Clinical trial results:
A Safety and Pharmacokinetic Study of Single Agent REGN2810 in Pediatric Patients with Relapsed or Refractory Solid or Central Nervous System (CNS) Tumors and a Safety and Efficacy Trial of REGN2810 in Combination with Radiotherapy in Pediatric Patients with Newly Diagnosed Diffuse Intrinsic Pontine Glioma, Newly Diagnosed High-Grade Glioma, or Recurrent High-Grade Glioma

Summary

EudraCT number	2023-000604-19
Trial protocol	Outside EU/EEA
Global end of trial date	10 May 2023

Results information

Result version number	v1 (current)
This version publication date	25 November 2023
First version publication date	25 November 2023

Trial information

Trial identification

Sponsor protocol code	R2810-ONC-1690

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03690869
WHO universal trial number (UTN)	-
Other trial identifiers	Pacific Pediatric Neuro-Oncology Consortium (PNOC): PNOC 013 (CC#160825)

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, United States, NY 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals Inc., 001 844-734-6643, clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002007-PIP02-17
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To confirm the safety, characterize the pharmacokinetics (PK) and anticipate recommended phase 2 dose (RP2D) of REGN2810 for children with recurrent or refractory solid or CNS tumors
To confirm the safety and anticipated RP2D of REGN2810 given concomitantly with conventionally fractionated or hypofractionated radiation among participants with newly diagnosed diffuse intrinsic pontine glioma (DIPG) and high-grade glioma (HGG) and with re-irradiation in participants with recurrent HGG
To assess PK of REGN2810 in pediatric participants with newly diagnosed DIPG, newly diagnosed HGG, or recurrent HGG when given in combination with radiation
To assess anti-tumor activity of REGN2810 in combination with radiation in improving overall survival at 12 months (OS12) among participants with newly diagnosed DIPG and recurrent HGG and in improving progression-free survival at 12 months (PFS12) among participants with newly diagnosed HGG

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	03 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 57
Worldwide total number of subjects	57
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	21
Adolescents (12-17 years)	27
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

65 participants had been screened and 57 participants had been enrolled and had received at least 1 dose of REGN2810 at time of study termination (Sponsor decision)

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Solid Tumors (Phase 1)

Arm description:

Participants with recurrent or refractory solid tumors received REGN2810 intravenous (IV) infusion every 2 weeks

Arm type	Experimental
Investigational medicinal product name	cemiplimab (monotherapy)
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously as monotherapy in Phase 1

Arm title	CNS Tumors (Phase 1)

Arm description:

Participants with recurrent or refractory Central Nervous System (CNS) tumors received REGN2810 IV infusion every 2 weeks

Arm type	Experimental
Investigational medicinal product name	cemiplimab (monotherapy)
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously as monotherapy in Phase 1

Arm title	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)

Arm description:

Participants with newly diagnosed Diffuse Intrinsic Pontine Glioma (ndDIPG) received combination REGN2810 IV infusion + radiation therapy (conventionally fractionated radiation therapy [CRT] or hypofractionated radiation therapy [HYRT])

Arm type	Experimental

Investigational medicinal product name	cemiplimab (maintenance)
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in combination with radiation and then used as maintenance therapy

Arm title	Newly Diagnosed HGG (ndHGG) (Efficacy Phase)

Arm description:

Participants with newly diagnosed High-grade Glioma (ndHGG) received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)

Arm type	Experimental
Investigational medicinal product name	cemiplimab (maintenance)
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in combination with radiation and then used as maintenance therapy

Arm title	Recurrent HGG (rHGG) (Efficacy Phase)

Arm description:

Participants with rHGG received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)

Arm type	Experimental
Investigational medicinal product name	cemiplimab (maintenance)
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in combination with radiation and then used as maintenance therapy

Number of subjects in period 1	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)
Started	8	17	11
Completed	0	0	0
Not completed	8	17	11
Physician decision	1	-	-
Adverse event, non-fatal	-	1	-
Subject decision	-	1	-
Death	2	7	8
Other	2	6	3
Progressive Disease	3	1	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Newly Diagnosed HGG (ndHGG)	Recurrent HGG (rHGG) (Efficacy

	(Efficacy Phase)	Phase)
Started	12	9
Completed	1	0
Not completed	11	9
Physician decision	-	-
Adverse event, non-fatal	1	1
Subject decision	1	-
Death	2	3
Other	7	3
Progressive Disease	-	2
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Solid Tumors (Phase 1)
Reporting group description:	
Participants with recurrent or refractory solid tumors received REGN2810 intravenous (IV) infusion every 2 weeks	
Reporting group title	CNS Tumors (Phase 1)
Reporting group description:	
Participants with recurrent or refractory Central Nervous System (CNS) tumors received REGN2810 IV infusion every 2 weeks	
Reporting group title	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed Diffuse Intrinsic Pontine Glioma (ndDIPG) received combination REGN2810 IV infusion + radiation therapy (conventionally fractionated radiation therapy [CRT] or hypofractionated radiation therapy [HYRT])	
Reporting group title	Newly Diagnosed HGG (ndHGG) (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed High-grade Glioma (ndHGG) received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	
Reporting group title	Recurrent HGG (rHGG) (Efficacy Phase)
Reporting group description:	
Participants with rHGG received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	

