Multicenter Uveitis Steroid Treatment (MUST) Trial (MUST)

ClinicalTrials.gov Identifier: NCT00132691

Recruitment Status : Completed
First Posted : August 22, 2005
Results First Posted : July 30, 2012

Last Update Posted : November 25, 2016

Sponsor:

JHSPH Center for Clinical Trials

Collaborator:

National Eye Institute (NEI)

Information provided by (Responsible Party):

JHSPH Center for Clinical Trials

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition	Uveitis
Interventions	Drug: fluocinolone acetonide intraocular implant Drug: oral corticosteroid with immunosuppressive agents as needed
Enrollment	255

Participant Flow

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Recruitment Details	Eligible patients were enrolled at 23 uveitis centers in the US, the United Kingdom and Australia from 6 December 2005 to 9 December 2008.
Pre-assignment Details	579 patients were assessed for initial eligibility (e.g. through chart review). Patients who were potentially eligible and interested in joining the trial signed an informed consent and underwent a baseline visit to confirm eligibility. Eligible patients (255) were randomly assigned to systemic treatment or implant treatment.

Arm/Group Title	Flucinolone Acetonide Intraocular Implant	Standard Systemic Treatment
▼ Arm/Group Description	Local therapy with fluocinolone acetonide 0.59 mg implant (Retisert; Bausch & Lomb Inc.) in each eye with uveitis of sufficient severity to justify treatment with systemic corticosteroids	Systemic corticosteroid therapy with immunosuppression as indicated
Period Title: **Overall Study**		
Started	129 [1]	126 [2]
Completed	118 [3]	114 [4]
Not Completed	11	12
Reason Not Completed		
Lost to Follow-up	5	8
Missed 2-year visit	4	4
Death	2	0

[1] 129 participants were assigned to implant; 122 received implant

[2] 126 participants were assigned to systemic treatment; 121 received systemic therapy

[3] 118 participants completed the 2-year anniversary visit

[4] 114 participants completed the 2-year anniversary visit

Baseline Characteristics

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Arm/Group Title	Flucinolone Acetonide Intraocular Implant	Standard Systemic Treatment	Total
▼ Arm/Group Description	Local therapy with fluocinolone acetonide 0.59 mg implant (Retisert; Bausch & Lomb Inc.) in each eye with uveitis of sufficient severity to justify	Systemic corticosteroid therapy with immunosuppression as indicated	Total of all reporting groups

		treatment with systemic corticosteroids		
Overall Number of Baseline Participants		129	126	255
▼ Baseline Analysis Population Description		[Not Specified]		
Age, Continuous Mean (Standard Deviation) Unit of measure: Years				
	Number Analyzed	129 participants	126 participants	255 participants
		46 (15)	47 (15)	46 (15)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: Participants				
	Number Analyzed	129 participants	126 participants	255 participants
	Female	91 70.5%	100 79.4%	191 74.9%
	Male	38 29.5%	26 20.6%	64 25.1%
Race/Ethnicity, Customized Measure Type: Number	Number Analyzed	129 participants	126 participants	255 participants

Unit of measure: Participants				
White		72	70	142
Hispanic		18	15	33
Black		35	31	66
Other		4	10	14
Region of Enrollment Measure Type: Number Unit of measure: Participants	Number Analyzed	129 participants	126 participants	255 participants
United States		109	104	213
Australia		5	6	11
United Kingdom		15	16	31
Bilateral uveitis Measure Type: Number Unit of measure: Participants				
	Number Analyzed	129 participants	126 participants	255 participants
		116	108	224
Site of uveitis Measure Type: Number Unit of measure: Participants	Number Analyzed	129 participants	126 participants	255 participants

Intermediate		50	47	97
Posterior or Panuveitis		79	79	158
Associated systemic inflammatory disease Measure Type: Number Unit of measure: Participants	Number Analyzed	129 participants	126 participants	255 participants
Yes		36	33	69
no		93	93	186
Visual acuity 20/40 or better Measure Type: Number Unit of measure: Eyes				
	Number Analyzed	129 participants	126 participants	255 participants
		116	122	238
Active uveitis Measure Type: Number Unit of measure: Eyes				
	Number Analyzed	129 participants	126 participants	255 participants

