

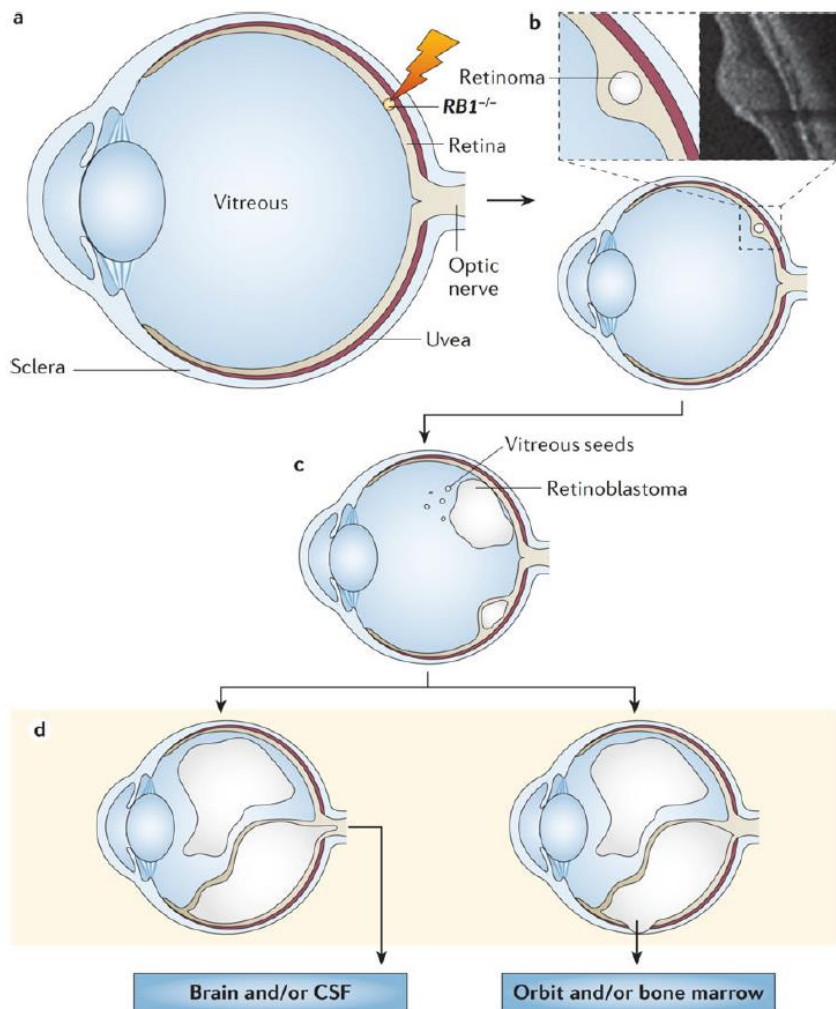
**VCN-01 is an encouraging therapy
against retinoblastoma**

IOVC 2021

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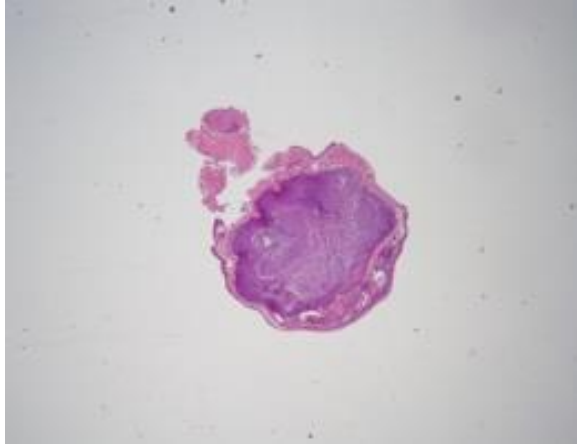
Retinoblastoma

Helen Dimaras¹, Timothy W. Corson², David Cobrinik³, Abby White⁴, Junyang Zhao⁵, Francis L. Munier⁶, David H. Abramson⁷, Carol L. Shields⁸, Guillermo L. Chantada⁹, Festus Njuguna¹⁰ and Brenda L. Gallie¹¹

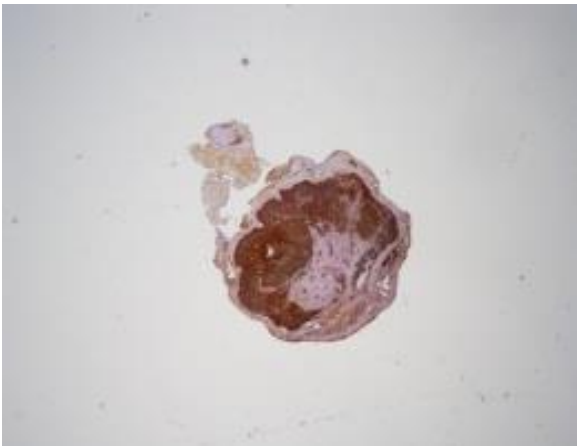


- Developmental intraocular tumor of the retina of the young child
- Average age at diagnosis: 2 years
- It rarely occurs in those older than 6 years
- Incidence 1 / 18,000 newborns
- Cause: biallelic mutation of the Rb1 gene
- Bilateral RB (with germline Rb1 mutation) 35%, unilateral RB (sporadic mutation) 65%

