

Supplementary Materials

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**Ocular Distribution and Pharmacodynamics of SF0166, a Topically Administered
v₃ Integrin Antagonist, for the Treatment of Retinal Diseases**

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Supplementary Table 1. Scoring scale for the laser-induced CNV model study in Dutch-Belted rabbits

Score	Description
Conjunctival Discharge	
0	Normal. No discharge.
1	Discharge above normal and present on the inner portion of the eye but not on the lids or hairs of the eyelids.
2	Discharge is abundant, easily observed and has collected on the lids and hairs of the eyelids.
3	Discharge has been flowing over the eyelids so as to wet the hairs substantially on the skin around the eye.
Conjunctival Congestion	
0	Normal. May appear blanched to reddish pink without perilimbal injection (except at the 12:00 and 6:00 positions) with vessels of the palpebral and bulbar conjunctiva easily observed.
1	A flushed, reddish color predominantly confined to the palpebral conjunctiva with some perilimbal injection but primarily confined to the lower and upper parts of the eye from the 4:00 to 7:00 and 11:00 to 1:00 positions.
2	Bright red color of the palpebral conjunctiva with accompanying perilimbal injection covering at least 75% of the circumference of the perilimbal region.
3	Dark, beefy red color with congestion of both the bulbar and palpebral conjunctiva along with pronounced perilimbal injection and the presence of petechia on the conjunctiva. The petechia generally predominates along the nictitating membrane and upper palpebral conjunctiva.
Conjunctival Swelling	
0	Normal or no swelling of the conjunctival tissue
1	Swelling above normal without eversion of the eyelids (easily discerned by noting upper and lower eyelids are positioned as in the normal eye); swelling generally starts in the lower cul-de-sac near the inner canthus.
2	Swelling with misalignment of the normal approximation of the lower and upper eyelids; primarily confined to the upper eyelid so that in the initial stages, the misapproximation of the eyelids begins by partial eversion of the upper eyelid. In this stage the swelling is confined generally to the upper eyelid with some swelling in the lower cul-de-sac.
3	Swelling definite with partial eversion of the upper and lower eyelids essentially equivalent. This can be easily observed by looking at the animal head-on and noting the position of the eyelids; if the eye margins do not meet, eversion has occurred.
4	Eversion of the upper eyelid is pronounced with less pronounced eversion of the lower eyelid. It is difficult to retract the lids and observe the perilimbal region.

Iris Involvement	
0	Normal iris without any hyperemia of the blood vessels.
1	Minimal injection of the secondary vessels but not tertiary vessels. Generally uniform but may be of greater intensity at the 12:00 to 1:00 or 6:00 position. If confined to this area, the tertiary vessels must be substantially hyperemic.
2	Minimal injection of tertiary vessels and minimal to moderate injection of the secondary vessels.
3	Moderate injection of the secondary and tertiary vessels with slight swelling of the iris stroma (the iris surface appears slightly rugose, usually most predominant near the 3:00 and 9:00 positions).
4	Marked injection of the secondary and tertiary vessels with marked swelling of the iris stroma. The iris appears rugose; may be accompanied by hemorrhage (hyphema) in the anterior chamber.
Cornea	
0	Normal cornea.
1	Some loss of transparency. Only the epithelium and/or the anterior half of the stroma are involved. The underlying structures are clearly visible although some cloudiness may be readily apparent.
2	Involvement of the entire thickness of the stroma. With diffuse illumination, the underlying structures are just barely visible (can still observe flare, iris, pupil response, and lens).
3	Involvement of the entire thickness of the stroma. With diffuse illumination, the underlying structures cannot be seen.
Surface Area of Cornea Involvement	
0	Normal.
1	1-25% area of stromal cloudiness.
2	26-50% area of stromal cloudiness.
3	51-75% area of stromal cloudiness.
4	76-100% area of stromal cloudiness.
Pannus	
0	No pannus (vascularization of the cornea).
1	Vascularization present but vessels have not invaded the entire cornea circumference.
2	Vessels have invaded 2 mm or more around entire corneal surface.
Pupillary Response	
0	Normal pupil response.
1	Sluggish or incomplete pupil response.
2	No pupil response.
3	No pupil response due to pharmacological blockage.

