Table 14.3.1.5b Summary of Treatment-Related Adverse Events by System Organ Class, Preferred Term, Treatment and Overall
(Safety Population)

Study Period: Controlled Treatment Period

Body System MedDRA Preferred Term	rhNGF 10 µg/ml (N=52)			rhNGF 20 µg/ml (N=52)			Vehicle Control (N=52)			Total (N=156)		
	N*	n	%	N*	n	%	N*	n	%	N*	n	%
Any Adverse Events	10	6	(11.5%)	15	9	(17.3%)	20	10	(19.2%)	45	25	(16.0%)
Eye disorders	7	5	(9.6%)	10	7	(13.5%)	16	9	(17.3%)	33	21	(13.5%)
Eye pain	0	0		4	4	(7.7%)	3	2	(3.8%)	7	6	(3.8%)
Blepharitis	1	1	(1.9%)	1	1	(1.9%)	1	1	(1.9%)	3	3	(1.9%)
Corneal neovascularisation	0	0		1	1	(1.9%)	1	1	(1.9%)	2	2	(1.3%)
Eye irritation	1	1	(1.9%)	0	0		1	1	(1.9%)	2	2	(1.3%)
Eye pruritus	0	0		1	1	(1.9%)	1	1	(1.9%)	2	2	(1.3%)
Vision blurred	0	0		0	0		2	2	(3.8%)	2	2	(1.3%)
Abnormal sensation in eye	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Asthenopia	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Conjunctival hyperaemia	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Corneal deposits	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Corneal epithelium defect	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Dry eye	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Eye discharge	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Eyelid oedema	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Eyelid pain	2	1	(1.9%)	0	0		0	0		2	1	(0.6%)

N* = Number of Events Reported, n = Number of Patients, % = Percentage of Patients.
Top N counts relate to the number of patients who have received each treatment in the specified study period. Patients allocated to Vehicle Control who are not completely healed at Week 8 are counted in the Vehicle Control group in the Controlled Treatment Period and their Uncontrolled Treatment group in the Uncontrolled Treatment Period and Follow-Up Period.
Percentages are calculated using the population number in each treatment group (N) as the denominator.
Treatment-Related Adverse Events are those events having a relationship to study treatment recorded as Possible, Probable or Highly Probable.
Body system and preferred terms are sorted by descending frequency of patient count in the Total column.
The data presented in this Table are contained in Listing 16.2.7.2b

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Table 14.3.1.5b Summary of Treatment-Related Adverse Events by System Organ Class, Preferred Term, Treatment and Overall
(Safety Population)

Study Period: Controlled Treatment Period

Body System MedDRA Preferred Term	rhNGF 10 µg/ml (N=52)			rhNGF 20 µg/ml (N=52)			Vehicle Control (N=52)			Total (N=156)		
	N*	n	%	N*	n	%	N*	n	%	N*	n	%
Eye disorders												
Lacrimation increased	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Macular fibrosis	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Ocular hyperaemia	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Photophobia	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Visual acuity reduced	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
General disorders and administration site conditions	1	1	(1.9%)	0	0		3	3	(5.8%)	4	4	(2.6%)
Disease progression	1	1	(1.9%)	0	0		2	2	(3.8%)	3	3	(1.9%)
Instillation site pain	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Nervous system disorders	2	2	(3.8%)	1	1	(1.9%)	1	1	(1.9%)	4	4	(2.6%)
Headache	1	1	(1.9%)	1	1	(1.9%)	1	1	(1.9%)	3	3	(1.9%)
Neuralgia	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Blood and lymphatic system disorders	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Neutropenia	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)

N* = Number of Events Reported, n = Number of Patients, % = Percentage of Patients.
Top N counts relate to the number of patients who have received each treatment in the specified study period. Patients allocated to Vehicle Control who are not completely healed at Week 8 are counted in the Vehicle Control group in the Controlled Treatment Period and their Uncontrolled Treatment group in the Uncontrolled Treatment Period and Follow-Up Period.
Percentages are calculated using the population number in each treatment group (N) as the denominator.
Treatment-Related Adverse Events are those events having a relationship to study treatment recorded as Possible, Probable or Highly Probable.
Body system and preferred terms are sorted by descending frequency of patient count in the Total column.
The data presented in this Table are contained in Listing 16.2.7.2b

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Table 14.3.1.5b Summary of Treatment-Related Adverse Events by System Organ Class, Preferred Term, Treatment and Overall
(Safety Population)

Study Period: Controlled Treatment Period

Body System MedDRA Preferred Term	rhNGF 10 µg/ml (N=52)			rhNGF 20 µg/ml (N=52)			Vehicle Control (N=52)			Total (N=156)		
	N*	n	%	N*	n	%	N*	n	%	N*	n	%
Cardiac disorders	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Arrhythmia	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Infections and infestations	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Corneal abscess	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Investigations	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Blood pressure increased	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)