		192	181	373
Visual acuity 20/200 or worse Measure Type: Number Unit of measure: Eyes				
	Number Analyzed	129 participants	126 participants	255 participants
		39	35	74

Outcome Measures

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1. Primary Outcome

Title	Change in Best-corrected Visual Acuity (Change in the Numbers of Letters Read From a Standard ETDRS Eye Chart) From Baseline to 24 Months in Eyes With Uveitis
Description	Best-corrected visual acuity was measured as the number of letters read from standard logarithmic visual acuity charts by study-certified examiners who were masked to treatment. Visual acuity was measured at all study visits. The primary outcome was eye-specific change in visual acuity from baseline to 2-year follow-up. Positive change values indicate improved vision while negative change values indicate vision has gotten worse. A change of 7.5 letters is considered clinically meaningful.
Time Frame	24 months

Outcome Measure Data

Analysis Population Description

The primary analysis was an intention-to-treat analysis; analysis was conducted "as randomized". Data from the 255 randomized participants were used in the analytic model. 232 of the 255 completed the 2 year outcome visit.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	A fluocinolone acetonide intravitreal implant (0.59 mg) was surgically placed by a study-certified surgeon was placed in each eligible eye. The first eye was implanted within 28 days of randomization and, if eligible, the second eye within the next 28 days. Prior to implant surgery, topical, periocular or systemic corticosteroids where used as needed to quiet the anterior chamber. Post-implant, systemic corticosteroids and immunosuppressive drugs were tapered and discontinued. If the second eye was not eligible for an implant initially but later became eligible, an implant was placed in the second eye at that time. The treatment algorithm included re-implantation upon reactivation and treatment per best medical judgment for failure to achieve inflammation control, treatment-limiting toxicity and systemic disease requiring systemic therapy.	Oral corticosteroids supplemented with immunosuppressive drugs if indicated were given according to published guidelines developed by an expert panel. For participants with active uveitis at baseline, 1 mg/kg/day up to 60 mg/day of prednisone was given until uveitis was controlled or 4 weeks had elapsed. When control was achieved, prednisone was tapered per study guidelines. Immunosuppressive drugs were added when uveitis was not initially controlled with prednisone alone, as corticosteroid-sparing agents when prednisone could not be tapered to 10 mg/day without reactivation of uveitis and for specific uveitis syndromes. Choice of immunosuppressant was made by the study ophthalmologist; immunosuppressant administration and monitoring for toxicity was conducted according to expert guidelines.
Overall Number of Participants Analyzed	129	126
Mean (Standard Error) Unit of Measure: letters		
	6.0 (1.4)	3.2 (1.4)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy

	Comments	Null hypothesis: There will be no difference in change in visual acuity between treatment groups. Assuming 67% bilateral disease, between eye correlation of 0.4, SD of 16 letters' change over 2 years and two-sided type 1 error rate of .05, a sample size of 250 provided 91% power (assuming 10% crossover) to detect a treatment difference of 7.5 standard ETDRS letters' change in visual acuity from baseline to 24 months.
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.16
	Comments	unadjusted
	Method	Generalized estimating equations, linear
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	2.79
	Confidence Interval	(2-Sided) 95% -1.16 to 6.68
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.03
	Estimation Comments	The treatment effect is a model-based comparison of within group treatment change from enrollment to 24 months (the difference of the differences - implant minus systemic).

2. Secondary Outcome

Title	Macular Edema
▼ Description	center point macular thickness >= 240 micrometers assessed on OCT (Stratus OCT-3 [Carl Zeiss Meditec, Dublin, CA]) as graded by Central Reading Center

Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description

All eyes with uveitis were included in the analysis (245 eyes of the 129 participants randomized to implant therapy and 234 eyes of the 126 participants randomized to systemic therapy)..

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with macular edema	245	234
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis		
	22 (14 to 30)	30 (21 to 40)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.071
	Comments	unadjusted
	Method	GEE, logistic
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Ratio of odds ratios
	Estimated Value	0.61
	Confidence Interval	(2-Sided) 95% 0.34 to 1.03
	Estimation Comments	For each treatment group the odds of macular edema at 2 yrs as compared to baseline was computed. The treatment effect is the ratio of these odds (implant divided by systemic).

