Bispecific trap-antibody inhibiting interleukin-6 and vascular endothelial growth factor (KSI-101): Phase 1b APEX Study in patients with macular edema secondary to inflammation (MESI)

First-Time End of Study Results

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Relevant Financial Disclosures: Consultant with Kodiak

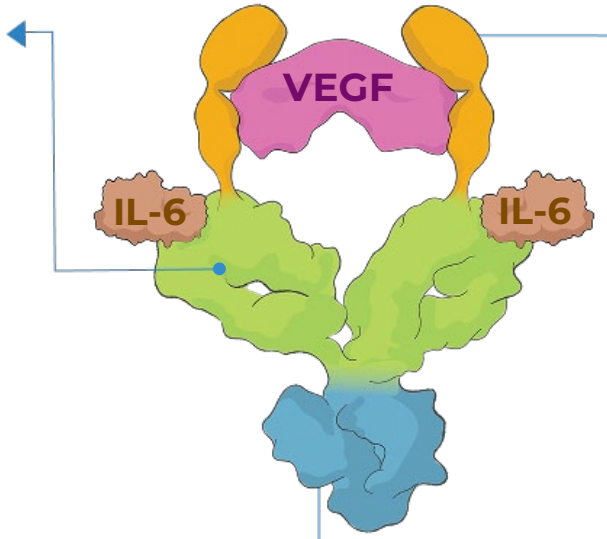
KSI-101 is a first-in-class, high-strength intravitreal biologic designed to target IL-6 mediated inflammation and VEGF-mediated vascular permeability simultaneously

KSI-101: high formulation strength (100 mg/mL)

Anti-IL-6 Antibody

Potent Anti-Inflammatory Effect

The anti-IL-6 antibody can inhibit up to two IL-6 molecules to block inflammation and normalize the blood retinal barriers



VEGF Trap

Broad VEGF Inhibition

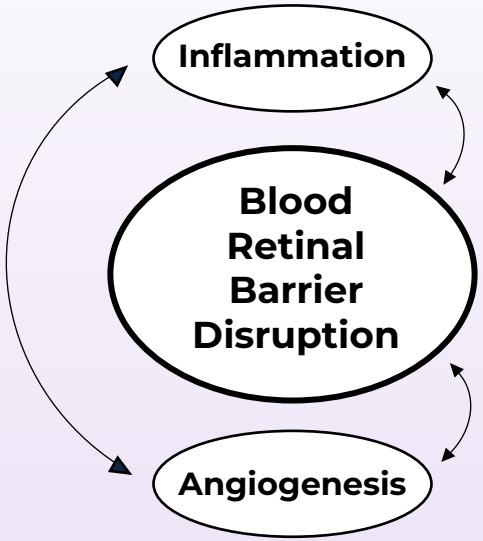
The VEGF trap mimics the native receptor and binds multiple targets including VEGF-A, VEGF-B and PIGF

Modified Fc

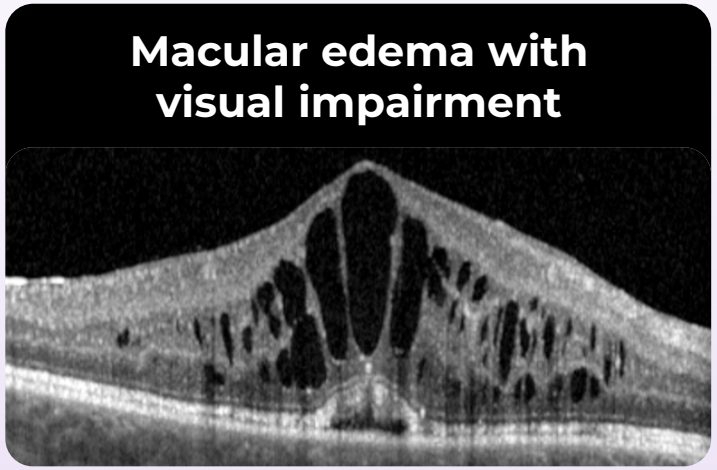
Immunologically inert antibody

What is macular edema secondary to inflammation (MESI)?

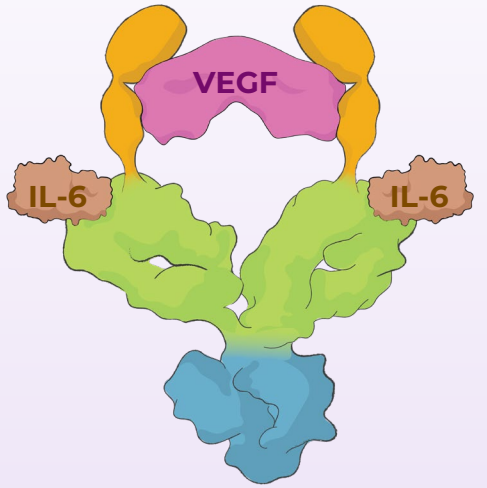
Common Pathophysiology



Common Clinical Presentation



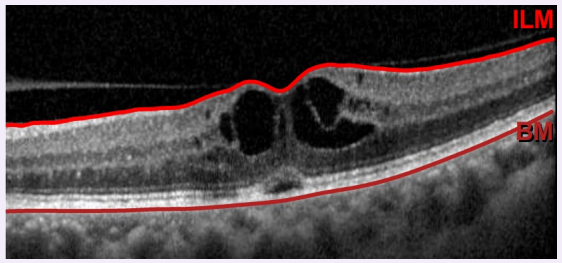
Unifying Therapy?



