NHS England

Evidence review:

Argus II retinal prosthesis for retinitis pigmentosa

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First published: December 2015

Updated: Not applicable

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Contents

1. Introduction

The Argus II retinal prosthesis system consists of video camera mounted on a pair of spectacles which communicates wirelessly with an implant placed surgically in the retina. The system stimulates the retina electrically with patterns which the brain is able to interpret as patterns of light.

2. Summary of results

The Argus II study group has studied a cohort of 30 patients and published several papers [4,6-9,11]. A total of 29 of 30 subjects had functioning Argus II Systems implants 3 years after implantation. Eleven subjects experienced a total of 23 serious device- or surgery-related adverse events. All were treated with standard ophthalmic care. As a group, subjects performed better with the system on than off on all visual function tests and functional vision assessments [11] but there is variation between patients and between tests.

In the real world assessment (FLORA) three years after implantation, 65% of 23 patients were graded 'positive' or 'mildly positive' (i.e. usually subjects who self-reported functional benefits that were not supported by assessors' observations)'. An economic study [10] modelled patients implanted at age 49 years with a 25 year time horizon. The incremental cost effectiveness ratio was 14 603 Euro (£10 634) per quality adjusted life year (QALY) for the base case, rising to 49 769 Euro (£36 206) with a shorter time horizon and different model assumptions. This study was populated with data from the Argus II cohort after two years of follow up.

3. Research questions

The research question is the effectiveness of the Argus II prosthesis in the treatment of visual loss due to retinitis pigmentosa.

Population: Patients with retinitis pigmentosa

Intervention: Argus II

Comparator: conventional standard of care

Outcome: Visual function, quality of life, adverse events.

4. Methodology

A search was undertaken on 25 August 2015 using PubMed, with 'Argus II retinal prosthesis' as the search term and 'clinical trial' as a filter:

(argus[All Fields] AND ii[All Fields] AND ("visual prosthesis"[MeSH Terms] OR

("visual"[All Fields] AND "prosthesis"[All Fields]) OR "visual prosthesis"[All Fields] OR ("retinal"[All Fields] AND "prosthesis"[All Fields]) OR "retinal prosthesis"[All Fields])) AND Clinical Trial[ptyp]

One study of cost effectiveness was identified.

5. Results

The PubMed search retrieved nine papers [1-9]. One study of cost effectiveness was identified by the PubMed suggestions system [10]. A further two papers were retrieved by citation tracking [11 – 12].

The Argus II study group has studied a cohort of 30 patients over three years or more. Twenty-nine patients had retinitis pigmentosa and one subject had choroideremia. Twenty- nine patients had bare light perception (i.e., the ability to detect very bright light) in both eyes, and one subject had no light perception (but was able to perceive light in response to trans-corneal electrical stimulation). The age at time of implant ranged from 28 to 77 years (average 58 years).

Outcomes were measured in three ways:

- Computerised tests of square localization, direction of motion and grating visual acuity;
- Find the Door and Follow the Line; and
- Functional Low Vision Observer Rated Assessment (FLORA).

FLORA[13] was developed specifically for this study at the request of the FDA to subjectively assess real-world benefit. Assessors interviewed the patient; observed the patient performing visual tasks (system on and off) in and around his or her home. The assessor then wrote a case study narrative to synthesize his or her judgment of the effect of the Argus II. All narratives were rated by a single independent rater for the effect of the system on subjects' lives: positive, mild positive (usually subjects who self-reported functional benefits that were not supported by assessors' observations), prior positive (subjects who self-reported positive effects in the past that could not be demonstrated at the time of the assessment), neutral, and negative.

On FLORA, 65% of 23 patients were rated positive or mildly positive (compared to previous) at three years.

On the functional tests, 89% of subjects performed significantly better with the system on than off for Square Localization, 56% for Direction of Motion, and 33% scored on the scale on Grating Visual Acuity with the system on (no subjects scored with the system off).

Seven subjects underwent elective revision surgeries in attempts to improve the position of the array.