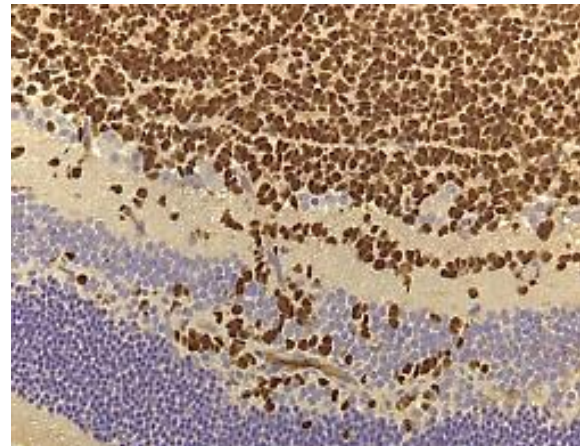
Retinoblastoma orthotopic models



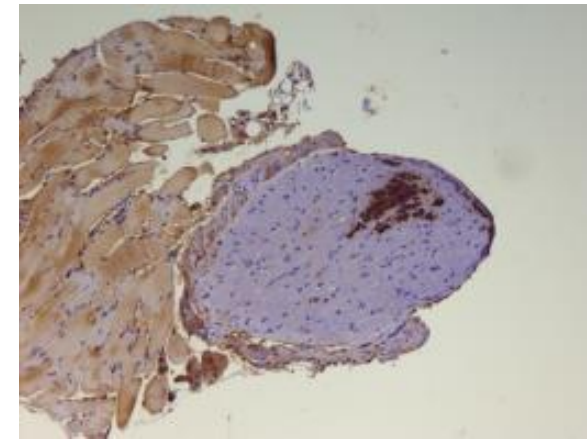
H&E



Anti-human Nuclei



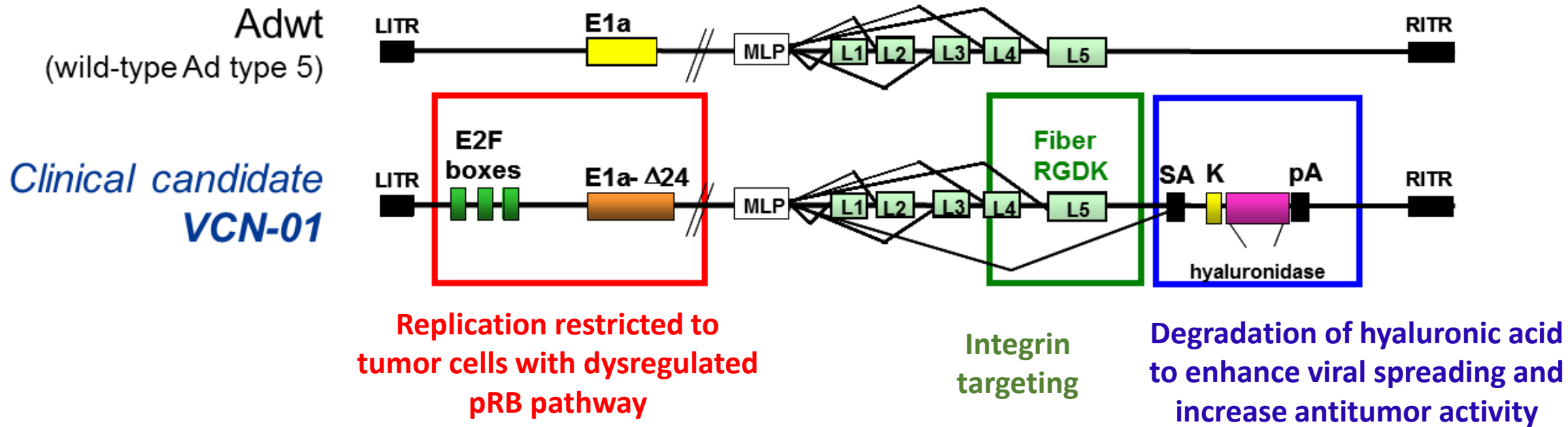
Retinal tumor invasion



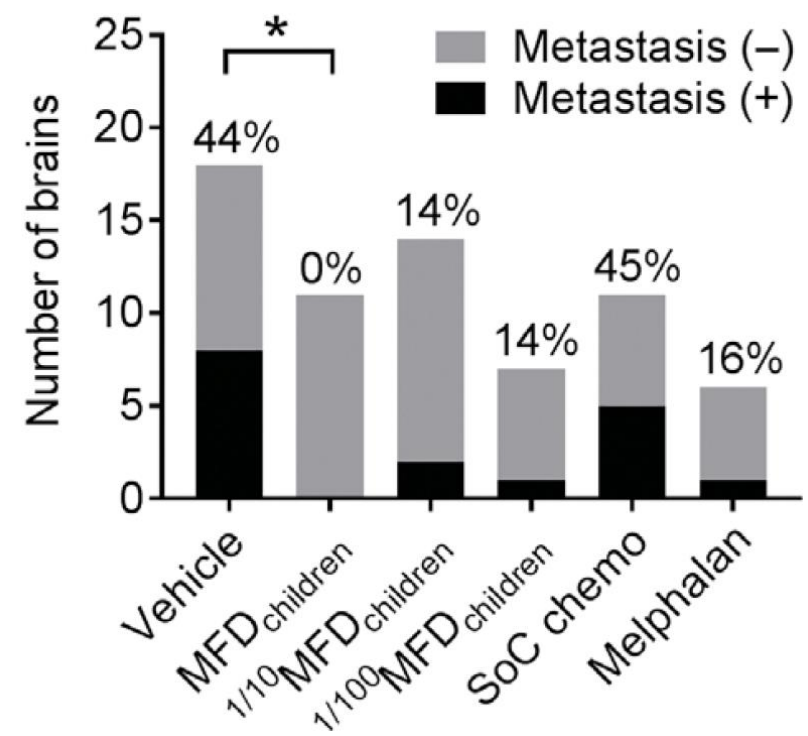
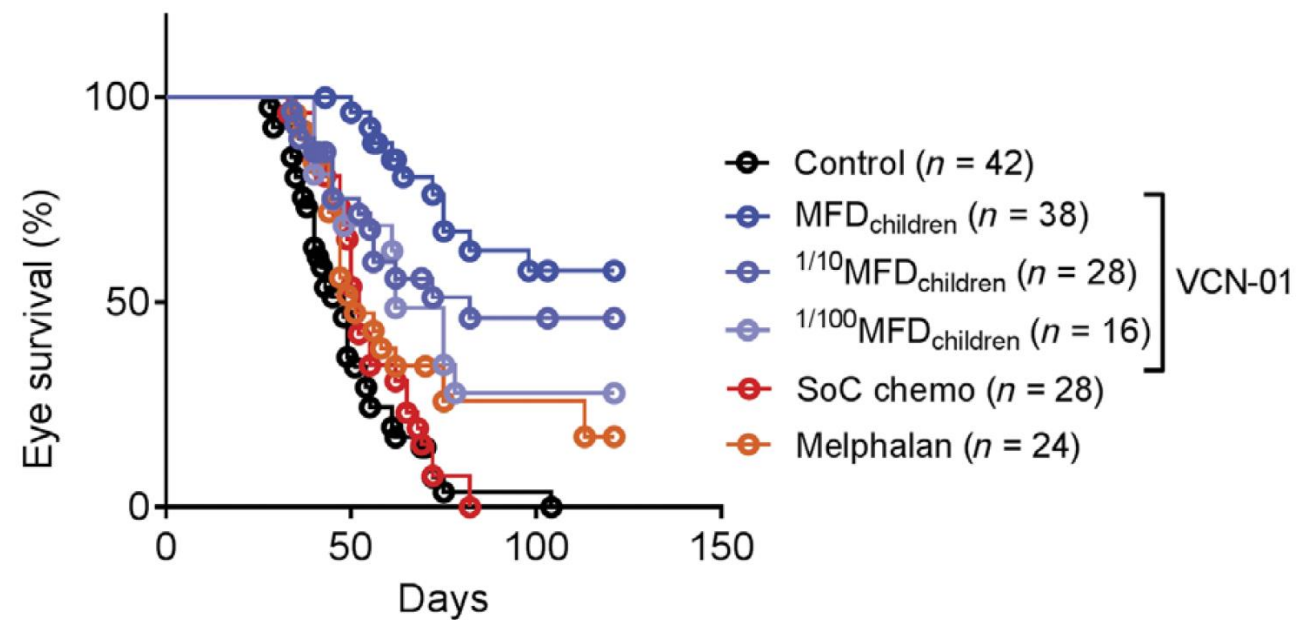
Optic nerve invasion

VCN-01

“First-in-Class oncolytic adenovirus that remodels tumour matrix”



