Clinical trial results:
Triamcinolone acetonide to prevent PVR in eyes undergoing vitreoretinal surgery for open globe trauma

Summary

EudraCT number	2007-005138-35
Trial protocol	GB
Global end of trial date	30 May 2014

Results information

Result version number	v1 (current)
This version publication date	28 June 2019
First version publication date	28 June 2019
Summary attachment (see zip file)	End of Study Summary Report (AOT End of Study Final Report.pdf)

Trial information

Trial identification

Sponsor protocol code	CHAD1024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Moorfields Eye Hospital NHS Foundation Trust
Sponsor organisation address	162 City Road, London, United Kingdom, EC1V 2PD
Public contact	Tania West (R&D office), Moorfields Eye Hospital, 020 72, moorfields.resadmin@nhs.net
Scientific contact	Tania West (R&D office), Moorfields Eye Hospital, 020 72533411, moorfields.resadmin@nhs.net

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2014
Global end of trial reached?	Yes
Global end of trial date	30 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a pilot RCT to investigate the the effect of the use of peroperative intravitreal triamcinilone acetate in the development of proliferative vitreoretinopathy following open globe trauma.

Protection of trial subjects:

safety and data reviewed by Moorfields internal DMC

Background therapy:

Surgical repair of ocular trauma

Evidence for comparator:

Eyes sustaining penetrating or open globe trauma (OGT) are a group at high risk of severe visual impairment. Retinal detachment is common in these eyes and multiple surgical interventions are often necessary 12, 13. PVR is the commonest cause of recurrent retinal detachment and visual loss in eyes with open globe trauma. It is estimated to occur in 10-45% of all OGT. 8-14

8. Cardillo JA, Stout JT, LaBree L, et al. Post-traumatic proliferative vitreoretinopathy. The epidemiologic profile, onset, risk factors, and visual outcome. Ophthalmology 1997;104(7):1166-73.
9. Spiegel D, Nasemann J, Nawrocki J, Gabel VP. Severe ocular trauma managed with primary pars plana vitrectomy and silicone oil. Retina 1997;17(4):275-85.
10. Framme C, Roider J. [Epidemiology of open globe injuries]. Klin Monbl Augenheilkd 1999;215 (5):287-93.
11. Mittra RA, Mieler WF. Controversies in the management of open-globe injuries involving the posterior segment. Surv Ophthalmol 1999;44(3):215-25.
12. Stryjewski TP, Andreoli CM, Eliott D. Retinal detachment after open globe injury. Ophthalmology 2014;121(1):327-33.
13. Andreoli MT, Andreoli CM. Surgical rehabilitation of the open globe injury patient. Am J Ophthalmol 2012;153(5):856-60.
14. Desai P, MacEwen CJ, Baines P, Minassian DC. Incidence of cases of ocular trauma admitted to hospital and incidence of blinding outcome. Br J Ophthalmol 1996;80(7):592-6.

Actual start date of recruitment	01 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

40 patients with open globe ocular trauma recruited between September 20111 and November 2013

Pre-assignment

Screening details:

45 patients screened for inclusion - 4 failed to meet inclusion criteria, one declined participation

Period 1

Period 1 title	recruitment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Blinding implementation details:

Patient and assessor blinded
Investigator - surgeon - providing treatment , (no placebo) not blinded

Arms

Arm title	Treatment

Arm description:

TREATMENT GROUP
a. Pre-operative Treatment
Guttae Prednisolone forte 2 hourly for up to one week.
b. Per-operative Treatment
4mg of intravitreal triamcinolone acetonide will be injected into the vitreous cavity following injection of silicone oil at the end of procedure
40mg of triamcinolone acetonide will be given as a posterior subtenons injection prior to suturing the conjunctiva.
c. Post-operative Treatment
Hourly g. Predforte for 1 week followed by a tapering regimen for 3-26 weeks thereafter depending on the degree of post-operative inflammation and cystoid macular oedema.
50mg flurbiprofen orally bid for 1 week

Arm type	Experimental
Investigational medicinal product name	triamcinolone acetonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraocular use

Dosage and administration details:

Intraoperative treatment: (a) 4 mg/0.1 ml of intravitreal triamcinolone acetonide (Bristol Myers Squibb, UK) was injected into the vitreous cavity following closure of the scleral ports at the end of procedure, (b) 40 mg/1 mL of triamcinolone acetonide (Bristol Myers Squibb, UK) was administered as a posterior subtenons injection prior to suturing the conjunctiva and (c) standard subconjunctival antibiotic injection of cefuroxime 125 mg or gentamicin was administered

Investigational medicinal product name	prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Conjunctival use

Dosage and administration details:

(a) Guttae prednisolone forte hourly for 1 week followed by a tapering regimen for 3–26 weeks thereafter depending on the degree of postoperative inflammation and cystoid macular oedema,

Investigational medicinal product name	flurbiprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg flurbiprofen orally twice daily for 1 week and

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Investigator administers treatment and there is no placebo

Number of subjects in period 1[2]	Treatment
Started	20
Completed	20

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Investigator administers treatment and sees trial medication - no placebo

