Table 14.3.1.6b Summary of Serious 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	5	3	(5.8%)	10	9	(17.3%)	5	5	(9.6%)	20	17	(10.9%)
Eye disorders	1	1	(1.9%)	2	2	(3.8%)	3	3	(5.8%)	6	6	(3.8%)
Visual acuity reduced	0	0		1	1	(1.9%)	1	1	(1.9%)	2	2	(1.3%)
Corneal endotheliitis	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Corneal epithelium defect	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Corneal oedema	0	0		0	0		1	1	(1.9%)	1	1	(0.6%)
Eye inflammation	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
General disorders and administration site conditions	0	0		2	2	(3.8%)	2	2	(3.8%)	4	4	(2.6%)
Disease progression	0	0		2	2	(3.8%)	2	2	(3.8%)	4	4	(2.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	1	(1.9%)	1	1	(1.9%)	0	0		2	2	(1.3%)
Malignant neoplasm progression	1	1	(1.9%)	1	1	(1.9%)	0	0		2	2	(1.3%)
Vascular disorders	0	0		2	2	(3.8%)	0	0		2	2	(1.3%)
Aortic dissection	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Venous thrombosis	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.
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 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Myocardial infarction	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Ear and labyrinth disorders	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Vertigo	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Immune system disorders	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Corneal graft rejection	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Infections and infestations	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Diverticulitis	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Renal and urinary disorders	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Renal colic	0	0		1	1	(1.9%)	0	0		1	1	(0.6%)
Respiratory, thoracic and mediastinal disorders	1	1	(1.9%)	0	0		0	0		1	1	(0.6%)
Respiratory distress	1	1	(1.9%)	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.
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 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	1	1	(10.0%)	1	1	(7.7%)	2	2	(8.7%)
Eye disorders	0	0		1	1	(7.7%)	1	1	(4.3%)
Visual acuity reduced	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%)

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.
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 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	22	10	(16.1%)	7	6	(9.2%)	2	2	(6.9%)	31	18	(11.5%)
Respiratory, thoracic and mediastinal disorders	2	2	(3.2%)	1	1	(1.5%)	1	1	(3.4%)	4	4	(2.6%)
Respiratory failure	0	0		1	1	(1.5%)	1	1	(3.4%)	2	2	(1.3%)
Dyspnoea	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Epistaxis	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Cardiac disorders	3	3	(4.8%)	0	0		0	0		3	3	(1.9%)
Arrhythmia	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Cardiac failure	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Myocardial infarction	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Eye disorders	4	2	(3.2%)	1	1	(1.5%)	0	0		5	3	(1.9%)
Corneal epithelium defect	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Corneal neovascularisation	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Corneal opacity	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Neurotrophic keratopathy	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Ulcerative keratitis	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.
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.
The data presented in this Table are contained in Listing 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	%
Gastrointestinal disorders	2	2	(3.2%)	0	0		0	0		2	2	(1.3%)
Diverticular perforation	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Nausea	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
General disorders and administration site conditions	1	1	(1.6%)	1	1	(1.5%)	0	0		2	2	(1.3%)
Disease progression	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Impaired healing	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Infections and infestations	2	2	(3.2%)	0	0		0	0		2	2	(1.3%)
Corneal abscess	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Herpes ophthalmic	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Injury, poisoning and procedural complications	0	0		2	1	(1.5%)	1	1	(3.4%)	3	2	(1.3%)
Clavicle fracture	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Fall	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Femur fracture	0	0		0	0		1	1	(3.4%)	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.
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.
The data presented in this Table are contained in Listing 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	%
Renal and urinary disorders	1	1	(1.6%)	1	1	(1.5%)	0	0		2	2	(1.3%)
Bladder prolapse	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Renal colic	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Vascular disorders	4	2	(3.2%)	0	0		0	0		4	2	(1.3%)
Aortic dissection	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Aortic rupture	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Diabetic vascular disorder	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Shock haemorrhagic	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Investigations	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Blood pressure increased	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Metabolism and nutrition disorders	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Decreased appetite	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Nervous system disorders	0	0		1	1	(1.5%)	0	0		1	1	(0.6%)
Syncope	0	0		1	1	(1.5%)	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.
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.
The data presented in this Table are contained in Listing 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42

Table 14.3.1.6b Summary of Serious 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	%
Reproductive system and breast disorders	1	1	(1.6%)	0	0		0	0		1	1	(0.6%)
Uterine prolapse	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.
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.
The data presented in this Table are contained in Listing 14.3.2.1b

Program path: \Dompe\rhNGF\NGF0212\Stat\programs\tables\rtae.sas Executed: 16OCT2015, 09:42