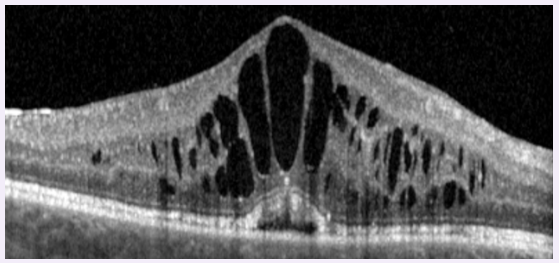
KSI-101

MESI is a heterogenous group of diseases that clinically present with macular edema and visual impairment, which are caused by a common pathophysiology: inflammation and blood retinal barrier disruption

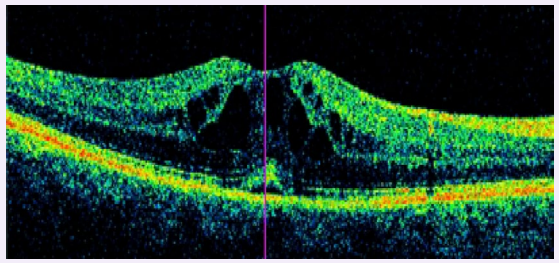
MESI comprises a heterogenous group of diseases with a common, readily identifiable clinical presentation: macular edema with visual impairment



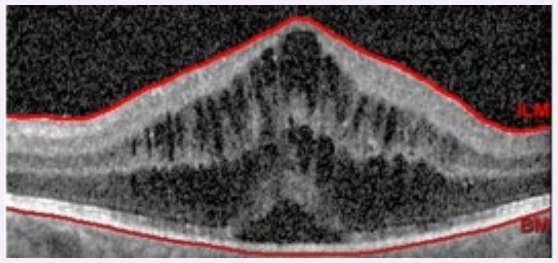
Anterior



Intermediate



Posterior



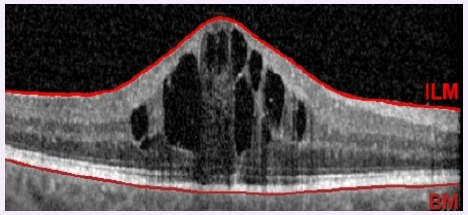
Panuveitis

Location of Inflammation

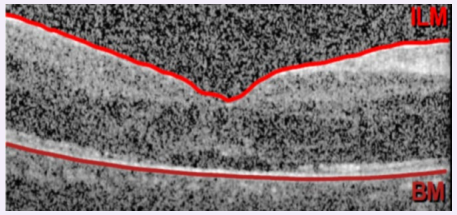
Irrespective of the anatomical location of the inflammation or the specific etiology, the clinical presentation is the same: macular edema