Reporting group values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)
Number of subjects	8	17	11
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	3	12	6
Adolescents (12-17 years)	5	5	3
Adults (18-64 years)	0	0	2
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	11.0	9.5	9.6
standard deviation	± 4.60	± 4.05	± 5.87
Gender Categorical Units: Subjects			
Male	5	10	3
Female	3	7	8

Reporting group values	Newly Diagnosed HGG (ndHGG) (Efficacy Phase)	Recurrent HGG (rHGG) (Efficacy Phase)	Total

Number of subjects	12	9	57
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	1	22
Adolescents (12-17 years)	9	5	27
Adults (18-64 years)	3	3	8
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	16.4	15.3	
standard deviation	± 3.63	± 3.94	-
Gender Categorical Units: Subjects			
Male	8	6	32
Female	4	3	25

End points

End points reporting groups

Reporting group title	Solid Tumors (Phase 1)
Reporting group description:	
Participants with recurrent or refractory solid tumors received REGN2810 intravenous (IV) infusion every 2 weeks	
Reporting group title	CNS Tumors (Phase 1)
Reporting group description:	
Participants with recurrent or refractory Central Nervous System (CNS) tumors received REGN2810 IV infusion every 2 weeks	
Reporting group title	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed Diffuse Intrinsic Pontine Glioma (ndDIPG) received combination REGN2810 IV infusion + radiation therapy (conventionally fractionated radiation therapy [CRT] or hypofractionated radiation therapy [HYRT])	
Reporting group title	Newly Diagnosed HGG (ndHGG) (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed High-grade Glioma (ndHGG) received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	
Reporting group title	Recurrent HGG (rHGG) (Efficacy Phase)
Reporting group description:	
Participants with rHGG received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	
Subject analysis set title	ndDIPG: REGN2810 + HYRT (Efficacy Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ndDIPG received combination REGN2810 IV infusion + hypofractionated radiation therapy (HYRT)	
Subject analysis set title	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with newly diagnosed diffuse Intrinsic pontine glioma (ndDIPG) received combination REGN2810 IV infusion + conventionally fractionated radiation therapy (CRT)	
Subject analysis set title	ndHGG: REGN2810 + HYRT (Efficacy Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with ndHGG received combination REGN2810 IV infusion + HYRT	
Subject analysis set title	ndHGG: REGN2810 + CRT (Efficacy Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with newly diagnosed high-grade glioma (ndHGG) received combination REGN2810 IV infusion + CRT	
Subject analysis set title	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with rHGG received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	
Subject analysis set title	Cohort A Phase 1 ST (DLT AS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (0 to <12 years) with recurrent or refractory solid tumors (ST); Dose limiting toxicity analysis set (DLT AS)	
Subject analysis set title	Cohort B Phase 1 ST (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (12 to <18 years) with recurrent or refractory ST; DLT analysis set

Subject analysis set title	Cohort C Phase 1 CNS (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (0 to <12 years) with recurrent or refractory Central Nervous System (CNS) tumors; DLT analysis set

Subject analysis set title	Cohort D Phase 1 CNS (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (12 to <18 years) with recurrent or refractory CNS tumors; DLT analysis set

Subject analysis set title	Cohort E Efficacy Phase ndDIPG (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (3 to <12 years) with ndDIPG; DLT analysis set

Subject analysis set title	Cohort F Efficacy Phase ndDIPG (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (12 to 25 years) with ndDIPG; DLT analysis set

Subject analysis set title	Cohort H Efficacy Phase ndHGG (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (12 to 25 years) with ndHGG; DLT analysis set

Subject analysis set title	Cohort I Efficacy Phase rHGG (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (3 to <12 years) with rHGG; DLT analysis set

Subject analysis set title	Cohort J Efficacy Phase rHGG (DLT AS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (12 to 25 years) with rHGG; DLT analysis set

Subject analysis set title	Phase 1: 3mg/kg Q2W (AAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received REGN2810 3 milligrams/kilogram (mg/kg) once every 2 weeks (Q2W); anti-drug antibody analysis set (AAS)

Subject analysis set title	Phase 1: 4.5mg/kg Q2W (AAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received REGN2810 4.5mg/kg Q2W; AAS

Subject analysis set title	Efficacy Phase: 3mg/kg Q2W (AAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received REGN2810 3mg/kg Q2W + radiation therapy (CRT or HYRT); AAS

Subject analysis set title	Efficacy Phase: 4.5mg/kg Q2W (AAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received REGN2810 4.5mg/kg Q2W + radiation therapy (CRT or HYRT); AAS

Subject analysis set title	Cohort A Phase 1 ST 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants (0 to <12 years) with recurrent or refractory ST received REGN2810 3mg/kg Q2W; Pharmacokinetic Analysis Set (PKAS)

