopathological findings
6	Hicks	Case series Multi-site	322	15-89 mths	Large numbers, some technique variation Complications in 46% (incl melt in 26%) 62% retention at 2 years VA data not clear, compromised by other ocular pathology + complications. Quoted 2 lines of improvement if uncomplicated.
7	Bleckman	Case series	4	6 months	VA 6 /15 to count fingers Short follow-up. 1 melt
8	Crawford	Case series	2	12 months	Main focus of paper was surgical method
KeraKlear					

No.	**Name**	**Type**	**Patients**	**Follow-up**	**Comment**
1	Studeny	Case series	3	6-24 mths	3/3 implanted. 2/3 achieved 6/60 vision or better after 1 year (1 died)
2	Alio	Case series	15	7-21 mths	9/15 good anatomical results, 6 complications. No eye better than counting fingers vision.
3	Alio	Case report	1	1 month	Aim of paper to demonstrate surgical technique.
Legeais					
No.	**Name**	**Type**	**Patients**	**Follow-up**	**Comment**
1	Hollick	Case series	7	12-48 mths	1 successful case, vision 6/12 6/7 were extruded after 2-28 months

Clinical Opinion:

AlphaCor

- This has been the most widely used alternative to the Boston KPro. All papers listed consist of case series, mostly single centre, with few patient numbers and clinical follow-up.
- The first 5 papers listed (published within the last decade) present results for a total of 32 patients. The most useful paper is Hicks (2006), reporting outcomes for 322 cases. Taking this paper alone, the incidence of complications is frequent. Unfortunately visual outcomes are not clearly expressed.

Taking account of these published results coupled with the fact that this device is no longer in production, clinical opinion is that there is insufficient evidence to recommend this device for commissioning by the NHS

KeraKlear

- The KeraKlear is designed for use in patients in whom standard grafts are likely to fail. It differs from other keratoprostheses in that it is implanted in the stroma without anterior chamber penetration.
- The few cases published have short follow-up and poor visual outcomes in almost all cases and frequent complications.

Taking account of these published results clinical opinion is that there is insufficient evidence to recommend this device for commissioning by the NHS.

Legais

- This device was used in a small case series, with universal poor outcomes.

Taking account of these published results clinical opinion is that there is insufficient evidence to recommend this device for commissioning by the NHS

Conclusion: Clinical Opinion

Having reviewed NICE MIB91 (2017), NICE IPG534 (2015) and the supplementary literature listed this paper, it is the combined clinical opinion that at the current time, only the Boston Keratoprosthesis has sufficient evidence to recommend it for commissioning by the NHS.