VCN-01 improves ocular survival and inhibits metastasis in retinoblastoma xenografts



Intravitreal administration of VCN-01 in patients



POPULATION

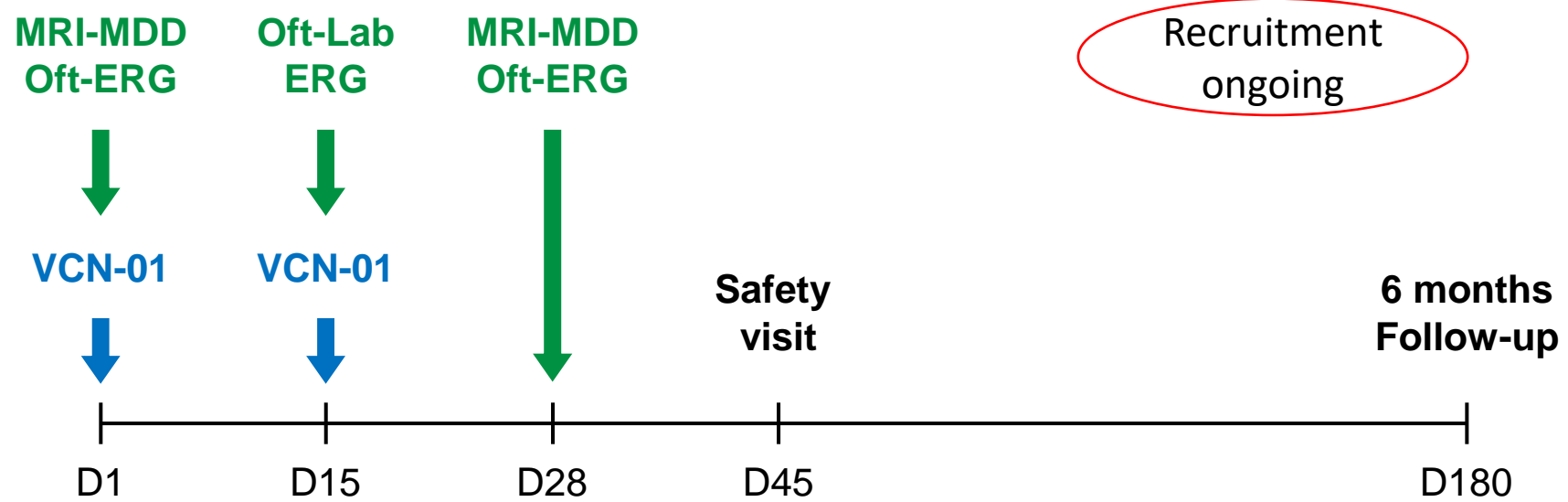
Children (2-6 years) with retinoblastoma
 Two intravitreal administrations 2 weeks interval
 Endpoints: Safety profile and Antitumoural Activity (retardation of enucleation)