Subject analysis set title	Cohort B Phase 1 ST 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (12 to <18 years) with recurrent or refractory ST received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort C Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (0 to <12 years) with recurrent or refractory CNS tumors received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort D Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (12 to <18 years) with recurrent or refractory CNS received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort C Phase 1 CNS 4.5mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (0 to <12 years) with recurrent or refractory CNS tumors received REGN2810 4.5mg/kg Q2W; PKAS	
Subject analysis set title	Cohort F Efficacy Phase ndDIPG 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (12 to 25 years) with ndDIPG received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort H Efficacy Phase ndHGG 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (12 to 25 years) with ndHGG received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort J Efficacy Phase rHGG 3mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (12 to 25 years) with rHGG received REGN2810 3mg/kg Q2W; PKAS	
Subject analysis set title	Cohort E Efficacy Phase ndDIPG 4.5mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (3 to <12 years) with ndDIPG received REGN2810 4.5mg/kg Q2W; PKAS	
Subject analysis set title	Cohort I Efficacy Phase rHGG 4.5mg/kg Q2W (PKAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants (3 to <12 years) with rHGG received REGN2810 4.5mg/kg Q2W; PKAS	

Primary: Number of severe (National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] Grade 3/4/5) TEAEs

End point title	Number of severe (National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] Grade 3/4/5) TEAEs[1][2]

End point description:

NCI CTCAE version 4.0 was utilized for AE grading of severity: Grade 1 (Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated); Grade 2 (Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL); Grade 3 (Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL); Grade 4 (Life-threatening consequences; urgent intervention indicated); Grade 5 (Death related to AE). Safety analysis set (SAF): All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated). Number of NCI grade 3/4/5 Treatment-Emergent Adverse Events (AEs) reported

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	8	13	20	13

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Events	6	13	20	

Statistical analyses

No statistical analyses for this end point

Primary: Number of treatment-emergent adverse events (TEAEs)

End point title	Number of treatment-emergent adverse events (TEAEs)[3][4]

End point description:

Safety analysis set (SAF): All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	61	129	148	62

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Events	94	128	203	

Statistical analyses

No statistical analyses for this end point

Primary: Number of severe (NCI CTCAE Grade 3/4/5) treatment-emergent sponsor identified irAEs

End point title	Number of severe (NCI CTCAE Grade 3/4/5) treatment-emergent sponsor identified irAEs[5][6]

End point description:

NCI CTCAE v. 4.0 was utilized for AE grading of severity: Grade 1 (Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated); Grade 2 (Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL); Grade 3 (Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL); Grade 4 (Life-threatening consequences; urgent intervention indicated); Grade 5 (Death related to AE). SAF: All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	0	0	1	2

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Events	0	2	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of treatment-emergent sponsor identified immune-related adverse events (irAEs)

End point title	Number of treatment-emergent sponsor identified immune-related adverse events (irAEs)[7][8]

End point description:

SAF: All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	1	0	3	4

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Events	5	4	9	

Statistical analyses

No statistical analyses for this end point

Primary: Number of severe (NCI CTCAE Grade 3/4/5) AESIs

End point title	Number of severe (NCI CTCAE Grade 3/4/5) AESIs[9][10]

End point description:

AESIs for this study include any AE (NCI CTCAE v.4.0) that meets dose-limiting toxicity (DLT) criteria, Grade 2 ≤ infusion-related reactions, Grade 2 ≤ allergic/hypersensitivity reactions, Grade 3 ≤ immune-related AE (irAE) (or grade 2 ≤ Uveitis). (NCI CTCAE v. 4.0 AE grading of severity: Grade 1 [Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated]; Grade 2 [Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL]; Grade 3 [Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL]; Grade 4 [Life-threatening consequences; urgent intervention indicated]; Grade 5 [Death related to AE]). SAF: All enrolled participants who received any study treatment in each study phase. Participants analyzed according to treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	0	1	1	3

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	

Units: Events	2	2	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of adverse events of special interest (AESIs)

End point title	Number of adverse events of special interest (AESIs)[11][12]

End point description:

AESIs for this study include any AE (NCI CTCAE v.4.0) that meets dose-limiting toxicity (DLT) criteria, Grade 2 ≤ infusion-related reactions, Grade 2 ≤ allergic/hypersensitivity reactions, Grade 3 ≤ immune-related AE (irAE) (or grade 2 ≤ Uveitis). (NCI CTCAE v. 4.0 AE grading of severity: Grade 1 [Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated]; Grade 2 [Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL]; Grade 3 [Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL]; Grade 4 [Life-threatening consequences; urgent intervention indicated]; Grade 5 [Death related to AE]). SAF: All enrolled participants who received any study treatment in each study phase. Participants analyzed according to treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Events	0	1	2	5

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Events	2	2	8	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with at least one lab abnormality (NCI-CTCAE All Grades) in Hematology, Electrolytes, Liver, Chemistry

End point title	Number of participants with at least one lab abnormality (NCI-CTCAE All Grades) in Hematology, Electrolytes, Liver, Chemistry[13][14]

End point description:

Number of participants with New or Worsened laboratory abnormalities (NCI-CTCAE All Grades) reported in Hematology, Electrolytes, Liver, Chemistry; NCI CTAE v. 4.0: Grade 1 (Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated); Grade 2 (Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL); Grade 3 (Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL); Grade 4 (Life-threatening consequences; urgent intervention indicated); Grade 5 (Death related to AE). SAF: All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated).