3. Secondary Outcome

Title	Uveitis Activity
▼ Description	Uveitis activity was determined by clinician assessment at each study visit. The study ophthalmologist evaluated each eye as active, inactive/never had uveitis or cannot assess.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
All eyes with uveitis were included in the analysis (245 eyes of the 129 participants randomized to implant therapy and 234 eyes of the 126 participants randomized to systemic therapy).

Arm/Group Title	Fluocinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	245	234
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis		
	12 (06 to 20)	29 (21 to 39)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Fluocinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.001
	Comments	unadjusted
	Method	GEE, logistic

	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Ratio of odds ratios
	Estimated Value	.29
	Confidence Interval	(2-Sided) 95% .13 to .60
	Estimation Comments	For each treatment group the odds of uveitis activity at 2 years as compared to baseline was computed. The treatment effect represents the ratio of these odds (implant divided by systemic).

4. Secondary Outcome

Title	Intraocular Pressure - Incident IOP Greater Than or Equal to 30 mm Hg
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126

Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	234	229
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	32.8 (27.1 to 39.2)	6.3 (3.7 to 10.3)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<.0001
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	6.08
	Confidence Interval	(2-Sided) 95% 3.32 to 11.15

	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of experiencing an IOP of 30 mmHg or greater. The systemic arm was the reference group.

5. Secondary Outcome

Title	Intraocular Pressure - Incident IOP Greater Than or Equal to 24 mm Hg
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	234	228

Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	53.1 (46.9 to 59.7)	18.7 (14.2 to 24.5)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<.0001
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	3.59
	Confidence Interval	(2-Sided) 95% 2.34 to 5.50
	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of experiencing an IOP of 24 mmHg or greater. The systemic arm was the reference group

6. Secondary Outcome

Title	Intraocular Pressure - Incident IOP Elevation >= 10 mmHg Above Baseline
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Fluocinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	235	230
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		

	51.8 (45.5 to 58.3)	15.5 (11.4 to 20.9)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Fluocinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<.0001
	Comments	unadjusted
	Method	Cox proportional hazards with RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	4.28
	Confidence Interval	(2-Sided) 95% 2.78 to 6.58
	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of experiencing an IOP that was 10mmHg or greater than the baseline value. The systemic arm was the reference group.

7. Secondary Outcome

Title	Glaucoma - Incident
▼ Description	Glaucoma was diagnosed by a glaucoma specialist through review of visual fields, clinical data, and fundus images.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Fluocinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	212	202
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	16.5 (12.1 to 22.2)	4.0 (2.0 to 7.8)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Fluocinolone Acetonide Implant, Systemic Therapy

	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.0008
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	4.19
	Confidence Interval	(2-Sided) 95% 1.82 to 9.63
	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of developing glaucoma. The systemic arm was the reference group.

8. Secondary Outcome

Title	Intraocular Pressure (IOP) - Incident Use of IOP-lowering Medical Therapy (Percentage of Eyes With Uveitis That Were Not Being Treated With IOP-lowering Medical Therapy at Baseline and Underwent IOP Lowering Therapy During the 24 Month Follow-up.
▼ Description	The percentage of subjects who used topical or systemic treatment for elevated IOP at any time during the 2 year follow-up and were not on IOP-lowering therapy at baseline is reported.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description

Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes	201	203
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	61.1 (54.3 to 67.8)	20.1 (15.1 to 26.3)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<.0001
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE

	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	4.16
	Confidence Interval	(2-Sided) 95% 2.67 to 6.47
	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of using an IOP-lowering therapy. The systemic arm was the reference group.

9. Secondary Outcome

Title	Intraocular Pressure - IOP-lowering Surgery
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126

Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	233	226
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	26.2 (21.0 to 32.4)	3.7 (1.9 to 7.2)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	8.40
	Confidence Interval	(2-Sided) 95% 3.39 to 20.82

	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of having surgery to lower IOP. The systemic arm was the reference group.

10. Secondary Outcome

Title	Cataract - Incident Cataract
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Eyes with uveitis, not participants, were analyzed. Eyes with prevalent complications or missing data at enrollment were were excluded from the risk set.

