EVALUATING THE TRUE RATE OF RECURRENCE OF NON-INFECTIOUS POSTERIOR SEGMENT UVEITIS FOLLOWING TREATMENT WITH AN INJECTABLE FLUOCINOLONE ACETONIDE INSERT (FAi)

Dilraj Grewal, MD

Associate Professor of Ophthalmology, Duke Eye Center

Director of Grading, Duke Reading Center

Durham, NC

On behalf of the Eyepoint Study Investigators

Duke Eye Center

DISCLOSURES

- Research Support: EyePoint, GILEAD
- Consultant: EyePoint, Allergan, Alimera

SUMMARY

- Over half of the recurrences in the 36-month phase 3 clinical trial were imputed as a result of confounding systemic medication use rather than a study eye recurrence.
  - Reasons for the use of confounding medications could include treatment of non-ocular conditions or fellow eye inflammation.
- The true, observed rate of recurrence in study eyes treated with FAi is likely lower than the 56% that has been reported.
  - May be as low as 43%

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OBJECTIVE

- Systemic anti-inflammatory and immunosuppressive treatments used for non-ocular or fellow-eye inflammation confound study-eye outcomes when evaluating monocular local treatment of non-infectious posterior segment uveitis (NIU-PS)

- The conservative analysis treats the use of confounding systemic medications as an imputed recurrence

- This post-hoc analysis reviewed each imputed recurrence and characterized the reasons for the use of confounding systemic medications to determine the true recurrence rates in the FAi and sham injection groups

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STUDY METHODS

Study Design

- 33 sites/N=129 in double masked, randomized, prospective, sham-controlled study
- 2:1 randomization to 0.18 mg fluocinolone acetonide insert (FAi) or Sham
- Multinational: US, UK, Germany, Hungary, Israel, India

Patients

- ≥ 1Y history of recurrent NIPU requiring:
  - 3M systemic therapy; or ≥ 2 steroid injections
- Enrolled patients required to have < 10 AC cells/HPF, ≤ 2+VH, and ≥15 ETDRS letters
- 6 mmHg < IOP < 21 mmHg without meds
- No recent history of 0.59 mg fluocinolone acetonide intravitreal implant (36M), dexamethasone intravitreal implant (6M), or ocular steroid injections (3M)
- Systemic meds had to be tapered over ≤ 3m

Study Endpoints

- Recurrence of uveitis defined as:
  - ≥ 2 step increase in vitreous haze; or
  - ≥ 15 letter loss of VA
  - Imputed for confounding and/or rescue treatment or for missing data
- BCVA
- Resolution of macular edema (Y/N)

Safety

- Adverse events
- IOP-lowering medications and surgeries
- Cataract and cataract surgeries

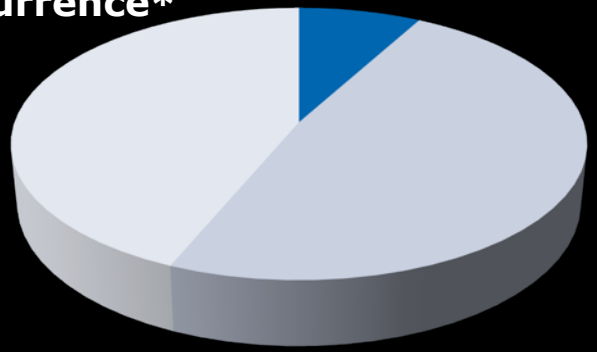
BASELINE DEMOGRAPHICS

	FAi (N=87)	SHAM (N=42)
Age (years)	48.3 ± 13.9	48.3 ± 13.7
Male Female	42.5% 57.5%	31.0% 69.0%
Duration of Uveitis (years)	7.8 ± 6.7	5.6 ± 6.8
Vitreous Haze ≥ 1+	44.8%	50.0%
BCVA (letters)	66.9 ± 15.5	64.9 ± 15.5
IOP (mmHg)	13.9 ± 3.1	13.6 ± 3.2

RESULTS: 36M NIU-PS RECURRENCE RATE

38/87 (43.7%)
No Recurrence*

FAi



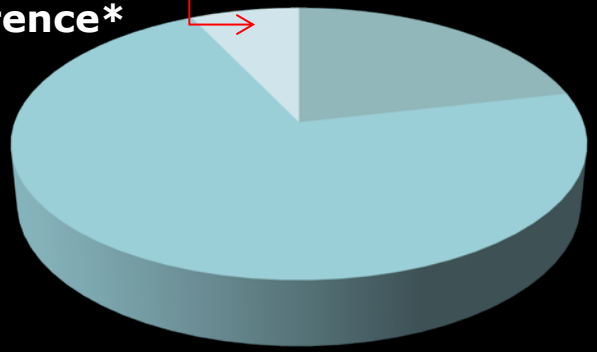
7/87 Observed (8.0%)
42/87 Imputed (48.3%)

35/87 (40%) Imputed recurrences due to adjunctive med use in FAi group

- **27/87 (31.0%) systemic treatments**
- 8/87 (9.2%) local injections

3/42 (7.1%)
No Recurrence*

Sham



9/42 Observed (21.4%)
30/42 Imputed (71.4%)