End point type	Primary

End point timeframe:

Up to 36 months

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Participants				
≥ 1 lab abnormality (All Grades) Hematology	7	13	5	5
≥ 1 lab abnormality (All Grades) Electrolytes	6	7	6	4
≥ 1 lab abnormality (All Grades) Liver	3	8	6	3
≥ 1 lab abnormality (All Grades) Chemistry	8	13	5	5

End point values	ndHGG: REGN2810 +	ndHGG: REGN2810 +	rHGG: REGN2810 +	

	HYRT (Efficacy Phase)	CRT (Efficacy Phase)	CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	6	9	
Units: Participants				
≥ 1 lab abnormality (All Grades) Hematology	5	6	9	
≥ 1 lab abnormality (All Grades) Electrolytes	3	6	8	
≥ 1 lab abnormality (All Grades) Liver	1	6	6	
≥ 1 lab abnormality (All Grades) Chemistry	5	5	8	

Statistical analyses

No statistical analyses for this end point

Primary: Number of deaths

End point title	Number of deaths[15][16]

End point description:

SAF: All enrolled participants who have received any study treatment (at least one dose of any component of study treatment in a combination therapy) in each study phase. Participants analyzed according to the study treatment received (as treated).

End point type	Primary

End point timeframe:

From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting includes subject analysis sets

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	8	17	6	5
Units: Deaths	6	13	5	5

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	7	9	
Units: Deaths	3	4	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who developed dose limiting toxicities (DLTs) (Phase 1)

End point title	Number of participants who developed dose limiting toxicities (DLTs) (Phase 1)[17]

End point description:

Dose limiting toxicity analysis set, Phase 1: All DLT-evaluable participants treated with monotherapy cemiplimab. DLT evaluable participants are defined as those participants who have completed the corresponding DLT observation period and those participants who discontinued early due to the development of a DLT.

End point type	Primary

End point timeframe:

Baseline to 28 days

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort A Phase 1 ST (DLT AS)	Cohort B Phase 1 ST (DLT AS)	Cohort C Phase 1 CNS (DLT AS)	Cohort D Phase 1 CNS (DLT AS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	5	9	5
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who developed DLTs (Efficacy Phase)

End point title	Number of participants who developed DLTs (Efficacy Phase)[18]

End point description:

Efficacy Phase: The first 6 DLT-evaluable participants of each disease cohort by age group who are treated with cemiplimab + radiotherapy during 3+3 safety run-in. DLT evaluable participants are defined as those who have completed the corresponding DLT observation period and those participants who discontinued early due to the development of a DLT.

End point type	Primary

End point timeframe:

Up to 4 weeks post radiation therapy

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort E Efficacy Phase ndDIPG (DLT AS)	Cohort F Efficacy Phase ndDIPG (DLT AS)	Cohort H Efficacy Phase ndHGG (DLT AS)	Cohort I Efficacy Phase rHGG (DLT AS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	5	6	1
Units: Participants	1	1	0	0

End point values	Cohort J Efficacy Phase rHGG (DLT AS)			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Elimination half-life (t1/2) of functional cemiplimab (REGN2810) in serum

End point title	Elimination half-life (t1/2) of functional cemiplimab (REGN2810) in serum[19]

End point description:

Pharmacokinetic Analysis Set (PKAS): All treated participants who received any amount of study drug (Safety Analysis Set [SAF]) and had at least 1 non-missing functional cemiplimab measurement following the first dose of cemiplimab up to the end of study. PKAS: Based on the actual treatment received (as treated)

End point type	Primary

End point timeframe:

Up to 24 months

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort A Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort B Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort C Phase 1 CNS 3mg/kg Q2W (PKAS)	Cohort D Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[20]	0[21]	0[22]	0[23]
Units: milligrams/Liter (mg/L)				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[20] - t1/2 will be later estimated by population PK analysis (PopPK)

[21] - t1/2 will be later estimated by population PK analysis (PopPK)

[22] - t1/2 will be later estimated by population PK analysis (PopPK)

[23] - t1/2 will be later estimated by population PK analysis (PopPK)

End point values	Cohort C Phase 1 CNS 4.5mg/kg Q2W	Cohort F Efficacy Phase ndDIPG	Cohort H Efficacy Phase ndHGG 3mg/kg	Cohort J Efficacy Phase rHGG 3mg/kg

	(PKAS)	3mg/kg Q2W (PKAS)	Q2W (PKAS)	Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[24]	0[25]	0[26]	0[27]
Units: milligrams/Liter (mg/L)				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[24] - t1/2 will be later estimated by population PK analysis (PopPK)