Arm/Group Title	Fluocinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Overall Number of Units Analyzed Type of Units Analyzed: Eyes with uveitis	54	50

Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of eyes with uveitis at risk		
	90.7 (81.3 to 96.6)	44.9 (32.3 to 59.8)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Fluocinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	unadjusted
	Method	Cox proportional hazards w/ RE
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	4.12
	Confidence Interval	(2-Sided) 95% 2.21 to 7.67
	Estimation Comments	A Cox proportional hazards model with a random effect to account for between-eye correlation was used to estimate the relative hazard of developing a cataract. The systemic arm was the reference group.

11. Secondary Outcome

Title	Change in Self-reported Vision-related Function as Measured by the National Eye Institute 25-Item Visual Function Questionnaire (NEI-VFQ 25) Vision Targeted Composite Score From Baseline to 24 Months
▼ Description	The NEI-VFQ 25 measures the effect of visual disability/symptoms with generic health and task-oriented domains. The range for the composite score is 0 to 100; higher scores are associated with better visual function. A change of 4 to 6 points is considered to be a clinically meaningful difference.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
[Not Specified]

Arm/Group Title	Fluocinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy	Participants randomized to receive systemic therapy
Overall Number of Participants Analyzed	129	126
Mean (Standard Error) Unit of Measure: units on a scale (composite score)		
	11.44 (1.67)	6.80 (1.58)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Fluocinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]

	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.043
	Comments	unadjusted
	Method	GEE, linear
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	4.64
	Confidence Interval	(2-Sided) 95% 0.14 to 9.15
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.30
	Estimation Comments	The treatment effect is a model-based comparison of within group treatment change from enrollment to 24 months (the difference of the differences - implant minus systemic).

12. Secondary Outcome

Title	Change in SF-36 Mental Component Score From Baseline to 24 Months
▼ Description	Self-reported health related QoL was measured with the SF 36 survey. The mental component score for the SF 36 is a summary measure of mental health primarily based on the social functioning, role emotional, mental health and vitality domains. The score is scaled to a population norm with a mean of 50 and standard deviation of 10. Higher scores represent better outcomes. The mean change in scores between baseline and 24 months was calculated for each treatment group.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description

[Not Specified]

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126
Mean (Standard Error) Unit of Measure: units on a scale		
	2.55 (1.11)	-1.1 (1.15)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.023
	Comments	unadjusted
	Method	GEE, linear
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	3.62
	Confidence Interval	(2-Sided) 95% 0.49 to 6.76

Parameter Dispersion	Type: Standard Error of the mean Value: 1.60
Estimation Comments	The treatment effect is a model-based comparison of within group treatment change from enrollment to 24 months (the difference of the differences - implant minus systemic)

13. Secondary Outcome

Title	Change in SF-36 Physical Component Score From Baseline to 24 Months
▼ Description	Self-reported health related QoL was measured with the SF 36 survey. The physical component score for the SF 36 is a summary measure of physical health primarily based on the physical functioning, role physical, bodily pain and general health domains of the survey. The score is scaled to a population norm with a mean of 50 and standard deviation of 10. Higher scores represent better outcomes. The mean change in scores between baseline and 24 months was calculated for each treatment group. A 3 to 5 point difference is considered to be clinically meaningful.
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
[Not Specified]

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	129	126

Mean (Standard Error) Unit of Measure: units on a scale		
	1.15 (0.83)	-1.8 (0.90)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.016
	Comments	unadjusted
	Method	Generalized Estimating Equations
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	2.95
	Confidence Interval	(2-Sided) 95% 0.54 to 5.36
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.23
	Estimation Comments	The treatment effect is a model-based comparison of within group treatment change from enrollment to 24 months (the difference of the differences - implant minus systemic).

14. Secondary Outcome

Title	Hyperlipidemia - Incident

▼ Description	LDL greater than or equal to 160 mg/mL
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Number of participants at risk were included in the analysis

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	97	104
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of participants at risk		
	9.8 (5.2 to 18.0)	11.0 (6.3 to 19.1)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other

	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.84
	Comments	unadjusted
	Method	Regression, Cox
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.91
	Confidence Interval	(2-Sided) 95% 0.39 to 2.15
	Estimation Comments	A Cox proportional hazards model was used to evaluate the relative hazard of hyperlipidemia for the implant and systemic treatments. The systemic treatment is the reference group.