DOSAGE

Dose escalation in monotherapy:

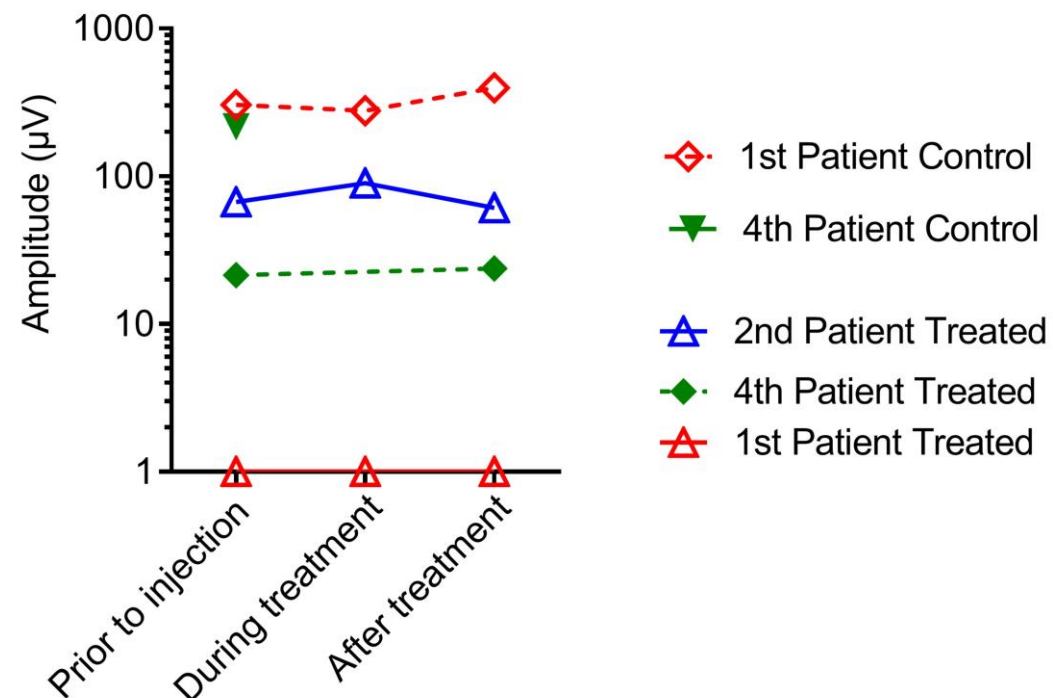
- 2E9 vp/eye 1 patient ✓
- 2E10 vp/eye 3 patients → 3 ✓
- 2E10 vp/eye 1-3 patients → ongoing

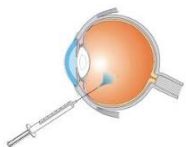


Safety FSJD-RTB Trial					
Adverse Reaction (Preferred Term)	Nº patients treated*	All grades		Grade ≥3	
		Nº patients observed	%	Nº patients observed	%
Uveitis	4	2	50%	2	50%
Periflebitis	4	1	25%	0	0%

- ✓ VCN-01 is well tolerated after intravitreal administration, although some degree of turbidity and vitritis associated to intravitreal inflammation is observed.
- ✓ Inflammation is managed with local and systemic administration of anti-inflammatory drugs.
- ✓ VCN-01 does not change the retinal function.