[25] - t1/2 will be later estimated by population PK analysis (PopPK)

[26] - t1/2 will be later estimated by population PK analysis (PopPK)

[27] - t1/2 will be later estimated by population PK analysis (PopPK)

End point values	Cohort E Efficacy Phase ndDIPG 4.5mg/kg Q2W (PKAS)	Cohort I Efficacy Phase rHGG 4.5mg/kg Q2W (PKAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[28]	0[29]		
Units: milligrams/Liter (mg/L)				
median (full range (min-max))	(to)	(to)		

Notes:

[28] - t1/2 will be later estimated by population PK analysis (PopPK)

[29] - t1/2 will be later estimated by population PK analysis (PopPK)

Statistical analyses

No statistical analyses for this end point

Primary: Trough concentration (Ctrough) of functional cemiplimab (REGN2810) in serum

End point title	Trough concentration (Ctrough) of functional cemiplimab (REGN2810) in serum[30]

End point description:

Ctrough (trough concentration) of functional cemiplimab in serum; Pharmacokinetic analysis set (PKAS): All treated participants who received any amount of study drug (SAF) and had at least 1 non-missing functional cemiplimab measurement following the first dose of cemiplimab up to the end of study (based on actual treatment received [as treated]).

End point type	Primary

End point timeframe:

Up to 24 months

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort A Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort B Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort C Phase 1 CNS 3mg/kg Q2W (PKAS)	Cohort D Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3[31]	5[32]	3[33]	5[34]
Units: mg/L				
median (full range (min-max))				
Ctrough - after 1st dose	16.7 (14.0 to 16.8)	23.9 (21.1 to 27.2)	33.8 (27.9 to 36.5)	28.5 (19.6 to 42.2)

Ctrough - week 16	39.4 (39.4 to 39.4)	78.6 (78.6 to 78.6)	99999 (99999 to 99999)	66.1 (66.1 to 66.1)

Notes:

[31] - week 16 n = 1, Median value = Full Range (min-max) value

[32] - week 16 n = 1, Median value = Full Range (min-max) value

[33] - week 16 n = 0

[34] - week 16 n = 1

End point values	Cohort C Phase 1 CNS 4.5mg/kg Q2W (PKAS)	Cohort F Efficacy Phase ndDIPG 3mg/kg Q2W (PKAS)	Cohort H Efficacy Phase ndHGG 3mg/kg Q2W (PKAS)	Cohort J Efficacy Phase rHGG 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8[35]	4[36]	11[37]	5[38]
Units: mg/L				
median (full range (min-max))				
Ctrough - after 1st dose	48.3 (32.9 to 63.8)	39.7 (33.9 to 41.9)	26.0 (17.4 to 36.3)	36.3 (25.2 to 178)
Ctrough - week 16	113 (113 to 113)	82.4 (65.7 to 104)	94.3 (84.5 to 247)	78.5 (57.0 to 134)

Notes:

[35] - week 16 n = 1

[36] - week 16 n = 4

[37] - week 16 n = 7

[38] - week 16 n = 5

End point values	Cohort E Efficacy Phase ndDIPG 4.5mg/kg Q2W (PKAS)	Cohort I Efficacy Phase rHGG 4.5mg/kg Q2W (PKAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[39]	1[40]		
Units: mg/L				
median (full range (min-max))				
Ctrough - after 1st dose	35.8 (32.4 to 49.6)	38.5 (38.5 to 38.5)		
Ctrough - week 16	122 (13.1 to 159)	70.0 (70.0 to 70.0)		

Notes:

[39] - week 16 n = 5

[40] - n = 1; Median value = Full Range (min-max) value

Statistical analyses

No statistical analyses for this end point

Primary: Peak concentration (Cmax) of functional cemiplimab (REGN2810) in serum

End point title	Peak concentration (Cmax) of functional cemiplimab (REGN2810) in serum[41]

End point description:

Cmax (peak concentration) of functional cemiplimab in serum; Pharmacokinetic Analysis Set (PKAS): All treated participants who received any amount of study drug (SAF) and had at least 1 non-missing functional cemiplimab measurement following the first dose of cemiplimab up to the end of study (based on actual treatment received [as treated]).

