Clinical trial results:
A phase 3 multi-centre double-masked randomised controlled trial of adjunctive intraocular and periocular steroid (triamcinolone acetonide) versus standard treatment in eyes undergoing vitreoretinal surgery for open globe trauma; the adjunctive steroid combination in ocular trauma (ASCOT) trial

Summary

EudraCT number	2014-002193-37
Trial protocol	GB
Global end of trial date	30 September 2020

Results information

Result version number	v1 (current)
This version publication date	01 December 2021
First version publication date	01 December 2021

Trial information

Trial identification

Sponsor protocol code	CHAD1031

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	Hayley Boston, Moorfields Eye Hospital NHS Foundation Trust, 0044 20 7253 3411 x2937 , moorfields.resadmin@nhs.net
Scientific contact	Daniela Narvaez, Moorfields Eye Hospital NHS Foundation Trust, 207253341 020 7253 3411 x2937 , 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	17 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2020
Global end of trial reached?	Yes
Global end of trial date	30 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In patients who have sustained an open globe injury (severe trauma) and are undergoing vitrectomy surgery as a result(procedure to clear the gel in the back of the eye) , does the use of a steroid injection into and around the eye improve the visual outcome at 6 months?

Protection of trial subjects:

Trial subjects were able to access the trial team and raise any issues. trail subjects were seen and dealt with promptly by hospital vitreoretinal services which are configured to manage acute and urgent situations.

Background therapy:

Standard vitreoretinal surgical care for penetrating eye injuries.

Evidence for comparator:

Multiple publications on vitreoretinal surgical outcomes in trauma:
Desai, P., et al., Incidence of cases of ocular trauma admitted to hospital and incidence of blinding outcome. Br J Ophthalmol, 1996. 80(7): p. 592-6.
Pinna, A., et al., Epidemiology, visual outcome, and hospitalization costs of open globe injury in northern Sardinia, Italy. Ophthalmic Epidemiol, 2007. 14(5): p. 299-305.
Cillino, S., et al., A five-year retrospective study of the epidemiological characteristics and visual outcomes of patients hospitalized for ocular trauma in a Mediterranean area. BMC Ophthalmol, 2008. 8: p. 6.
Cardillo, J.A., et al., Post-traumatic proliferative vitreoretinopathy. The epidemiologic profile, onset, risk factors, and visual outcome. Ophthalmology, 1997. 104(7): p. 1166-73.
Spiegel, D., et al., Severe ocular trauma managed with primary pars plana vitrectomy and silicone oil. Retina, 1997. 17(4): p. 275-85.
Framme, C. and J. Roider, [Epidemiology of open globe injuries]. Klin Monbl Augenheilkd, 1999. 215(5): p. 287-93.
Mittra, R.A. and W.F. Mieler, Controversies in the management of open-globe injuries involving the posterior segment. Surv Ophthalmol, 1999. 44(3): p. 215-25.

Actual start date of recruitment	01 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 280
Worldwide total number of subjects	280
EEA total number of subjects	0

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)	220
From 65 to 84 years	45
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

Recruitment of 280 cases took place between December 2014 and March 2020

Pre-assignment

Screening details:

792 patient screened

Period 1

Period 1 title	Recruitment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Monitor, Data analyst, Assessor, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

Intra0cular and sub Tenons triamcinolone acetonide

Arm type	Experimental
Investigational medicinal product name	triamcinolone acetonide
Investigational medicinal product code	
Other name	Kenolog
Pharmaceutical forms	Suspension for injection
Routes of administration	Subconjunctival use, Intraocular use

Dosage and administration details:

steroid combination (triamcinolone acetonide) - 4mg/0.1ml into the vitreous cavity and 40mg/1ml subtenons
given at the end of vitreoretinal surgery

Arm title	Control

Arm description:

Standard vitreoretinal surgery

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Treatment	Control
Started	143	137
Completed	130	129
Not completed	13	8
Consent withdrawn by subject	2	1
Lost to follow-up	7	7
Protocol deviation	4	-

Period 2	
Period 2 title	Follow up and end point
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Monitor, Data analyst, Assessor, Investigator

Arms	
Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

Intra0cular and sub Tenons triamcinolone acetonide

Arm type	Experimental
Investigational medicinal product name	triamcinolone acetonide
Investigational medicinal product code	
Other name	Kenolog
Pharmaceutical forms	Suspension for injection
Routes of administration	Subconjunctival use, Intraocular use