Stable Electroretinographic signals





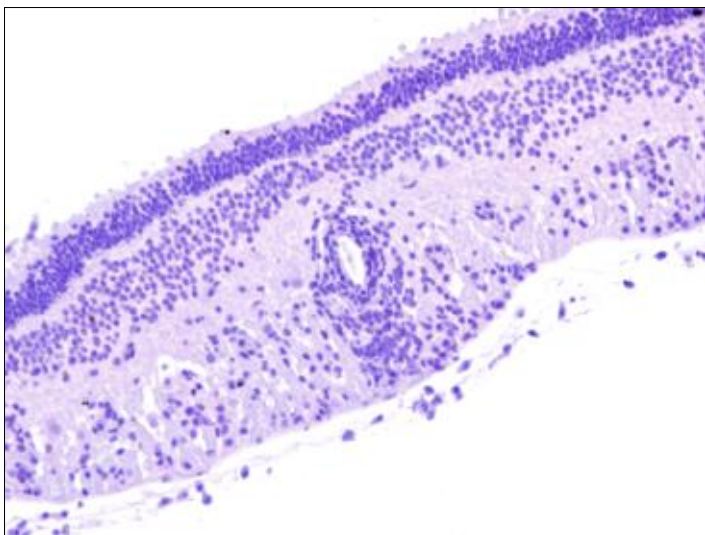
First patient

2 years- old patient

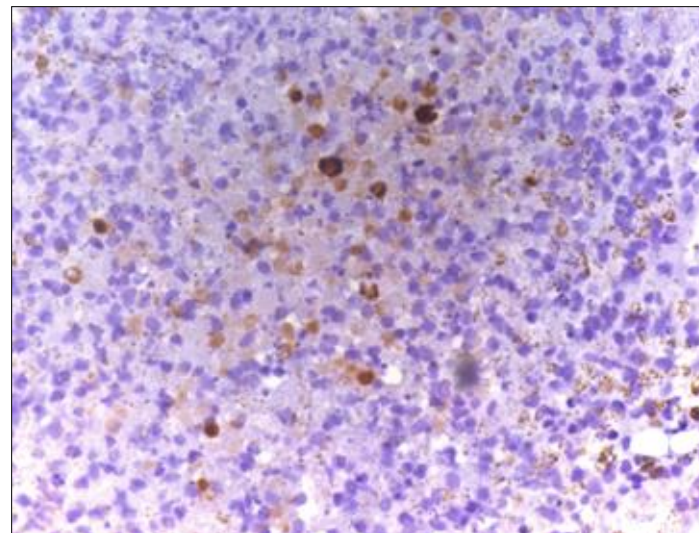
Dose: 2E9 vp/eye

Eye was enucleated 28 days after 2nd VCN-01 admin

Conserved retina



Necrotic tumor



α -E1A IHC

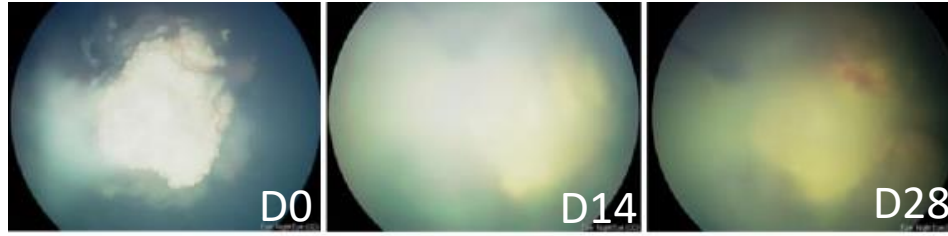
*E1A protein expression is associated with **tumour necrosis***

*Lack of E1A expression in normal retina confirms **selective VCN-01 replication***

VCN-01 significantly reduces the number of vitreous seeds

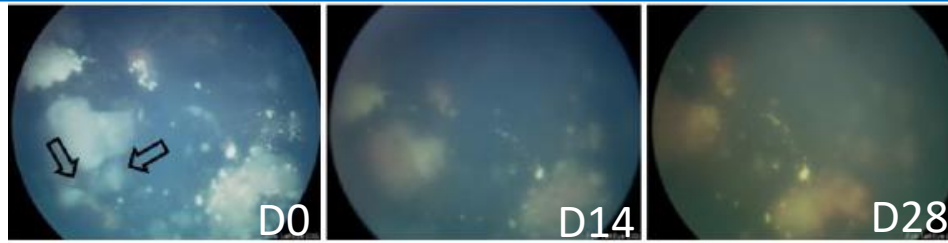
Patient & Dose

1st 2E+9vp



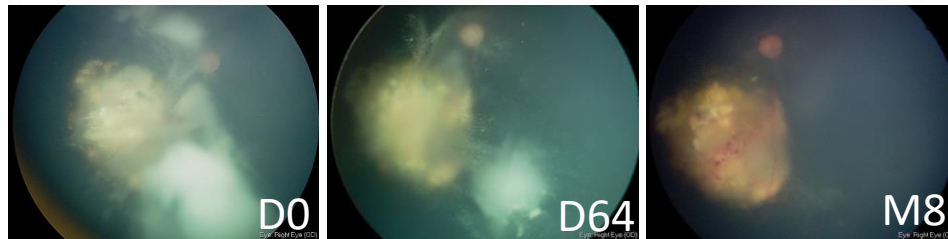
Enucleation Date	Enucleation Reason	Clinical Evaluation
D42	Vitritis-associated turbidity precluding monitoring the tumor activity	Necrosis without clear evidence of tumor seed reduction

2nd 2E+10vp



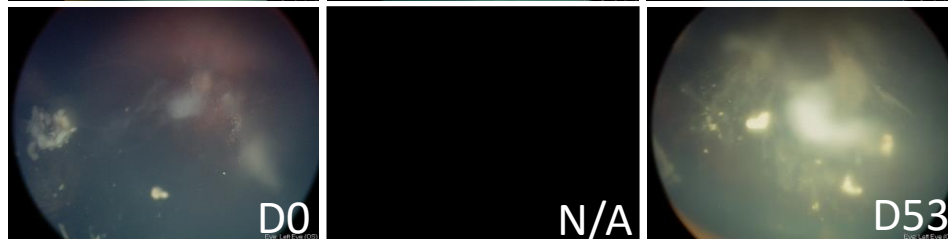
D61	Vitritis-associated turbidity precluding monitoring the tumor activity	Reduction of tumoral vitreous seeds in size and number
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3rd 2E+10vp



-	-	Complete Regression
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4th 2E+10vp