End point type	Primary

End point timeframe:

Up to 24 months

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort A Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort B Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort C Phase 1 CNS 3mg/kg Q2W (PKAS)	Cohort D Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3[42]	5[43]	3[44]	5[45]
Units: mg/L				
median (full range (min-max))				
Cmax - after 1st dose	58.2 (52.0 to 86.9)	73.5 (63.4 to 87.9)	92.2 (87.9 to 101)	68.3 (60.9 to 101)
Cmax - week 16	122 (122 to 122)	136 (136 to 136)	144 (144 to 144)	112 (112 to 112)

Notes:

[42] - week 16 n = 1, Median value = Full Range (min-max) value

[43] - week 16 n = 1, Median value = Full Range (min-max) value

[44] - week 16 n = 1, Median value = Full Range (min-max) value

[45] - week 16 n = 1, Median value = Full Range (min-max) value

End point values	Cohort C Phase 1 CNS 4.5mg/kg Q2W (PKAS)	Cohort F Efficacy Phase ndDIPG 3mg/kg Q2W (PKAS)	Cohort H Efficacy Phase ndHGG 3mg/kg Q2W (PKAS)	Cohort J Efficacy Phase rHGG 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9[46]	4[47]	11[48]	5[49]
Units: mg/L				
median (full range (min-max))				
Cmax - after 1st dose	152 (76.0 to 202)	95.1 (65.5 to 106)	71.8 (6.41 to 88.0)	88.8 (69.5 to 124)
Cmax - week 16	236 (236 to 236)	221 (164 to 256)	165 (143 to 200)	179 (119 to 234)

Notes:

[46] - week 16 n = 1, Median value = Full Range (min-max) value

[47] - week 16 n = 4

[48] - week 16 n = 8

[49] - week 16 n = 5

End point values	Cohort E Efficacy Phase ndDIPG 4.5mg/kg Q2W (PKAS)	Cohort I Efficacy Phase rHGG 4.5mg/kg Q2W (PKAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[50]	1[51]		
Units: mg/L				
median (full range (min-max))				
Cmax - after 1st dose	105 (93.7 to 130)	123 (123 to 123)		
Cmax - week 16	209 (99.2 to 297)	225 (225 to 225)		

Notes:

[50] - week 16 n = 5

[51] - n =1, Median value = Full Range (min-max) value

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve (AUC) of functional cemiplimab (REGN2810) in serum

End point title	Area under the concentration-time curve (AUC) of functional cemiplimab (REGN2810) in serum[52]

End point description:

Pharmacokinetic Analysis Set (PKAS): All treated participants who received any amount of study drug (SAF) and had at least 1 non-missing functional cemiplimab measurement following the first dose of cemiplimab up to the end of study. PKAS: Based on the actual treatment received (as treated)

End point type	Primary

End point timeframe:

Up to 24 months

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	Cohort A Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort B Phase 1 ST 3mg/kg Q2W (PKAS)	Cohort C Phase 1 CNS 3mg/kg Q2W (PKAS)	Cohort D Phase 1 CNS 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[53]	0[54]	0[55]	0[56]
Units: mg/L				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[53] - AUC will be later estimated by population PK analysis (PopPK)

[54] - AUC will be later estimated by PopPK

[55] - AUC will be later estimated by PopPK

[56] - AUC will be later estimated by PopPK

End point values	Cohort C Phase 1 CNS 4.5mg/kg Q2W (PKAS)	Cohort F Efficacy Phase ndDIPG 3mg/kg Q2W (PKAS)	Cohort H Efficacy Phase ndHGG 3mg/kg Q2W (PKAS)	Cohort J Efficacy Phase rHGG 3mg/kg Q2W (PKAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[57]	0[58]	0[59]	0[60]
Units: mg/L				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[57] - AUC will be later estimated by PopPK

[58] - AUC will be later estimated by PopPK

[59] - AUC will be later estimated by PopPK

[60] - AUC will be later estimated by PopPK

End point values	Cohort E Efficacy Phase ndDIPG 4.5mg/kg Q2W (PKAS)	Cohort I Efficacy Phase rHGG 4.5mg/kg Q2W (PKAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[61]	0[62]		
Units: mg/L				
median (full range (min-max))	(to)	(to)		

Notes:

[61] - AUC will be later estimated by PopPK

[62] - AUC will be later estimated by PopPK

Statistical analyses

No statistical analyses for this end point

Primary: Overall survival (OS) rate at 12 months for participants with newly diagnosed DIPG and recurrent HGG

End point title	Overall survival (OS) rate at 12 months for participants with newly diagnosed DIPG and recurrent HGG[63]

End point description:

OS is defined as the time from randomization to the date of death due to any cause. A participant who has not died will be censored at the last date that participant is documented to be alive; Full analysis set (FAS) (Efficacy Phase): All ndDIPG and ndHGG participants assigned to radiation treatment by Interactive web response system (IWRS) at randomization. Participants analyzed according to treatment assigned during randomization. Includes all screen-pass and eligible participants with rHGG; All deaths due to any cause occurring on/before cut-off date in the FAS were used in the OS analysis. A participant who had not died/was lost to follow up at time of analysis cut-off date was censored at last date participant was documented to be alive

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[63] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndDIPG: REGN2810 + CRT (Efficacy Phase)	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	6	5[64]	9	
Units: Percent of survival at 12 months				
number (confidence interval 95%)	33.3 (4.6 to 67.6)	0.0 (0 to 0)	31.3 (4.8 to 64.1)	

Notes:

[64] - 0 to 0 Confidence Interval (95%) = Not evaluable

Statistical analyses

No statistical analyses for this end point

Primary: Progression-free survival (PFS) rate at 12 months for participants with newly diagnosed HGG

End point title	Progression-free survival (PFS) rate at 12 months for participants with newly diagnosed HGG[65]

End point description:

PFS at 12 months; FAS includes two parts: All ndDIPG and ndHGG participants to whom the radiation treatment has been assigned by the IWRS at randomization. This is the intent to treat (ITT) population for these two disease cohorts. Per ITT principle, these patients will be analyzed according to the treatment they have been assigned to during the randomization. All recurrent HGG patients who have pass screening and are deemed to be eligible for this study.