Specific Etiology

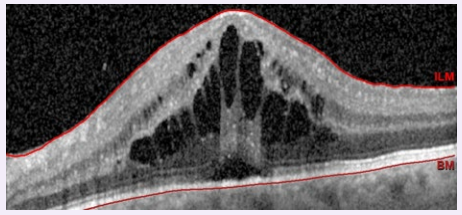
Idiopathic



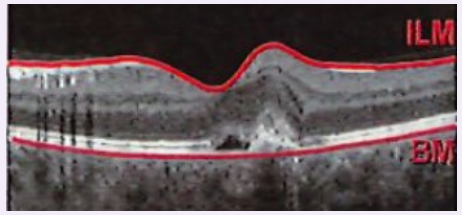
Juvenile Idiopathic Arthritis



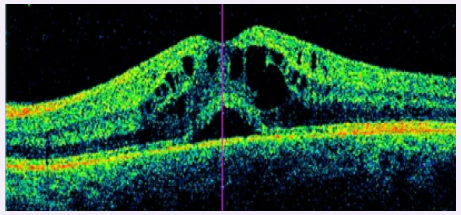
Focal Chorioretinal inflammation



Punctate Inner Choroidopathy

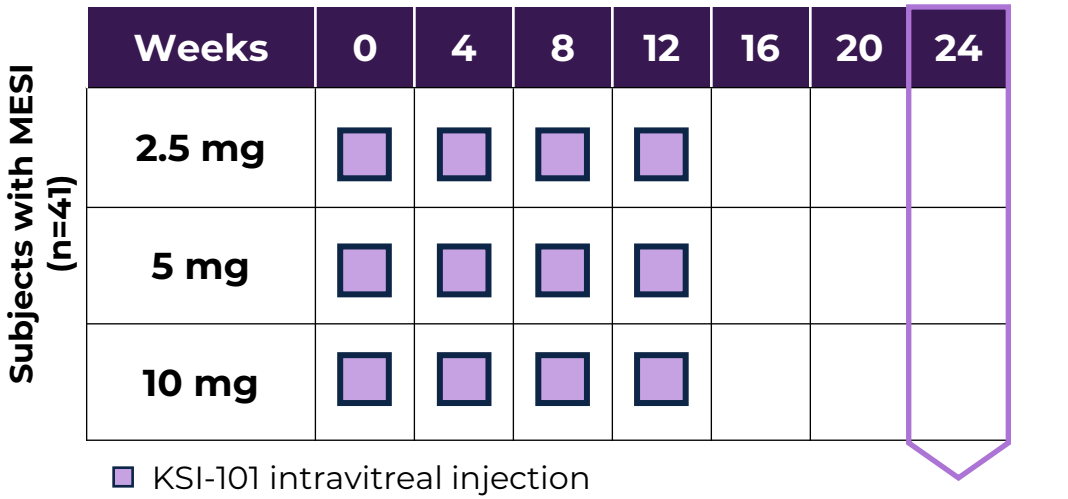


Post-Operative Macular Edema



Phase 1b APEX study: multiple dose study of KSI-101 in patients with MESI

Study Design: Ongoing, Open-label Phase 1b in MESI



Key inclusion criteria

- Macular edema secondary to inflammation (MESI)
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic
- Active leakage as evidenced by fluorescein angiogram
- OCT CST of ≥320 microns
- BCVA score ≤75 and ≥25 (20/32 to 20/320 Snellen equivalent)

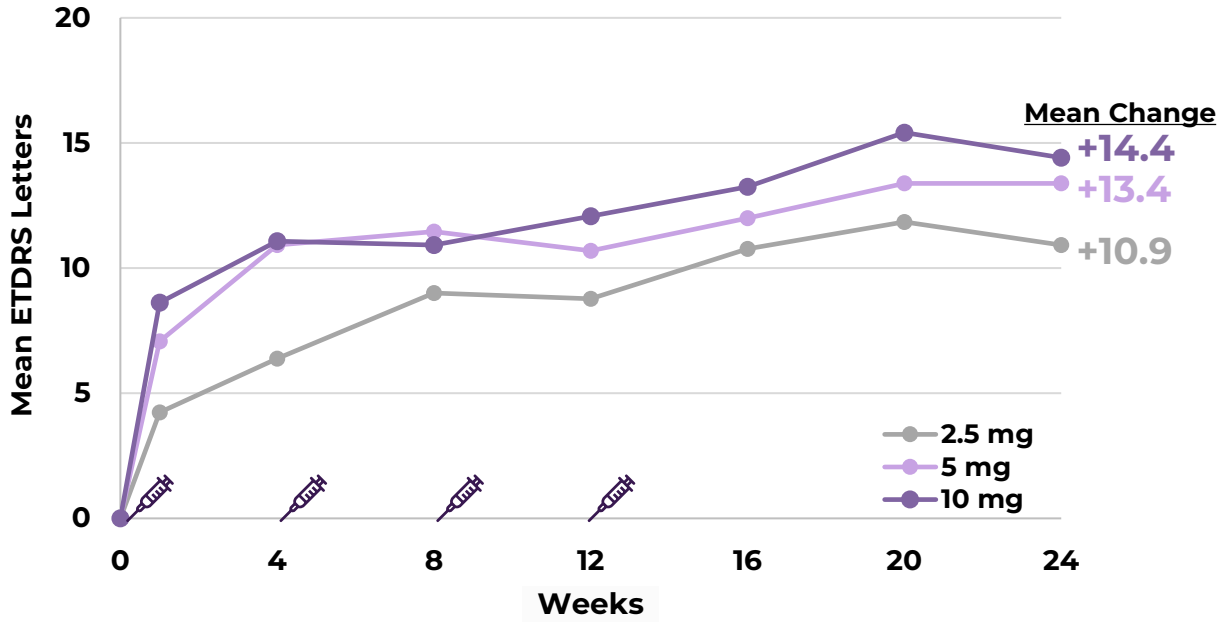
Baseline Characteristics

	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)	All KSI-101 (N=41)
Age, years, mean (SD)	74.2 (11.6)	67.4 (8.1)	67.5 (18.8)	69.6 (13.7)
Female, n (%)	8 (61.5)	7 (50.0)	8 (57.1)	23 (56.1)
Race, White, n (%)	11 (84.6)	11 (78.6)	14 (100)	36 (87.8)
MESI disease duration, months, mean (SD)	12.2 (21.0)	1.7 (1.2)	15.8 (37.2)	11.1 (26.5)
Inflammation anatomical location, n (%)				
Anterior	0	2 (14.3)	0	2 (4.9)
Intermediate	1 (7.7)	0	2 (14.3)	3 (7.3)
Posterior	10 (76.9)	6 (42.9)	10 (71.4)	26 (63.4)
Panuveitis	2 (15.4)	6 (42.9)	2 (14.3)	10 (24.4)
Patients with active inflammation, n (%)	3 (23.1)	11 (78.6)	5 (35.7)	19 (46.3)
Unilateral MESI, n (%)	9 (69.2)	6 (42.9)	5 (35.7)	20 (48.8)
BCVA, ETDRS Letters, mean (SD)	62.7 (7.4)	65.6 (7.9)	62.1 (8.4)	63.5 (7.9)
Snellen equivalent	~20/50	~20/50	~20/63	~20/50
OCT CST, µm, mean (SD) (Site reported)	461.7 (137.7)	487.0 (124.1)	528.6 (157.3)	493.2 (139.7)
OCT CST, µm, mean (SD) (Reading Center Data)	451.3 (143.3)	488.7 (121.8)	517.7 (159.7)	486.8 (141.5)
Lens Status, pseudophakic, n (%)	9 (69.2)	13 (92.9)	11 (78.6)	33 (80.5)

Final results from the APEX Study in MESI.