15. Secondary Outcome

Title	Hypertension Diagnosis Requiring Treatment
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Participants with prevalent complications or missing data at enrollment were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.

Overall Number of Participants Analyzed	88	88
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of participants		
	4.6 (1.8 to 11.9)	10.5 (5.6 to 19.3)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.13
	Comments	unadjusted
	Method	Regression, Cox
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.40
	Confidence Interval	(2-Sided) 95% 0.13 to 1.29
	Estimation Comments	A Cox proportional hazards model was used to evaluate the relative

		hazard of hypertension for the implant and systemic treatments. The systemic treatment is the reference group.

16. Secondary Outcome

Title	Diabetes Mellitus
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
Participants with prevalent complications or missing data at enrollment were excluded from the risk set.

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	105	114
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of participants		
	1.0 (0.1 to 6.6)	3.6 (1.4 to 9.4)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Flucinolone Acetonide Implant, Systemic Therapy
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	P-Value	0.24
	Comments	unadjusted
	Method	Regression, Cox
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.26
	Confidence Interval	(2-Sided) 95% 0.03 to 2.44
	Estimation Comments	A Cox proportional hazards model was used to evaluate the relative hazard of diabetes mellitus for the implant and systemic treatments. The systemic treatment is the reference group.

17. Secondary Outcome

Title	Mortality
▼ Description	[Not Specified]
Time Frame	24 months

▼ Outcome Measure Data

▼ Analysis Population Description
[Not Specified]

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description:	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.
Overall Number of Participants Analyzed	126	124
Measure Type: Number Number (95% Confidence Interval) Unit of Measure: percentage of participants		
	1.6 (0.4 to 6.3)	0 [1] (NA to NA)

[1] no deaths reported in systemic group

Adverse Events

Go to

Time Frame	2 years
Adverse Event Reporting Description	[Not Specified]

Arm/Group Title	Flucinolone Acetonide Implant	Systemic Therapy
▼ Arm/Group Description	Participants randomized to receive implant therapy.	Participants randomized to receive systemic therapy.

All-Cause Mortality

	Flucinolone Acetonide Implant		Systemic Therapy	
	Affected / at Risk (%)		Affected / at Risk (%)	
Total	--/--		--/--	

Serious Adverse Events

	Flucinolone Acetonide Implant		Systemic Therapy	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	75/129 (58.14%)		47/126 (37.30%)	
Cardiac disorders				
Pericardial drain placement *	0/129 (0.00%)	0	1/126 (0.79%)	1
Hypertension *	7/129 (5.43%)	12	3/126 (2.38%)	5
Cardiovascular *	2/129 (1.55%)	2	4/126 (3.17%)	5
Endocrine disorders				
Total thyroidectomy *	0/129 (0.00%)	0	1/126 (0.79%)	1
Eye disorders				
Endophthalmitis *	3/129 (2.33%)	3	0/126 (0.00%)	0
Glaucoma *	7/129 (5.43%)	11	1/126 (0.79%)	2
Hypotony *	4/129 (3.10%)	4	2/126 (1.59%)	2
Ocular Hypertension *	32/129 (24.81%)	54	5/126 (3.97%)	6
Retinal Detachment *	4/129 (3.10%)	5	1/126 (0.79%)	1
Vitreous Hemorrhage *	14/129 (10.85%)	15	4/126 (3.17%)	5
Bleb revision *	1/129 (0.78%)	1	0/126 (0.00%)	0
Complication of Kenalog injection *	1/129 (0.78%)	1	0/126 (0.00%)	0
Enucleation *	0/129 (0.00%)	0	1/126 (0.79%)	1
Hospitalization for cataract surgery *	0/129 (0.00%)	0	1/126 (0.79%)	2
Retisert wound dehiscence *	1/129 (0.78%)	1	0/126 (0.00%)	0
Choroidal neovascularization *	1/129 (0.78%)	1	0/126 (0.00%)	0