D53	Retinal detachment associated to previous chemotherapies	No viable tumor was found at enucleation
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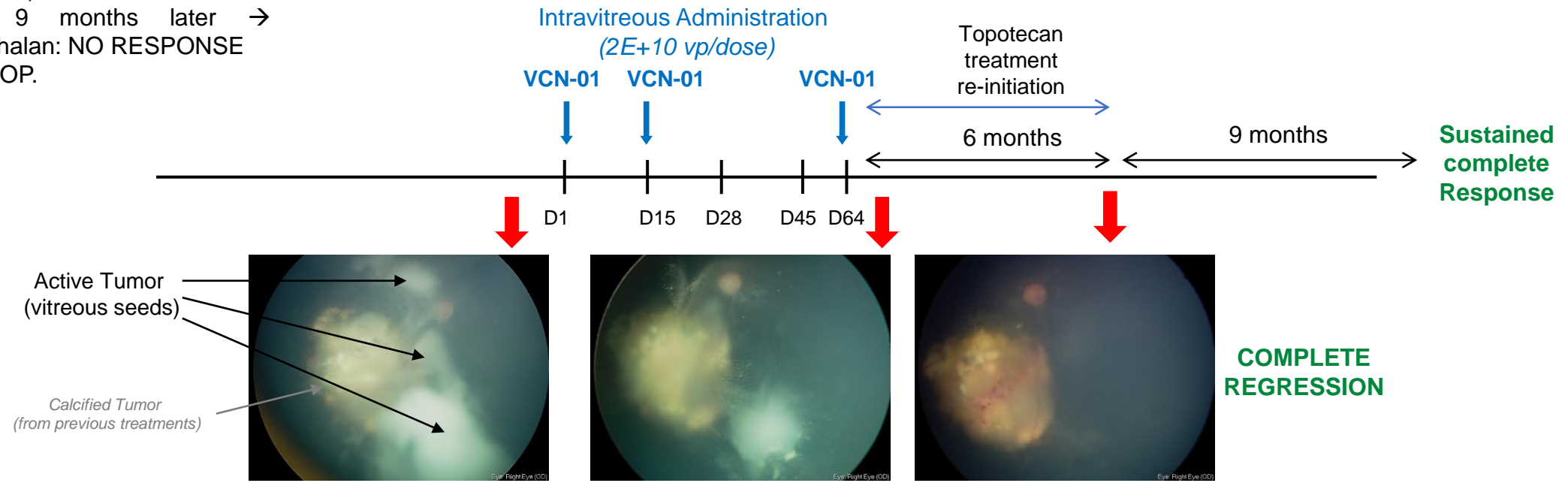
VCN-01 is clinically effective in pediatric retinoblastoma patients

3rd Patient 3-years old ♂

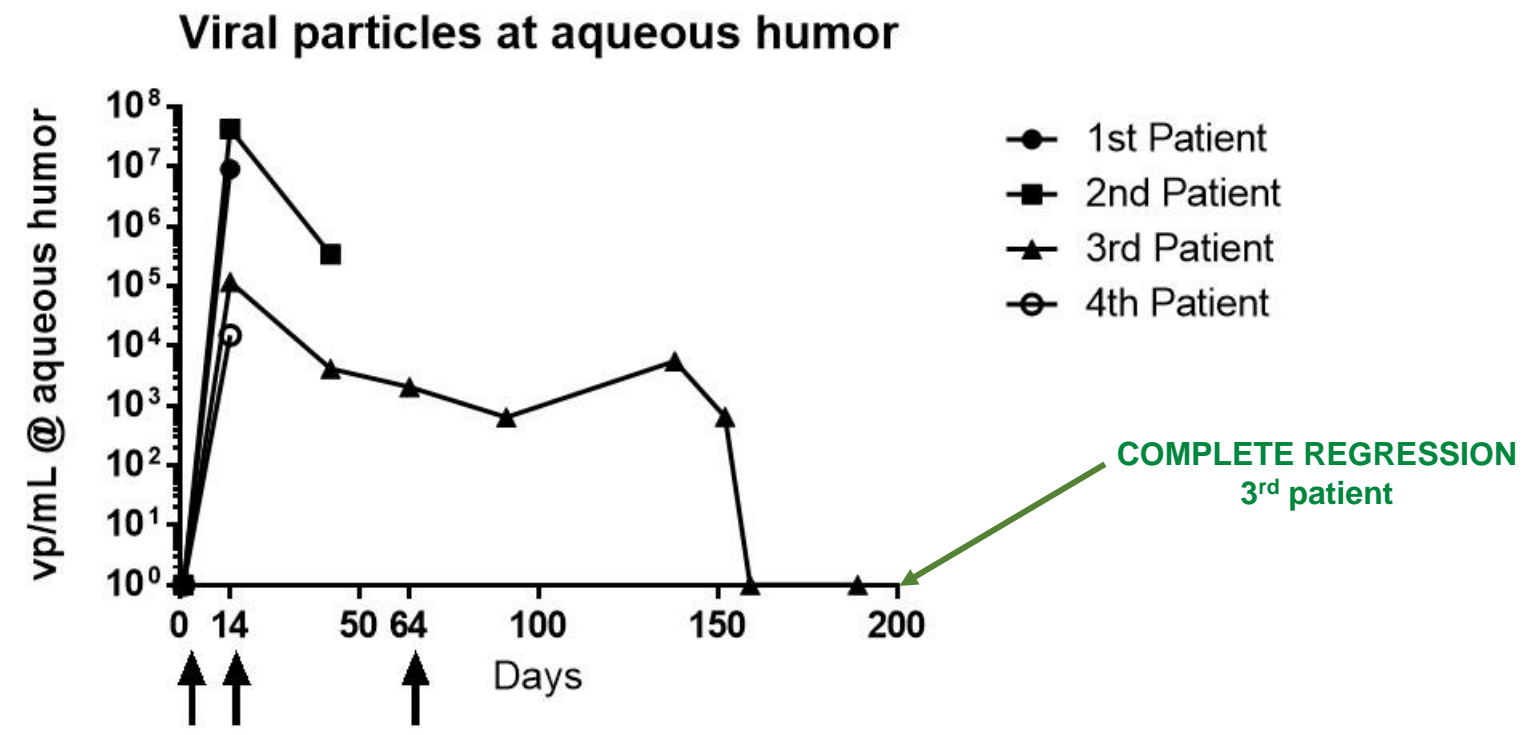
Bilateral retinoblastoma (with germline Rb1 mutation), with 1st eye already enucleated.

Previous treatments:

- Systemic chemotherapy CBP/VP-16/VCR (followed by intraarterial dosing of topotecan/melphalan).
- Tumor relapse 9 months later → Intravitreal melphalan: NO RESPONSE
- Chemotherapy STOP.



VCN-01 replicated within retinoblastoma tumors over time



Viral particles at aqueous humor are observed over long periods of time, suggesting viral replication.