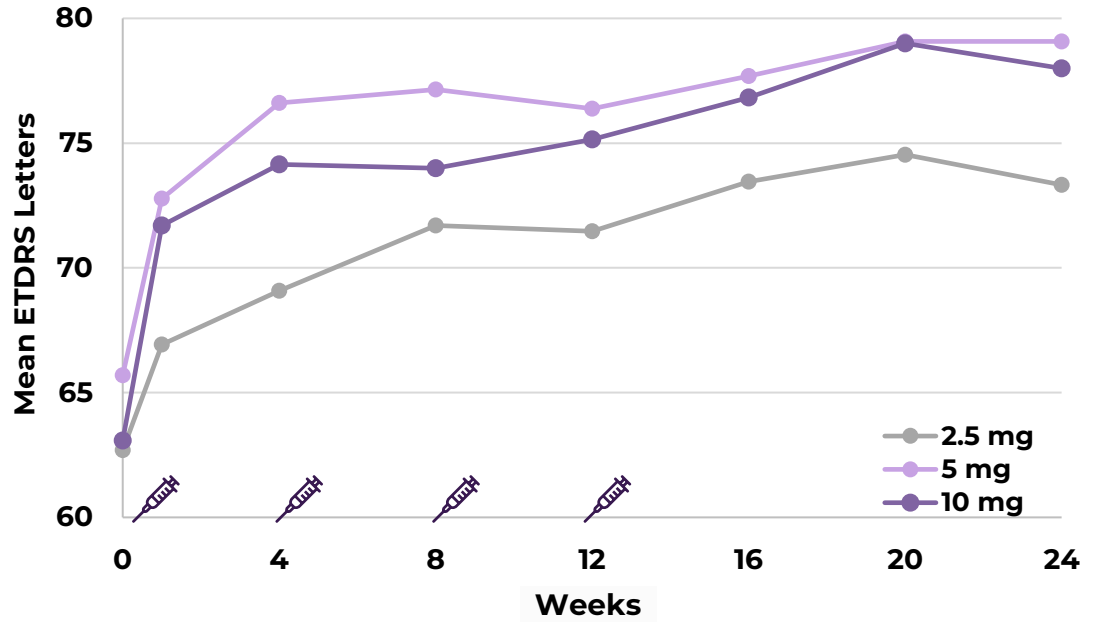
The top two dose levels achieve meaningful vision gains of >10 letters by Week 4 and continue to improve over time, achieving a 20/25 Snellen visual acuity by Week 20

Mean Change in BCVA over time



Dose Level	Sample Size							
2.5 mg	13	13	13	13	13	13	13	12
5 mg	13	13	13	13	13	13	13	13
10 mg	13	13	13	13	13	12	12	12

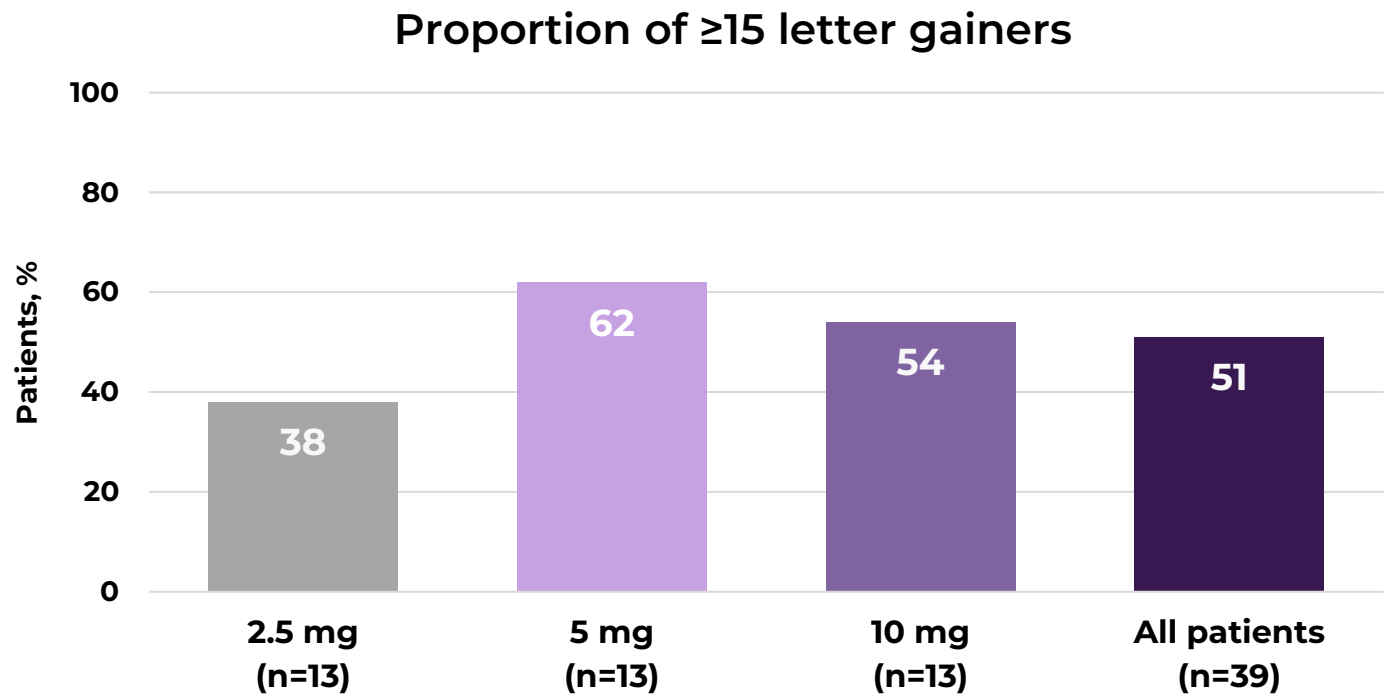
Observed BCVA over time



Dose Level	Sample Size							
2.5 mg	13	13	13	13	13	13	13	12
5 mg	13	13	13	13	13	13	13	13
10 mg	13	13	13	13	13	12	12	12

Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). One patient in the 10 mg dose level discontinued after Week 12 due to recurrent uveitis flare-up

More than half of patients achieved a ≥15 letter gain, with additional benefit observed in the top dose levels



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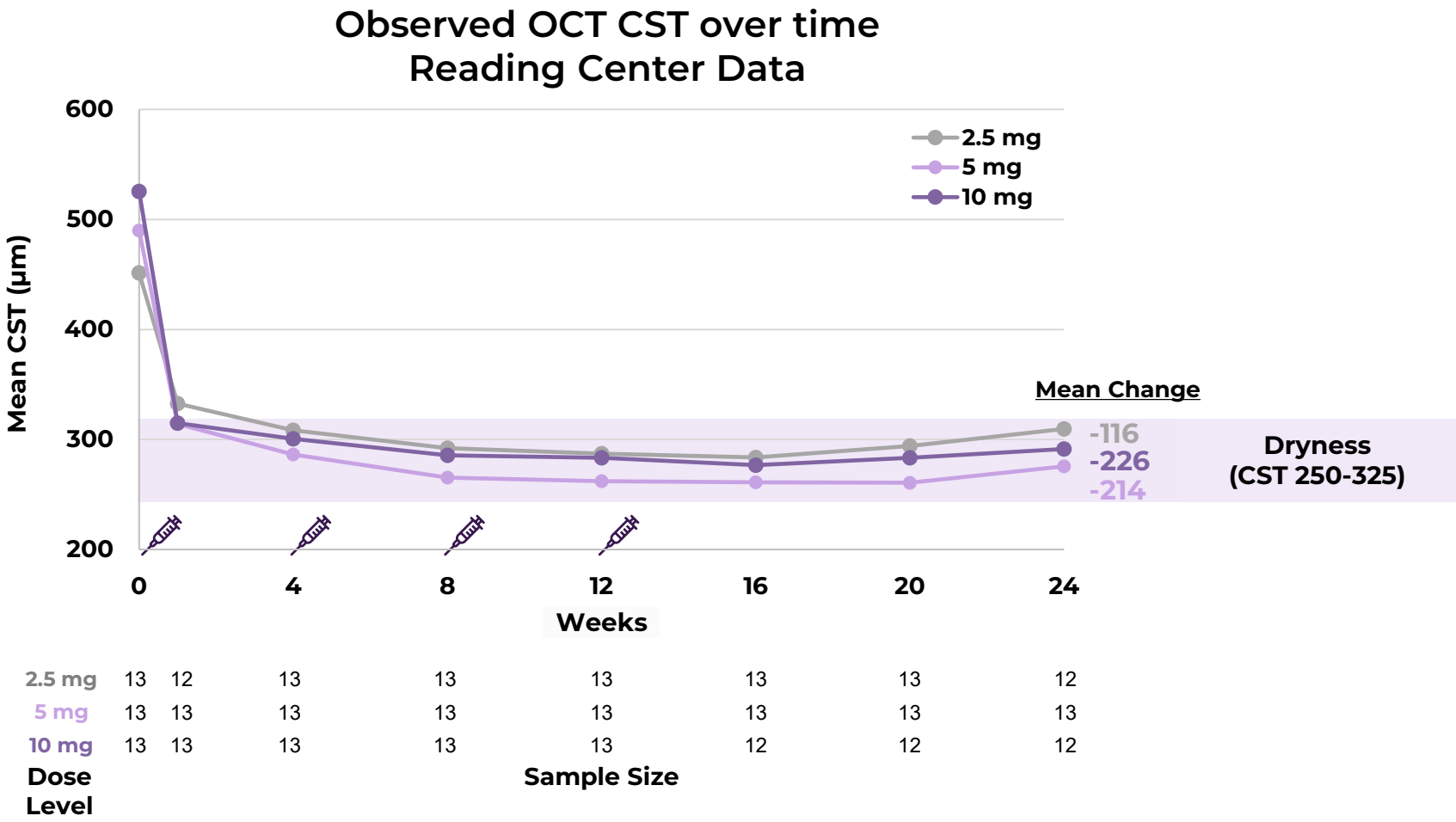
Meaningful anatomical improvements are rapidly achieved, with OCT CST levels <325 µm observed in the top two dose levels as early as Week 1, further deepening over time