Baseline characteristics

Reporting groups

Reporting group title	Treatment
Reporting group description:	
TREATMENT GROUP a. Pre-operative Treatment Guttae Prednisolone forte 2 hourly for up to one week. b. Per-operative Treatment 4mg of intravitreal triamcinolone acetonide will be injected into the vitreous cavity following injection of silicone oil at the end of procedure 40mg of triamcinolone acetonide will be given as a posterior subtenons injection prior to suturing the conjunctiva. c. Post-operative Treatment Hourly g. Predforte for 1 week followed by a tapering regimen for 3-26 weeks thereafter depending on the degree of post-operative inflammation and cystoid macular oedema. 50mg flurbiprofen orally bid for 1 week	

Reporting group values	Treatment	Total	
Number of subjects	20	20	
Age categorical			
Mean age in years (SD) 44 (16) 37 (13)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
34 male and 6 female subjects recruited			
Units: Subjects			
Female	2	2	
Male	18	18	

Subject analysis sets

Subject analysis set title	treatment group
Subject analysis set type	Intention-to-treat
Subject analysis set description: treatment group analysed v controls	
Subject analysis set title	control group
Subject analysis set type	Intention-to-treat
Subject analysis set description: analyse dv treatment group	

Reporting group values	treatment group	control group	
Number of subjects	20	20	
Age categorical			
Mean age in years (SD) 44 (16) 37 (13)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
34 male and 6 female subjects recruited			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: TREATMENT GROUP a. Pre-operative Treatment Guttae Prednisolone forte 2 hourly for up to one week. b. Per-operative Treatment 4mg of intravitreal triamcinolone acetonide will be injected into the vitreous cavity following injection of silicone oil at the end of procedure 40mg of triamcinolone acetonide will be given as a posterior subtenons injection prior to suturing the conjunctiva. c. Post-operative Treatment Hourly g. Predforte for 1 week followed by a tapering regimen for 3-26 weeks thereafter depending on the degree of post-operative inflammation and cystoid macular oedema. 50mg flurbiprofen orally bid for 1 week	
Subject analysis set title	treatment group
Subject analysis set type	Intention-to-treat
Subject analysis set description: treatment group analysed v controls	
Subject analysis set title	control group
Subject analysis set type	Intention-to-treat
Subject analysis set description: analyse dv treatment group	

Primary: The primary outcome measure was anatomic reapposition of

End point title	The primary outcome measure was anatomic reapposition of
End point description: primary outcome measure The primary outcome measure was anatomic reapposition of the remaining retina to the retinal pigment epithelium in the absence of an internal tamponade agent at 6 months postprimary vitrectomy surgery	
End point type	Primary
End point timeframe: 6 months	

End point values	Treatment	treatment group	control group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: patients	20	20	20	

Statistical analyses

Statistical analysis title	Analysis

Statistical analysis description:

The time taken to recruit patients is reported together with the number of patients who failed to provide outcome data. Baseline characteristics of the two groups were compared to assess the adequacy of randomisation. The OR of patients in whom anatomical retinal attachment remained at 6 months postprimary vitrectomy between the two treatment groups was reported with 95% CIs

Comparison groups	treatment group v control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.5 [2]
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.316
upper limit	3.904
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[1] - A total of 40 patients was considered a feasible number over the study period and expected to provide sufficient data to estimate the SD to power a definitive study

[2] - Not applicable

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Period of study - 6 month follow up

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	treatment

Reporting group description:

The number of adverse events (AEs) was comparable across both groups with 18 out of 20 adjunct patients suffering at least one AE compared with 16 of 20 control patients. There were no cases of postoperative endophthalmitis in either group. A slightly higher number of patients in the adjunct group (n=7, 35%) suffered at least one episode of elevated intraocular pressure (IOP) (>25 mm Hg) compared with five (25%) patients in the control group. . A higher median IOP was noted in the adjunct group at day 10, but this subsequently becomes comparable between the two groups. There were more cases of postoperative uveitis in the control group (n=5) in comparison to the adjunct group (n=2). An equal number of patients (n=5) suffered at least one episode of hypotony (IOP <6 mm Hg) during the trial.

Reporting group title	control

Reporting group description:

The number of adverse events (AEs) was comparable across both groups with 18 out of 20 adjunct patients suffering at least one AE compared with 16 of 20 control patients. There were no cases of postoperative endophthalmitis in either group. A slightly higher number of patients in the adjunct group (n=7, 35%) suffered at least one episode of elevated intraocular pressure (IOP) (>25 mm Hg) compared with five (25%) patients in the control group. The median IOP readings at each time point is displayed in the box plot of figure 3. A higher median IOP was noted in the adjunct group at day 10, but this subsequently becomes comparable between the two groups. There were more cases of postoperative uveitis in the control group (n=5) in comparison to the adjunct group (n=2). An equal number of patients (n=5) suffered at least one episode of hypotony (IOP <6 mm Hg) during the trial.

Serious adverse events	treatment	control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	treatment	control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)	13 / 20 (65.00%)	
Eye disorders			
raised iop	Additional description: raised intraocular pressure		
subjects affected / exposed	18 / 20 (90.00%)	13 / 20 (65.00%)	
occurrences (all)	18	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26546051