The Retinoblastoma Team



**Angel M.
Carcaboso**



**Guillermo
Chantada**



**Jaume
Català-Mora**



**Guillem
Pascual-Pasto**



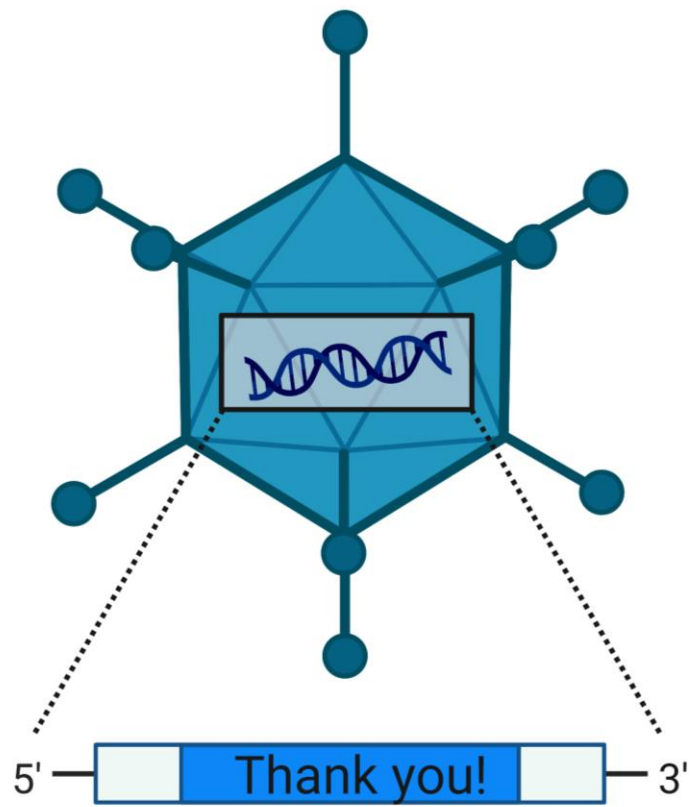
**Ramon
Alemany**



**Manel
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**Miriam
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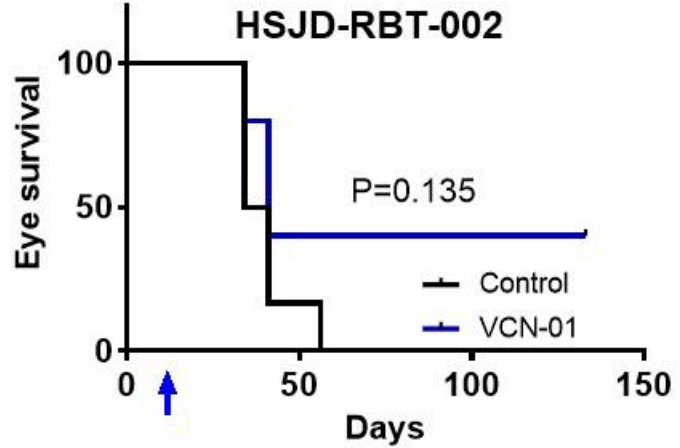
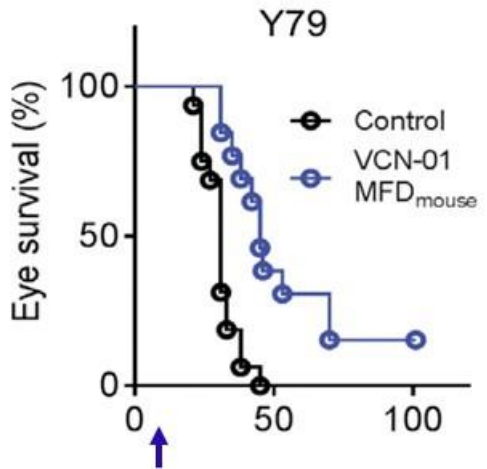


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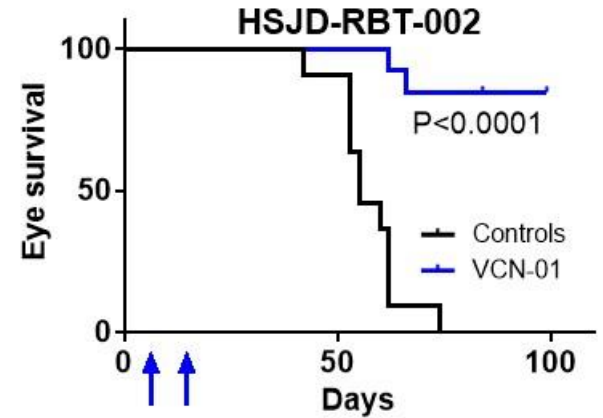
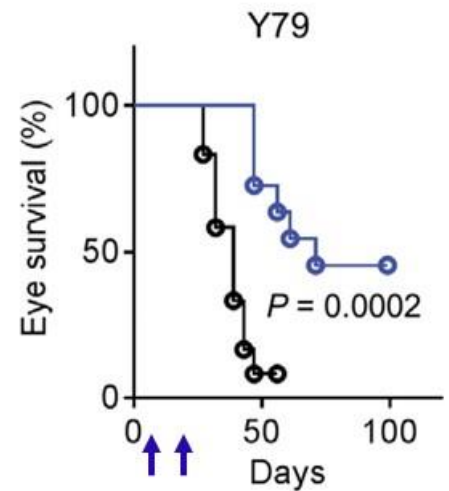
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Efficacy of single & double intravitreal VCN-01 in orthotopic retinoblastoma xenografts