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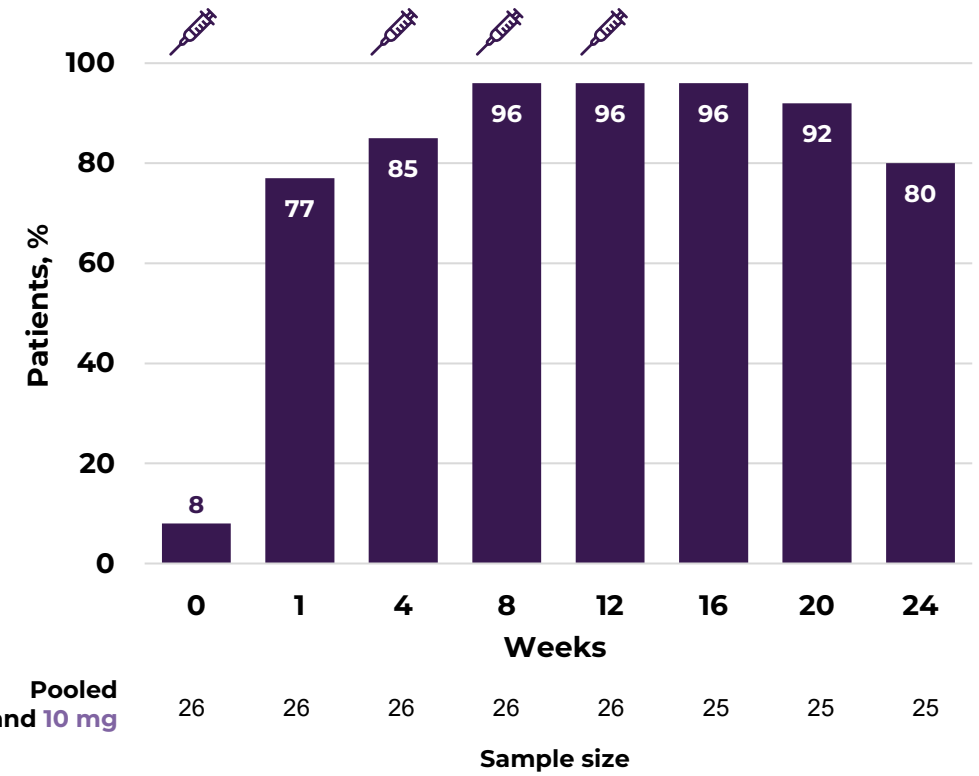
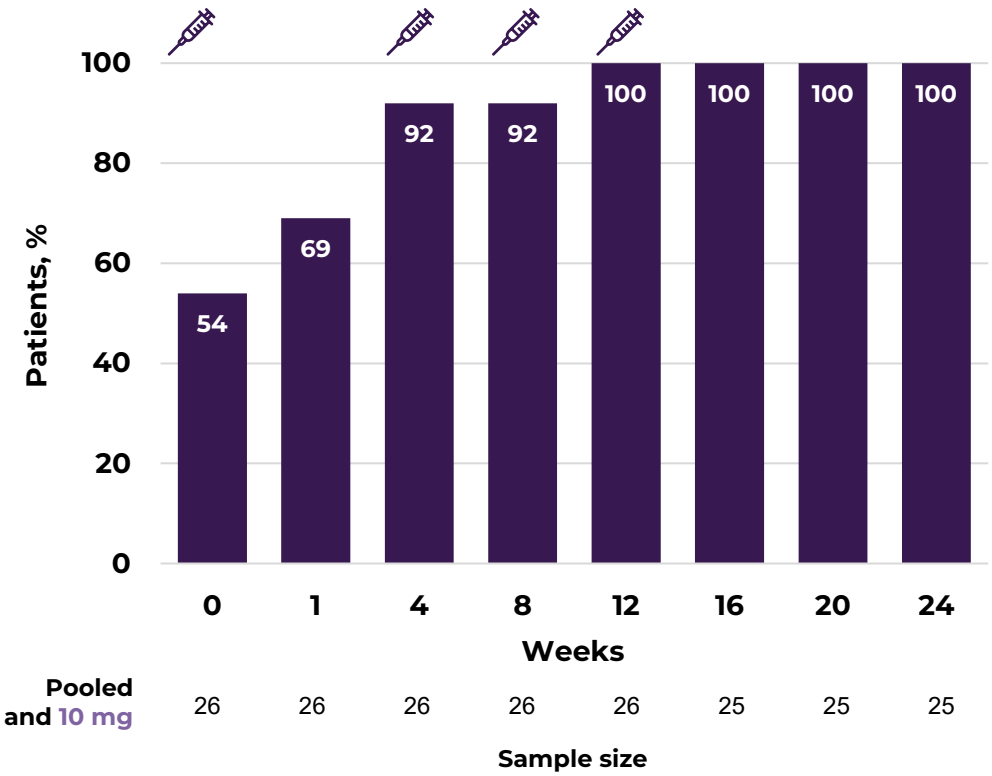
≥90% of patients in the top two dose levels achieved absence of both intraretinal and subretinal fluid. A recurrence in IRF was observed in some patients 8 to 12 weeks after the last study treatment

Proportion of patients in the 5 and 10 mg (pooled) dose level achieving absence of IRF



Proportion of patients in the 5 and 10 mg (pooled) dose level achieving absence of SRF



Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). One patient in the 10 mg dose level discontinued after Week 12 due to recurrent uveitis flare-up.