Dosage and administration details:

steroid combination (triamcinolone acetonide) - 4mg/0.1ml into the vitreous cavity and 40mg/1ml subtenons
given at the end of vitreoretinal surgery

Arm title	Control

Arm description:

Standard vitreoretinal surgery

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Treatment	Control
Started	130	129
Completed	130	129

Baseline characteristics

Reporting groups	
Reporting group title	Recruitment

Reporting group description: -

Reporting group values	Recruitment	Total	
Number of subjects	280	280	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Median age 43 years IQR 30 to 55 years			
Units: years			
median	43		
inter-quartile range (Q1-Q3)	30 to 55	-	
Gender categorical Units: Subjects			
Male	246	246	
Female	34	34	

End points

End points reporting groups	
Reporting group title	Treatment
Reporting group description: Intra0cular and sub Tenons triamcinolone acetonide	
Reporting group title	Control
Reporting group description: Standard vitreoretinal surgery	
Reporting group title	Treatment
Reporting group description: Intra0cular and sub Tenons triamcinolone acetonide	
Reporting group title	Control
Reporting group description: Standard vitreoretinal surgery	

Primary: Clinically meaningful change in visual acuity	
End point title	Clinically meaningful change in visual acuity
End point description:	
End point type	Primary
End point timeframe: 6 months	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	129		
Units: Nunber of particupants	61	57		

Statistical analyses

Statistical analysis title	Mixed logistic regression model
Comparison groups	Treatment v Control
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.994
Method	Regression, Linear
Parameter estimate	Odds ratio (OR)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.68

Secondary: Change in visual acuity - continuous

End point title	Change in visual acuity - continuous
End point description: Visual acuity change as a continuous measure	
End point type	Secondary
End point timeframe: 6 months	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	129		
Units: ETDRS letters				
number (not applicable)	19.4	19.3		

Statistical analyses

Statistical analysis title	Linear mixed regression model
Comparison groups	Treatment v Control
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.361
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.67
upper limit	3.52

Secondary: Stable complete retinal reattachment (without internal tamponade present) at 6 months

End point title	Stable complete retinal reattachment (without internal tamponade present) at 6 months

End point description:

End point type	Secondary

End point timeframe:
6 months

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	123		
Units: Number of paticipants	65	79		

Statistical analyses

Statistical analysis title	Mixed logistic regression model
Comparison groups	Treatment v Control
Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.99

Secondary: Retinal detachment with PVR within 6 months of vitrectomy

End point title	Retinal detachment with PVR within 6 months of vitrectomy

End point description:

End point type	Secondary

End point timeframe:
6 months

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	124		
Units: number of participants	42	35		

Statistical analyses

Statistical analysis title	Mixed logistic regression model
Comparison groups	Treatment v Control
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.327
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.27

Adverse events

Adverse events information

Timeframe for reporting adverse events:

6 months after trial finished recruitment

Adverse event reporting additional description:

Adverse events were recorded with clinical symptoms and accompanied with a simple, brief description of the event, including dates as appropriate. Adverse events were reported on the eCRF. Serious adverse events were reported in an expedited manner to the Sponsor for each participant for their duration in the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Treatment

Reporting group description:

Intra0cular and sub Tenons triamcinolone acetonide

Reporting group title	Control

Reporting group description:

Standard vitreoretinal surgery

Serious adverse events	Treatment	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 130 (3.85%)	0 / 129 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Eye disorders			
Central subretinal bleed			
subjects affected / exposed	1 / 130 (0.77%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elevated intraocular pressure			
subjects affected / exposed	2 / 130 (1.54%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

loss of eye	Additional description: due to the effects of injury		
subjects affected / exposed	1 / 130 (0.77%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	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	81 / 130 (62.31%)	66 / 129 (51.16%)	
Eye disorders			
Elevated intraocular pressure			
subjects affected / exposed	56 / 130 (43.08%)	45 / 129 (34.88%)	
occurrences (all)	56	45	
Retinal detachment			
subjects affected / exposed	28 / 130 (21.54%)	21 / 129 (16.28%)	
occurrences (all)	28	21	
uveitis			
subjects affected / exposed	6 / 130 (4.62%)	2 / 129 (1.55%)	
occurrences (all)	6	2	
endophthalmitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 129 (0.00%)	
occurrences (all)	1	0	
hypotony	Additional description: low intraocular pressure		
subjects affected / exposed	29 / 130 (22.31%)	35 / 129 (27.13%)	
occurrences (all)	29	35	

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