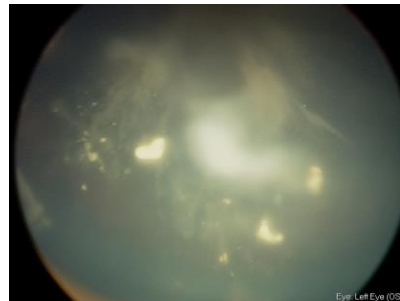
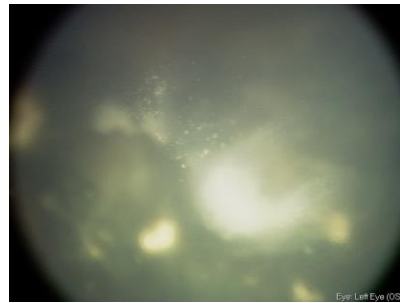
Single

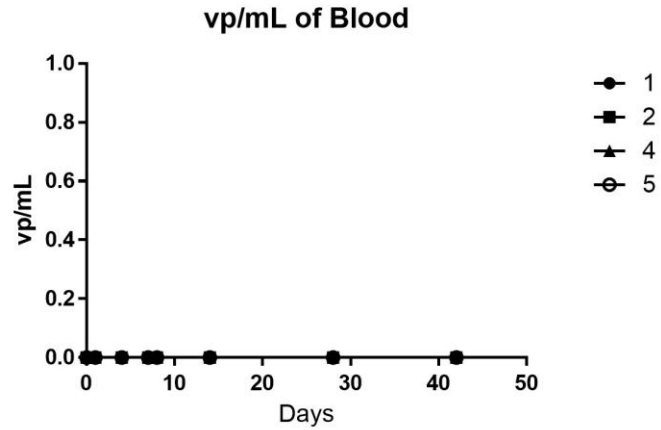


Double

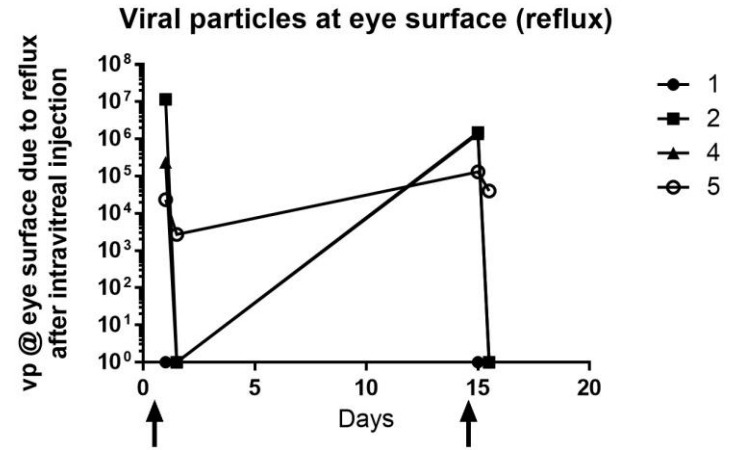


Patient 5. Received both doses of VCN-01 ITV and was enucleated on D53 due to retinal detachment associated to previous chemotherapies. **No tumor was found at enucleation.**

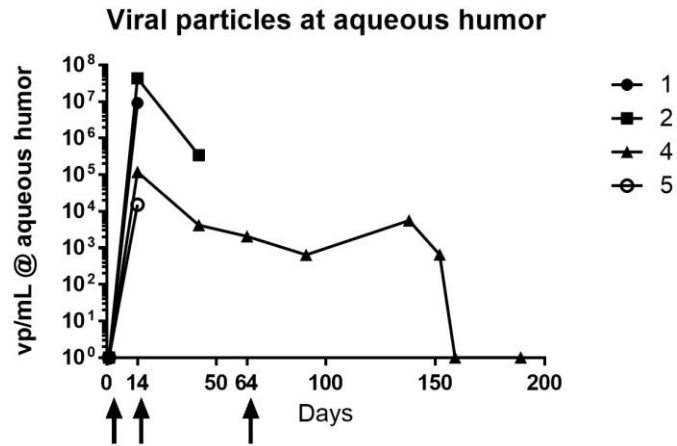




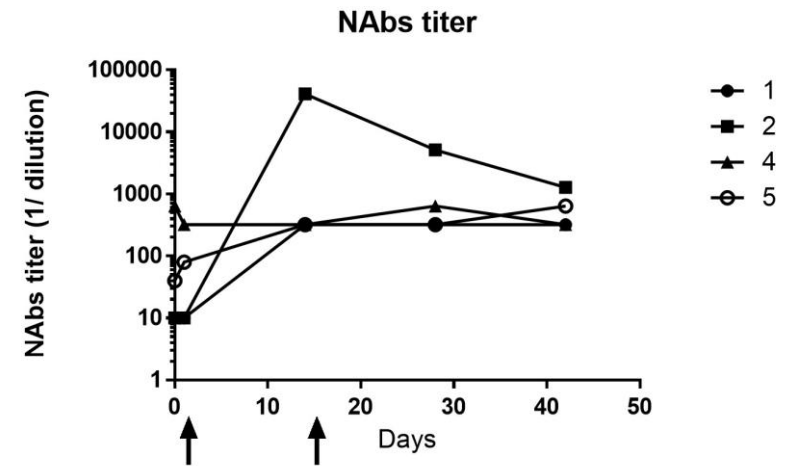
No virus is detected in blood after intravitreal administration



Viral reflux is observed at the eye surface after intravitreal administration



Viral particles at aqueous humor are observed over long periods of time, suggesting viral replication.



NAb titer is increased after VCN-01 administration