Hyphema *	1/129 (0.78%)	1	0/126 (0.00%)	0
Exposed suture *	1/129 (0.78%)	1	0/126 (0.00%)	0
Surgery to reposition shunt *	1/129 (0.78%)	1	0/126 (0.00%)	0
Iris bombe *	1/129 (0.78%)	1	0/126 (0.00%)	0
Exposed Ahmed valve *	1/129 (0.78%)	1	0/126 (0.00%)	0
Orbital cellulitis *	1/129 (0.78%)	1	0/126 (0.00%)	0
Revision of Ahmed valve *	1/129 (0.78%)	1	0/126 (0.00%)	0
Abnormal ERG *	0/120 (0.00%)	0	1/126 (0.79%)	1
Gastrointestinal disorders				
Diarrhea, dehydration *	0/129 (0.00%)	0	1/126 (0.79%)	1
Ileostomy takedown *	0/129 (0.00%)	0	1/126 (0.79%)	1
Perforated viscus lung cancer *	0/129 (0.00%)	0	1/126 (0.79%)	1
Exacerbation of intestinal fissure *	0/129 (0.00%)	0	1/126 (0.79%)	1
Gastrointestinal *	1/129 (0.78%)	3	2/126 (1.59%)	2
General disorders				
Prolonged hospitalization stay due to reaction *	1/120 (0.83%)	1	0/126 (0.00%)	0
Abdominal pain *	0/129 (0.00%)	0	1/126 (0.79%)	1
Flu-like reaction to Avonex *	0/129 (0.00%)	0	1/126 (0.79%)	1
Hospitalization *	0/129 (0.00%)	0	1/126 (0.79%)	1
Headache due to hypertension *	0/129 (0.00%)	0	1/126 (0.79%)	1
Hepatobiliary disorders				
Gall bladder surgery *	0/129 (0.00%)	0	2/126 (1.59%)	2
Abnormal laboratory value *	4/129 (3.10%)	5	1/126 (0.79%)	1
Immune system disorders				
Neuro Bechet's disease *	0/129 (0.00%)	0	1/126 (0.79%)	1
Infections and infestations				

Infection *	6/129 (4.65%)	9	5/126 (3.97%)	5
Injury, poisoning and procedural complications				
Torn medial meniscus *	1/129 (0.78%)	1	0/126 (0.00%)	0
Fracture *	1/129 (0.78%)	1	6/126 (4.76%)	6
Investigations				
Chest pain *	1/129 (0.78%)	2	3/126 (2.38%)	3
Musculoskeletal and connective tissue disorders				
Hip replacement *	2/129 (1.55%)	2	0/126 (0.00%)	0
Shoulder surgery *	0/129 (0.00%)	0	1/126 (0.79%)	1
Arthrosis due to aseptic necrosis *	0/129 (0.00%)	0	1/126 (0.79%)	1
Dislocation of hip *	0/129 (0.00%)	0	1/126 (0.79%)	1
Ankylosing spondylitis *	1/129 (0.78%)	1	0/126 (0.00%)	0
Hip pain *	0/129 (0.00%)	0	1/126 (0.79%)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Hospitalization for post-surgical observation of pharyngeal papilloma biopsy *	0/129 (0.00%)	0	1/126 (0.79%)	1
Cancer *	1/129 (0.78%)	1	3/126 (2.38%)	3
Nervous system disorders				
Anterior cervical dissection, fusion *	1/129 (0.78%)	1	0/126 (0.00%)	0
Psychiatric disorders				
Hospitalization for observation while on prednisone *	1/129 (0.78%)	1	0/126 (0.00%)	0
Psychotic episode *	0/129 (0.00%)	0	1/126 (0.79%)	1
Renal and urinary disorders				

Kidney stones *	1/129 (0.78%)	1	0/126 (0.00%)	0
Hemmorhagic cystitis *	0/129 (0.00%)	0	1/126 (0.79%)	1
Hydronephrosis *	1/129 (0.78%)	1	0/126 (0.00%)	0
Reproductive system and breast disorders				
Hysterectomy *	1/129 (0.78%)	1	1/126 (0.79%)	1
Precancerous cells right breast *	1/129 (0.78%)	1	0/126 (0.00%)	0
Cervical dysplasia *	1/129 (0.78%)	1	0/126 (0.00%)	0
Miscarriage *	1/129 (0.78%)	1	3/126 (2.38%)	3
Skin and subcutaneous tissue disorders				
Non-melanoma skin cancer *	1/129 (0.78%)	1	3/126 (2.38%)	7
Vascular disorders				
Thrombosis *	4/129 (3.10%)	4	2/126 (1.59%)	2