End point type	Primary

End point timeframe:

At 12 months

Notes:

[65] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only

End point values	ndHGG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5[66]	7		
Units: Percent of PFS at 12 months				
number (confidence interval 95%)	99999 (99999 to 99999)	20.0 (0.8 to 58.2)		

Notes:

[66] - 99999 = not evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-REGN2810 antibodies (ADA)

End point title	Number of participants with anti-REGN2810 antibodies (ADA)

End point description:

ADA status classified as: Positive; Pre-existing (baseline [BL] sample positive & all post BL ADA titers reported as < 9-fold BL titer value); Negative (all samples negative); ADA positive: Treatment-boosted (positive result at BL with ≥1 post BL titer result ≥9-fold BL titer value); Treatment-emergent (TE) (negative result or missing result at BL with ≥1 positive post BL result); TE: Persistent (positive result detected in ≥2 consecutive post BL samples separated by ≥ a 12/16-week post BL period with no ADA-negative results in-between, regardless of any missing samples; Indeterminate (positive result in last collection, regardless of any missing samples); Transient (not persistent or indeterminate, regardless of any missing samples); ADA analysis set (AAS): all treated participants who received any amount of cemiplimab (SAF) & had ≥1 non-missing ADA result following first dose of cemiplimab (based on actual treatment received [as treated]).

End point type	Secondary

End point timeframe:

1st follow-up visit, approximately 25 months

End point values	Phase 1: 3mg/kg Q2W (AAS)	Phase 1: 4.5mg/kg Q2W (AAS)	Efficacy Phase: 3mg/kg Q2W (AAS)	Efficacy Phase: 4.5mg/kg Q2W (AAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	5	19	7
Units: Participants				
Negative	16	5	17	6
Pre-existing immunoreactivity	0	0	1	0
Treatment-boosted response	0	0	0	0
Treatment-emergent (TE) response	0	0	1	1
- persistent TE response	0	0	0	0
- transient TE response	0	0	1	1
- indeterminate TE response	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

ORR is defined as the percentage of participants who have a confirmed complete response (CR) or partial response (PR), as determined per standard criteria between the date of first study treatment and the date of the first objectively documented progression or the date of receiving another anti-cancer systemic therapy, whichever came first.

End point type	Secondary

End point timeframe:

Approximately 24 months

End point values	Solid Tumors (Phase 1)	CNS Tumors (Phase 1)	Newly Diagnosed DIPG (ndDIPG) (Efficacy Phase)	Newly Diagnosed HGG (ndHGG) (Efficacy Phase)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	17	11	12
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 36.9)	0 (0.0 to 19.5)	0 (0.0 to 28.5)	8.3 (0.2 to 38.5)

End point values	Recurrent HGG (rHGG) (Efficacy Phase)			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percentage of participants				

number (confidence interval 95%)	0 (0.0 to 33.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to 90 days after the last dose of study treatment (up to 36 months)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Solid Tumors: REGN2810 monotherapy (Phase 1)
Reporting group description:	
Participants with recurrent or refractory solid tumors received REGN2810 intravenous (IV) infusion every 2 weeks	
Reporting group title	CNS Tumors: REGN2810 monotherapy (Phase 1)
Reporting group description:	
Participants with recurrent or refractory Central Nervous System (CNS) tumors received REGN2810 IV infusion every 2 weeks	
Reporting group title	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed Diffuse Intrinsic Pontine Glioma (ndDIPG) received combination REGN2810 IV infusion + conventionally fractionated radiation therapy (CRT)	
Reporting group title	ndDIPG: REGN2810 + HYRT (Efficacy Phase)
Reporting group description:	
Participants with ndDIPG received combination REGN2810 IV infusion + hypofractionated radiation therapy (HYRT)	
Reporting group title	ndHGG: REGN2810 + CRT (Efficacy Phase)
Reporting group description:	
Participants with newly diagnosed High-grade Glioma (ndHGG) received combination REGN2810 IV infusion + CRT	
Reporting group title	ndHGG: REGN2810 + HYRT (Efficacy Phase)
Reporting group description:	
Participants with ndHGG received combination REGN2810 IV infusion + HYRT	
Reporting group title	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)
Reporting group description:	
Participants with rHGG received combination REGN2810 IV infusion + radiation therapy (CRT or HYRT)	