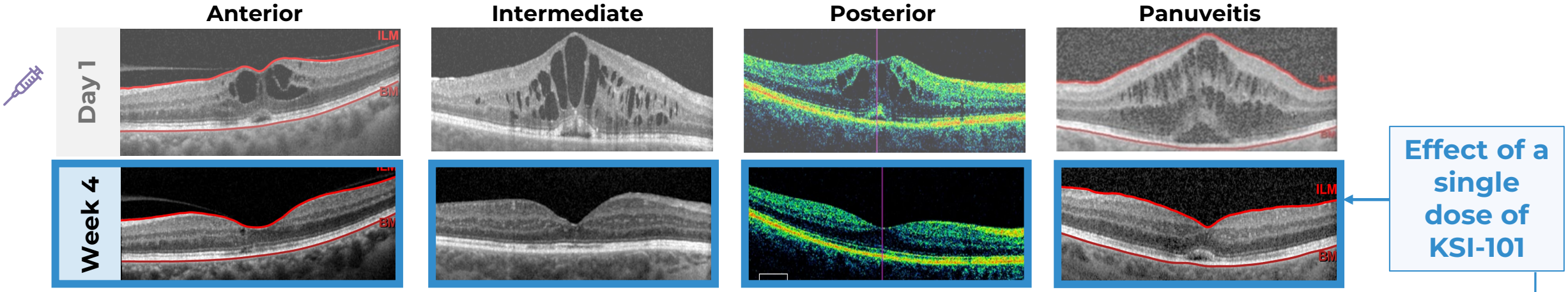
KSI-101 has been well-tolerated

	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)	All KSI-101 (N=41)
Summary of AEs in the Study eye, n (%)				
Subjects with ≥1 AEs	2 (15.4)	3 (21.4)	2 (14.3)	7 (17.1)
Treatment-related AEs	1 (7.7)[a]	1 (7.1)[b]	0	2 (4.9)
Serious AEs	0	0	0	0
Treatment-related serious AEs	0	0	0	0
Severe AEs	0	0	0	0
AEs leading to study discontinuation	0	1 (7.1)[b]	0	1 (2.4)
Selected AEs in the Study Eye, n (%)				
Intraocular inflammation (recurrent uveitis flare-up)	1 (7.7)[a]	1 (7.1)[b]	0	2 (4.9)
Occlusive retinal vasculitis	0	0	0	0
Cataract	0	0	0	0
Elevated IOP	0	0	0	0
Eye Pain	1 (7.7)[a]	0	0	1 (2.4)
Vitreous hemorrhage	1 (7.7)[a]	0	0	1 (2.4)

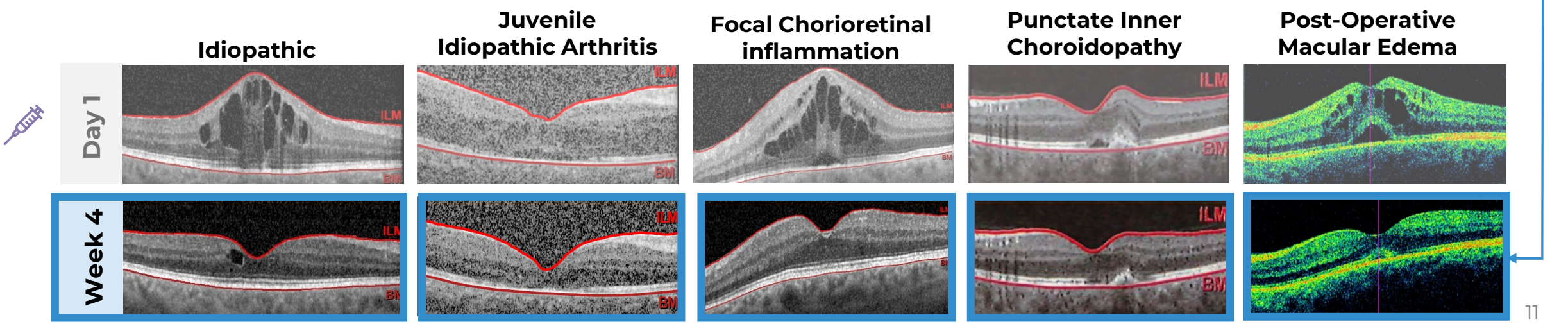
Final results from the APEX Study in MESI.
AE, Adverse event; IOP, intraocular pressure. Events are investigator reported. Adverse events are treatment-emergent events with start date ≥first study drug date and ≤last study drug date + 28 days.
[a] Same patient. Vitreous hemorrhage secondary to aqueous humor sampling at the Day 1 visit (pre-dose). The patient had 3+ AC cells and flare and 2+ vitreous haze ***prior*** to the Day 1 KSI-101 dose. The patient safely received all 4 doses of KSI-101 and is +26 letters in BCVA at their last visit and no intraocular inflammation.
[b] Same patient. Uveitis flare-up consistent with underlying disease.