27/42 (64.3%) Imputed recurrences due to adjunctive med use in sham group

- **9/42 (21.4%) systemic treatments**
- 18/42 (42.9%) local injections

*** P < 0.001**

RESPONDER ANALYSIS DEFINITIONS

RESPONDER	Patient would not have otherwise been considered to have had a recurrence during the 36M study period
NON-RESPONDER	Patient had subsequent findings that suggested their study eye uveitis was not adequately controlled
LIKELY RESPONDER	Reason for confounding systemic treatment was not completely clear or the duration of low dose confounding treatment was excessive
UNKNOWN	Insufficient information to make a judgement

POST-HOC REVIEW RESULTS

Imputed Recurrences due to systemic treatment

	FAi (N=27)	SHAM (N=9)
RESPONDER Fellow Eye Inflammation Non-Ocular*	10 (5) (5)	2 (0) (2)
NON-RESPONDER	12	6
LIKELY RESPONDER	2	0
UNKNOWN	3	1

* Non-ocular conditions treated with confounding systemic medications: Multiple Sclerosis (2), Arthritis, Sarcoidosis, Upper Respiratory Infection, Back Strain, Asthma

RESPONDER & LIKELY RESPONDER DETAILS

ID	Group	Tx Reason	Indication	Review Details
RESPONDERS				
04002	FAi	Non-Ocular	URI	Day 686 Methylprednisolone injection for bronchitis + carpal tunnel; Day 710 oral Prednisone for pneumonia; No recurrence or other confounding meds after
08002	FAi	Non-Ocular	Arthritis	Oral Prednisone tapered (Days 621-746) for oglioarthritis; Day 812 SC Abatacept for same; No recurrence or other confounding meds after
11005	FAi	Fellow Eye	Episcleritis	Oral Methylprednisolone tapered (Days 876-909) for fellow eye episcleritis unresponsive to difuprednate 0.05% drops; No recurrence or other confounding meds after
17001	FAi	Non-Ocular	MS	IV Methylprednisolone for worsening MS (Days 716-718); No recurrence or other confounding meds after
46001	FAi	Fellow Eye	Uveitis	Oral Prednisone tapered (Days 1076-1082) for fellow eye uveitis inadequately controlled with Triamcinolone Acetonide + Dexamethasone intravitreal implant; No recurrence or other confounding meds after
52002	FAi	Non-Ocular	Sarcoid	Low dose (5 mg/day) Prednisone used throughout the study; Fellow eye required local tx of uveitis indicating that dose was too low to confound
53002	FAi	Fellow Eye	ME	Day 1051 IM Methylprednisolone for fellow eye macular edema; No recurrence or other confounding meds after
73001	FAi	Fellow Eye	Vit Haze	Day 32 Prednisone for fellow eye vitreous haze; No recurrence or other confounding meds after
74001	FAi	Fellow Eye	Post-op	Oral Prednisone (1mg/day x 3 weeks) following fellow eye cataract surgery; No recurrence or other confounding meds after
95002	FAi	Non-Ocular	MS	Systemic Methylprednisolone started month 31 for MS prophylaxis; No recurrence or other confounding meds after
02002	Sham	Non-Ocular	Back Strain	Day 183 Methylprednisolone for back strain; No recurrence or other confounding meds after
13001	Sham	Non-Ocular	Asthma	Oral Prednisone tapered (Days 66-76) for worsening asthma; No recurrence or other confounding meds after
LIKELY RESPONDERS				
18006	FAi	Both	Multi	Oral Prednisone tapered (Days 244-285) for shingles; (Days 410-452) for gout; Day 1142 SC Adalimumab presumably for fellow eye uveitis; No recurrence or other confounding meds after
18009	FAi	Non-Ocular	Skin lesions	Oral Prednisone tapered (Days 404-1147) for lesions on extremities; Day 1142 SC Adalimumab for psoriasis; Good response for over 1 year prior to treatment of skin conditions

RESULTS: ADVERSE EVENTS

- The most common adverse events were cataract development and increases in intraocular pressure.
- AE details have been reported previously.

- Jaffe GJ, Foster CS, Pavesio CE, Paggiarino DA, Riedel GE. Effect of an Injectable Fluocinolone Acetonide Insert on Recurrence Rates in Chronic Noninfectious Uveitis Affecting the Posterior Segment: Twelve-Month Results. Ophthalmology. 2019 Apr;126(4):601-610.
- Jaffe GJ, Pavesio C, on behalf of the study investigators and sites, Effect of an Fluocinolone Acetonide Insert on Recurrence Rates in Noninfectious Intermediate, Posterior, or Panuveitis: 3-Year Results, Ophthalmology (2020), doi: https://doi.org/10.1016/j.ophtha.2020.04.001.

DISCUSSION

- 27/49 (55.1%) recurrences in FAi treated eyes in the 36-month phase 3 clinical trial were imputed as a result of confounding systemic medication use.
- The sole reason for designating the study eye a treatment failure in 10 FAi cases was the use of a confounding systemic medication
  - 5 cases were the result of systemic treatment of a non-ocular condition and 5 were the result of systemic treatment for fellow-eye inflammation
- The true, observed rate of recurrence in study eyes treated with FAi is likely lower than the 56% that has been reported.
  - May be as low as 43%
- The adverse event profile has been previously reported and contains no unanticipated side effects.