* Indicates events were collected by non-systematic assessment

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

	Flucinolone Acetonide Implant		Systemic Therapy	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	113/129 (87.60%)		113/126 (89.68%)	
Cardiac disorders				
Hypertension (systolic) †	27/129 (20.93%)	38	32/126 (25.40%)	62
Hypertension (diastolic) †	24/129 (18.60%)	39	30/126 (23.81%)	47
Eye disorders				
Ocular hypertension †	78/129 (60.47%)	246	29/126 (23.02%)	67
Glaucoma †	10/129 (7.75%)	13	2/126 (1.59%)	5

Hypotony †	26/129 (20.16%)	46	10/126 (7.94%)	28
Cataract †	40/129 (31.01%)	65	13/126 (10.32%)	15
Vitreous hemorrhage †	13/129 (10.08%)	15	2/126 (1.59%)	2
Gastrointestinal disorders				
Nausea *	5/129 (3.88%)	7	20/126 (15.87%)	24
Vomiting *	5/129 (3.88%)	5	11/126 (8.73%)	15
Diarrhea *	2/129 (1.55%)	2	12/126 (9.52%)	16
General disorders				
Headache *	25/129 (19.38%)	36	19/126 (15.08%)	21
Fatigue *	6/129 (4.65%)	7	11/126 (8.73%)	15
Infection *	52/129 (40.31%)	116	67/126 (53.17%)	178
Hepatobiliary disorders				
SGOT (AST) or SGPT (ALT) †	5/129 (3.88%)	9	8/126 (6.35%)	13
Immune system disorders				
Allergic reaction *	10/129 (7.75%)	16	9/126 (7.14%)	11
Metabolism and nutrition disorders				
Hyperglycemia (fasting) †	4/129 (3.10%)	4	10/126 (7.94%)	16
Hyperglycemia (casual) †	6/129 (4.65%)	8	10/126 (7.94%)	16
Hypoglycemia †	7/129 (5.43%)	8	6/126 (4.76%)	6
Triglyceride (high) †	10/129 (7.75%)	12	10/126 (7.94%)	12
Musculoskeletal and connective tissue disorders				
Osteoporosis †	12/129 (9.30%)	12	10/126 (7.94%)	10
Psychiatric disorders				
Mood *	4/129 (3.10%)	4	11/126 (8.73%)	12
Renal and urinary disorders				
BUN †	8/129 (6.20%)	8	10/126 (7.94%)	16

† Indicates events were collected by systematic assessment

* Indicates events were collected by non-systematic assessment

Limitations and Caveats

Go to

[Not Specified]

More Information

Go to

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact

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Publications of Results:

The Multicenter Uveitis Steroid Treatment (MUST) Trial Research Group; Writing Committee, Kempen JH, Altaweel MM, Holbrook JT, Jabs DA, Louis TA, Sugar EA, Thorne JE. Randomized Comparison of Systemic Anti-inflammatory Therapy Versus Fluocinolone Acetonide Implant for Intermediate, Posterior, and Panuveitis: The Multicenter Uveitis Steroid Treatment Trial. Ophthalmology. 2011 Oct;118(10):1916-1926. Epub 2011 Aug 15. PubMed PMID: 21840602; PubMed Central PMCID: PMC3191365. http://dx.doi.org/doi:10.1016/j.ophtha.2011.07.027

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Tomkins-Netzer O, Lightman SL, Burke AE, Sugar EA, Lim LL, Jaffe GJ, Altaweel MM, Kempen JH, Holbrook JT, Jabs DA; Multicenter Steroid Treatment Trial and Follow-up Study Research Group. Seven-Year Outcomes of Uveitic Macular Edema: The Multicenter Uveitis Steroid Treatment Trial and Follow-up Study Results. Ophthalmology. 2021 May;128(5):719-728. doi: 10.1016/j.ophtha.2020.08.035. Epub 2020 Sep 10.

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