Aqueous Flare	
0	None
1	1+
2	2+
3	3+
4	4+ (fibrin)
Cellular Flare	
0	None
1	1+
2	2+
3	3+
4	4+
Lens	
0	Lens clear.
1	Anterior (cortical/capsular).
2	Nuclear.
3	Posterior (cortical/optical).
4	Equatorial.
Vitreous	
0	Clear vitreous.
1	Few scattered opacities, fundus unimpaired.
2	Moderate scattered opacities, fundus details somewhat obscured.
3	Many opacities, marked blurring of fundus details.
4	Dense opacities, no fundus view.
Vitreous Hemorrhage	
0	None
1	1-25%
2	26-50%
3	51-75%
4	76-100%

Retinal Detachment	
0	None.
1	Rhegmatogenous (retinal detachment occurs when subretinal fluid accumulates in the potential space between the neurosensory retina and the underlying retinal pigment epithelium).
2	Exudative (occurs due to inflammation, injury, or vascular abnormalities that results in fluid accumulating underneath the retina without the presence of a hole, tear, or break).
3	Tractional (occurs when fibrous or fibrovascular tissue, caused by an injury, inflammation, or neovascularization that pulls the sensory retina from the retinal pigment epithelium).
Retinal Hemorrhage	
0	None
1	1-25%
2	26-50%
3	51-75%
4	76-100%
Choroidal/Retinal Inflammation	
0	None
1	Mild
2	Moderate
3	Severe

Supplementary Table 2. Scoring scale used to determine fluorescein angiography score for the VEGF-induced vascular leakage study in Dutch-Belted rabbits

Score	Description
0	Major vessels straight some tortuosity of smaller vessels, no vessel dilation
1	Increased tortuosity of major vessels and/or some vessel dilation
2	Leakage between major vessels, significant vessel dilation
3	Leakage between major and minor vessels, minor vessels still visible
4	Leakage between major and minor vessels, minor vessels poorly/not visible

Supplementary Table 3. Design for the VEGF-induced vascular leakage study in Dutch-Belted rabbits

Test Article	Dosing	Dose (mg/eye)	Dose Concentration (%)	Dose Volume (µL/eye)
SF0166	Ocular (Topical, OU, QD starting Day 1)	2.5	5	50
SF0166	Ocular (Topical, OU, BID starting Day 1)	1.25	2.5	50
SF0166	Ocular (Topical, OU, QD starting Day 1)	1.25	2.5	50
SF0166	Ocular (Topical, OU, BID starting Day 1)	0.5	1.0	50
Vehicle	Ocular (Topical, OU, QD starting Day 1)	—	—	50
Bevacizumab	Ocular (IVT, OU, single administration on Day 1)	1.25	2.5	50

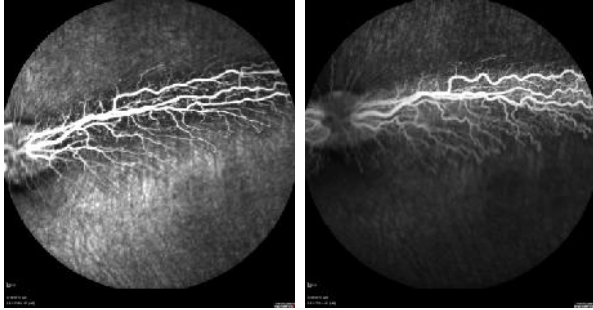
BID: twice daily; IVT: intravitreal; OU: both eyes; QD: once daily

Animals were dosed with test article starting Day 1. VEGF was injected on Day 3. N = 6 per group.