As of 1 year after implantation, 66.7% of subjects (20/30) had experienced no

device- or surgery-related SAEs. There were 18 SAEs among 10 subjects. The SAEs fell into 10 types, with hypotony, conjunctival dehiscence, conjunctival erosion, and presumed endophthalmitis (culture negative) being slightly more common than the others. There were also 2 subjects who under- went revision. At 3 years after implantation, there were a total of 23 SAEs among 11 subjects, with 2 additional SAE types. One subject's device was removed at 1.2 years to treat recurrent conjunctival erosion.

Other papers reported the results of various tests of visual function, including motion detection [4], letter reading [6], path tracing [7], spatial tracking [9], and navigation [12]. Improvements varied from task to task, with 96% (26/27) of patients showing improved accuracy on the tracking task, 54% better on motion detection and equivocal results for the navigation task.

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6. Appendix One

Grade	Study design			Outcomes				Reference	Other		
Grade of evidence	Study design	Study size	Intervention	Primary Outcome	Primary Result	Secondary Outcome	Secondary Result	Reference	Complications noted	Benefits noted	Comments
2++	Case series	n=30	Argus II prothesis					1			
2+	Cohort	n=13	Argus II prosthesis	Ability to detect motion	Fifteen subjects (54%) were able to perform the task significantly better with their prosthesis system than they were with their residual vision, 2 subjects had significantly better performance with their residual vision, and no difference was found for 11 subjects			4			
2+	Cohort	n=30	Argus II	Letter and word reading	21/30 patients in the cohort took part in the study. Results varied from letter to letter but for example for the letters L, T, E, J, F, H, I, U, patients recognized			6			

					72% and 18% respectively with the system switched on or off.						
2+	Cohort		Argus II study group	Tracing paths on a touchscreen	For right-angle/single-turn sets, average tracing error was reduced by 63% and tracing time increased by 156% when using the prosthesis, relative to residual vision. With mixed-angle/single-turn sets, error was reduced by 53% and time to complete tracing increased by 184%. Prosthesis use decreased error by 38% and increased tracing time by 252% for paths that incorporated two turns			*7*			Not clear why only 21 patients were reported in this study from the Argus II group
	Cohort		Argus II study group Interim safety and efficacy	Safety (the number, seriousness, and relatedness of adverse	Subjects performed statistically better with system ON			*8*			

			results (see reference 11 for longer follow up)	events) and visual function, as measured by 3 computer-based, objective tests: square localization, direction of motion, grating visual acuity	vs. OFF in the following tasks: object localization (96% of subjects); motion discrimination (57%); and discrimination of oriented gratings (23%). The best recorded visual acuity to date is 20/1260. Subjects' mean performance on Orientation and Mobility tasks was significantly better when the System was ON vs. OFF. Seventy percent of the patients did not have any serious adverse events (SAEs). The most common SAE reported was either conjunctival erosion or dehiscence over the extraocular implant and was						

					successfully treated in all subjects except in one which required explantation of the device without further complications						
	Cohort	n=30	Argus II study cohort	Spatial tracking	Ninety-six percent (26/27) of subjects showed a significant improvement in accuracy and 93% (25/27) show a significant improvement in repeatability with the system on compared with off			*9*			
	Cohort	n=4 patients with Argus; n= 5 age matched and n= 6 younger controlsl		Path reproduction and a triangle completion navigation task	Results suggested no benefit on the path reproduction task; two patients showed benefit on the triangle task.			*12*			

7. Appendix Two

Literature Search Terms

Assumptions / limits applied to search:	
Original search terms:	N/A
Updated search terms - Population	Patients with retinitis pigmentosa
Updated search terms - Intervention	Argus II
Updated search terms – Comparator	Supportive care.
Updated search terms – Outcome	*Critical to decision-making:* Visual function, quality of life, adverse effects *Important to decision-making:*
Inclusion criteria	**General inclusion criteria**
	Specific inclusion criteria
Exclusion criteria	**General exclusion criteria**
	Specific exclusion criteria