Single-dose KSI-101 demonstrates rapid, meaningful responses in MESI, independent of inflammation location or macular edema etiology

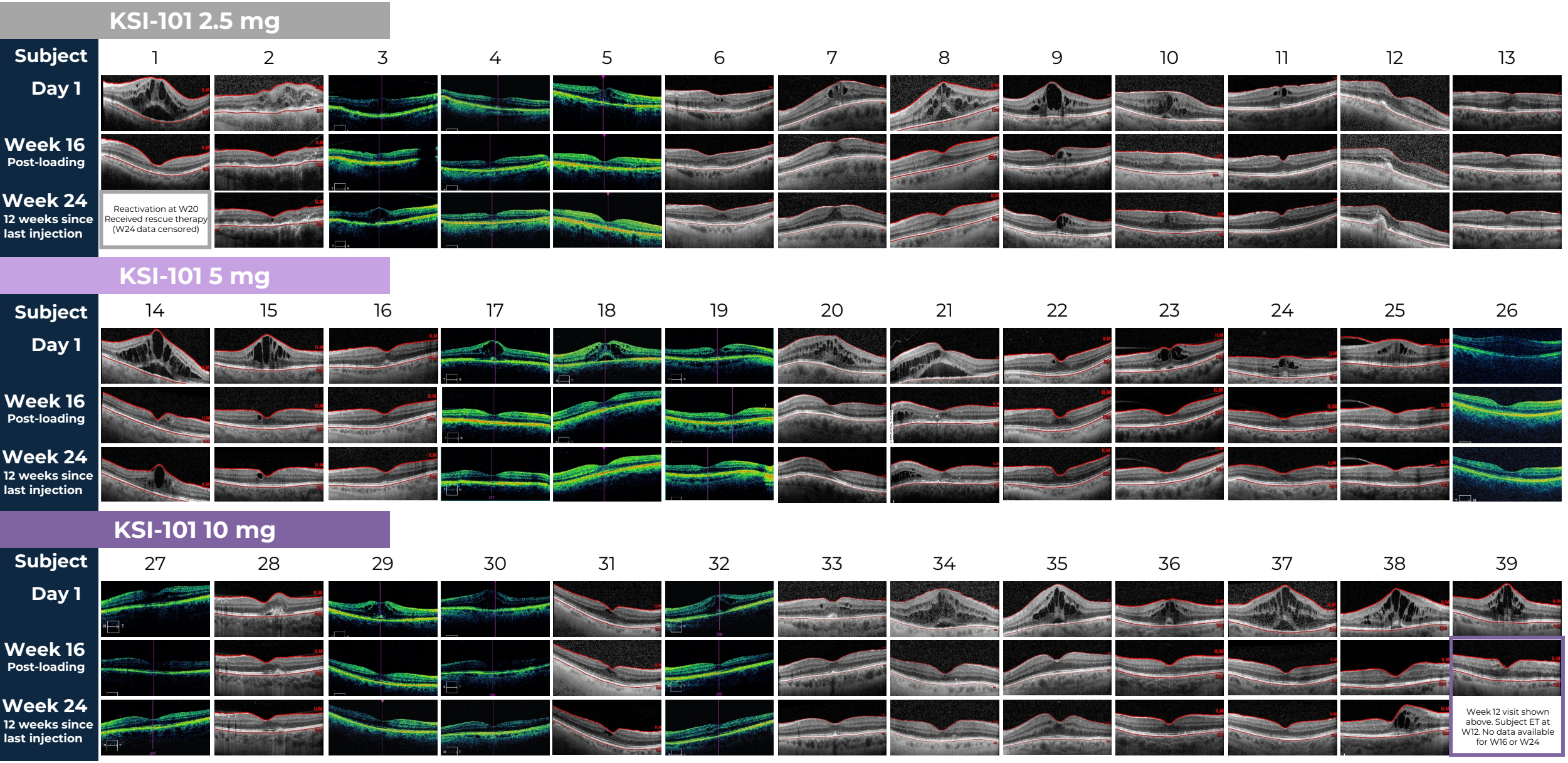
Location of Inflammation



Specific Macular Edema Etiology

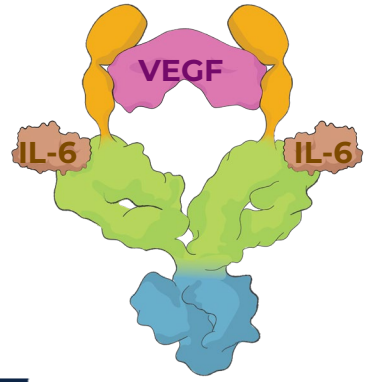


KSI-101 achieves dryness and normalizes the retinal architecture in the majority of patients



Based on positive APEX data, the 5 mg and 10 mg dose levels have advanced into the Phase 3 PEAK and PINNACLE studies in MESI

- **KSI-101 in MESI patients in APEX showed robust anatomic and visual responses**
  - Over half of patients achieved at least a ≥15 letter gain
  - >90% resolution of both IRF & SRF by Week 8
  - Consistent response irrespective of different underlying etiologies



KSI-101

	Fixed monthly dosing						Individualized dosing						
Weeks	**D1**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**
KSI-101 5 mg													
KSI-101 10 mg													
Sham													

- KSI-101 5 mg injection
- KSI-101 10 mg injection
- Sham injection
- Individualized treatment (PRN)
- Sham PRN

Primary endpoint: Mean change in BCVA from Day 1 to the average of Week 20 and Week 24

Key inclusion criteria

- Macular edema secondary to inflammation
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic
- Active leakage as evidenced by fluorescein angiogram
- OCT CST of ≥320 microns
- BCVA score ≤78 and ≥25 (~20/25 to 20/320 Snellen)

PEAK and PINNACLE Phase 3 Studies in MESI are actively enrolling

PEAK: NCT06990399. PINNACLE: NCT06996080