Vehicle

Baseline score = 0

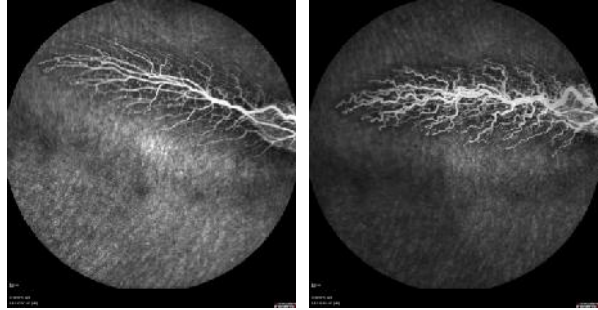
Day 8 score = 4



SF0166 1% BID

Baseline score = 0

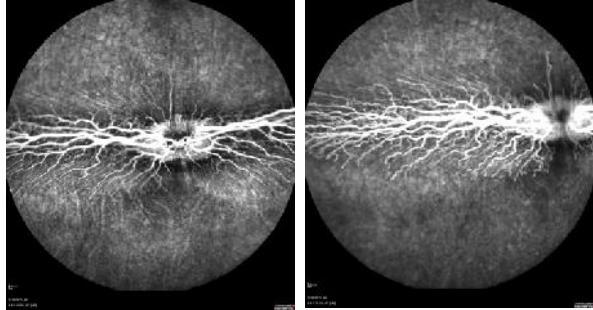
Day 8 score = 2



SF0166, 2.5% QD

Baseline score = 0

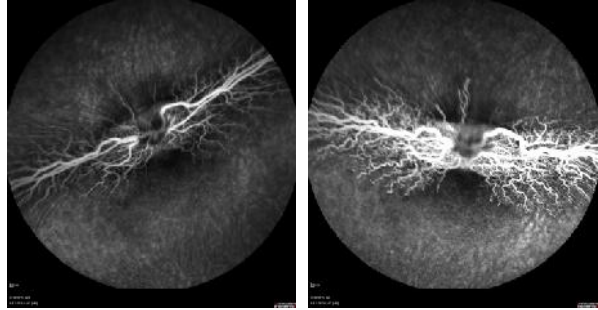
Day 8 score = 1



SF0166, 2.5% BID

Baseline score = 0

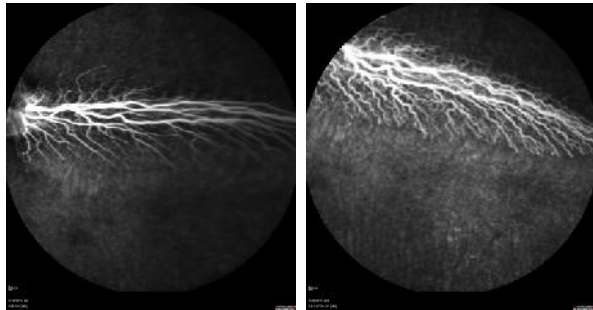
Day 8 score = 1



SF0166, 5% QD

Baseline score = 0

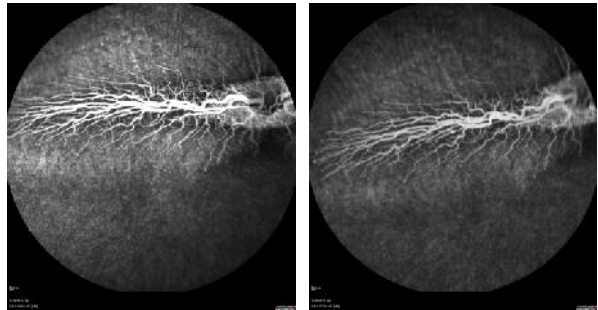
Day 8 score = 0



Bevacizumab

Baseline score = 0

Day 8 score = 0



Supplementary Figure 1. Representative fluorescein images from the VEGF-induced vascular leakage study in Dutch-Belted rabbits. Images were taken at baseline and Day 8.