N* = Number of Events Reported, n = Number of Patients, % = Percentage of Patients.
Top N counts relate to the number of patients who have received each treatment in the specified study period. Patients allocated to Vehicle Control who are not completely healed at Week 8 are counted in the Vehicle Control group in the Controlled Treatment Period and their Uncontrolled Treatment group in the Uncontrolled Treatment Period and Follow-Up Period.
Percentages are calculated using the population number in each treatment group (N) as the denominator.
Treatment-Related Adverse Events are those events having a relationship to study treatment recorded as Possible, Probable or Highly Probable.
Body system and preferred terms are sorted by descending frequency of patient count in the Total column.
The data presented in this Table are contained in Listing 16.2.7.2b

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Table 14.3.1.5b Summary of Treatment-Related Adverse Events by System Organ Class, Preferred Term, Treatment and Overall
(Safety Population)

Study Period: Uncontrolled Treatment Period

Body System MedDRA Preferred Term	rhNGF 10 µg/ml (N=10)			rhNGF 20 µg/ml (N=13)			Total (N=23)		
	N*	n	%	N*	n	%	N*	n	%
Any Adverse Events	2	2	(20.0%)	6	2	(15.4%)	8	4	(17.4%)
Eye disorders	0	0		6	2	(15.4%)	6	2	(8.7%)
Blepharitis	0	0		1	1	(7.7%)	1	1	(4.3%)
Conjunctival hyperaemia	0	0		1	1	(7.7%)	1	1	(4.3%)
Erythema of eyelid	0	0		1	1	(7.7%)	1	1	(4.3%)
Eye discharge	0	0		1	1	(7.7%)	1	1	(4.3%)
Eye irritation	0	0		1	1	(7.7%)	1	1	(4.3%)
Eye pain	0	0		1	1	(7.7%)	1	1	(4.3%)
General disorders and administration site conditions	1	1	(10.0%)	0	0		1	1	(4.3%)
Disease progression	1	1	(10.0%)	0	0		1	1	(4.3%)
Investigations	1	1	(10.0%)	0	0		1	1	(4.3%)
Blood creatinine increased	1	1	(10.0%)	0	0		1	1	(4.3%)

N* = Number of Events Reported, n = Number of Patients, % = Percentage of Patients.
Top N counts relate to the number of patients who have received each treatment in the specified study period. Patients allocated to Vehicle Control who are not completely healed at Week 8 are counted in the Vehicle Control group in the Controlled Treatment Period and their Uncontrolled Treatment group in the Uncontrolled Treatment Period and Follow-Up Period.
Percentages are calculated using the population number in each treatment group (N) as the denominator.
Treatment-Related Adverse Events are those events having a relationship to study treatment recorded as Possible, Probable or Highly Probable.
Body system and preferred terms are sorted by descending frequency of patient count in the Total column.
The data presented in this Table are contained in Listing 16.2.7.2b

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Table 14.3.1.5b Summary of Treatment-Related Adverse Events by System Organ Class, Preferred Term, Treatment and Overall
(Safety Population)

Study Period: Follow-Up Period

Body System MedDRA Preferred Term	rhNGF 10 µg/ml (N=62)			rhNGF 20 µg/ml (N=65)			Vehicle Control (N=29)			Total (N=156)		
	N*	n	%	N*	n	%	N*	n	%	N*	n	%
Any Adverse Events	1	1	(1.6%)	0	0		2	1	(3.4%)	3	2	(1.3%)
Eye disorders	0	0		0	0		2	1	(3.4%)	2	1	(0.6%)
Dry eye	0	0		0	0		1	1	(3.4%)	1	1	(0.6%)
Eyelid pain	0	0		0	0		1	1	(3.4%)	1	1	(0.6%)
Investigations	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Vital dye staining cornea present	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)

N* = Number of Events Reported, n = Number of Patients, % = Percentage of Patients.
Top N counts relate to the number of patients who have received each treatment in the specified study period. Patients allocated to Vehicle Control who are not completely healed at Week 8 are counted in the Vehicle Control group in the Controlled Treatment Period and their Uncontrolled Treatment group in the Uncontrolled Treatment Period and Follow-Up Period.
Percentages are calculated using the population number in each treatment group (N) as the denominator.
Treatment-Related Adverse Events are those events having a relationship to study treatment recorded as Possible, Probable or Highly Probable.
Body system and preferred terms are sorted by descending frequency of patient count in the Total column.
Events are categorised according to the last treatment received from the controlled or uncontrolled treatment periods.
Note: Patient 350002 was allocated to Vehicle Control in the Controlled Treatment Period and is categorised as such in this table; however, the AEs 'Dry eye' and 'Eye lid pain' occurred during follow-up, while the patient was being treated with an unscheduled course of rhNGF 10 µg/ml.
The data presented in this Table are contained in Listing 16.2.7.2b

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