Serious adverse events	Solid Tumors: REGN2810 monotherapy (Phase 1)	CNS Tumors: REGN2810 monotherapy (Phase 1)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	3 / 17 (17.65%)	2 / 5 (40.00%)
number of deaths (all causes)	6	13	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pseudoprogression			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Family stress			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body ingestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IIIrd nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Encephalitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	ndHGG: REGN2810 + HYRT (Efficacy Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	5 / 7 (71.43%)	2 / 5 (40.00%)
number of deaths (all causes)	5	4	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pseudoprogression			

subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Family stress			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body ingestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IIIrd nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Encephalitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 9 (55.56%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pseudoprogression			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Family stress			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foreign body ingestion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
IIIrd nerve disorder				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				

subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Drug reaction with eosinophilia and systemic symptoms				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Encephalitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhinovirus infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Solid Tumors: REGN2810 monotherapy (Phase 1)	CNS Tumors: REGN2810 monotherapy (Phase 1)	ndDIPG: REGN2810 + CRT (Efficacy Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	14 / 17 (82.35%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tumour pseudoprogression			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	3 / 5 (60.00%)
occurrences (all)	0	1	4
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Catheter site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Asthenia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)	7 / 17 (41.18%)	2 / 5 (40.00%)
occurrences (all)	2	9	2
Chills			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Peripheral swelling			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Social circumstances			
Family stress			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	2 / 17 (11.76%)	1 / 5 (20.00%)
occurrences (all)	2	2	1

Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Nasal congestion			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Apnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aspiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Laryngeal inflammation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Respiratory tract congestion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiration abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngeal ulceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Laryngeal oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Libido decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Personality change			

subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 8 (0.00%)	3 / 17 (17.65%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 17 (11.76%)	1 / 5 (20.00%)
occurrences (all)	1	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 17 (11.76%)	1 / 5 (20.00%)
occurrences (all)	1	2	2
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Lymphocyte count decreased			
subjects affected / exposed	3 / 8 (37.50%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	4	3	1
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	2
Amylase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			

subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Wound dehiscence			

subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Stoma site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Radiation skin injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	3
Procedural site reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal wound dehiscence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Incision site erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pseudomeningocele			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diastolic dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 8 (0.00%)	4 / 17 (23.53%)	2 / 5 (40.00%)
occurrences (all)	0	5	4
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Accessory nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysarthria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Facial nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	4 / 17 (23.53%)	1 / 5 (20.00%)
occurrences (all)	0	6	1
Somnolence			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Tremor			

subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Aphasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Auditory nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoglossal nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysmetria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Glossopharyngeal nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Hydrocephalus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Central nervous system necrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

IIIrd nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Memory impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
VIth nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Trigeminal nerve disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Thrombocytosis			

subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Anaemia			
subjects affected / exposed	3 / 8 (37.50%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	5	2	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Optic atrophy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Papilloedema			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eyelid function disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	4 / 17 (23.53%)	2 / 5 (40.00%)
occurrences (all)	1	6	5
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	2 / 5 (40.00%)
occurrences (all)	0	2	2
Nausea			
subjects affected / exposed	2 / 8 (25.00%)	2 / 17 (11.76%)	1 / 5 (20.00%)
occurrences (all)	2	3	1
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Abdominal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatitis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	2
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin atrophy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	2 / 8 (25.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Rash macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Adrenal insufficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperthyroidism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Pain in extremity			
subjects affected / exposed	1 / 8 (12.50%)	3 / 17 (17.65%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	2 / 8 (25.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	2	1	1
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Arthralgia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1
Arthritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Costochondritis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Infections and infestations			
Vaginal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin candida			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Mucosal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			

Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	4 / 17 (23.53%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Decreased appetite			
subjects affected / exposed	2 / 8 (25.00%)	3 / 17 (17.65%)	3 / 5 (60.00%)
occurrences (all)	2	4	3
Hypomagnesaemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 17 (11.76%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Hypermagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Increased appetite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Alkalosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ndDIPG: REGN2810 + HYRT (Efficacy Phase)	ndHGG: REGN2810 + CRT (Efficacy Phase)	ndHGG: REGN2810 + HYRT (Efficacy Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	7 / 7 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tumour pseudoprogression			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	2
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	2
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 7 (28.57%)	1 / 5 (20.00%)
occurrences (all)	3	3	1
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	3 / 7 (42.86%)	3 / 5 (60.00%)
occurrences (all)	1	3	5
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Family stress			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Apnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiration abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngeal ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Laryngeal oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Libido decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Restlessness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Personality change			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	5	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Blood bilirubin increased			

subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Lymphocyte count decreased			
subjects affected / exposed	3 / 6 (50.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	5	6	2
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	3 / 6 (50.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	2
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Haemoglobin increased			

subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Protein total decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
White blood cell count decreased			
subjects affected / exposed	2 / 6 (33.33%)	4 / 7 (57.14%)	0 / 5 (0.00%)
occurrences (all)	3	7	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Wound dehiscence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Stoma site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Radiation skin injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Procedural site reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal wound dehiscence			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Incision site erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pseudomeningocele			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Diastolic dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Headache			

subjects affected / exposed	3 / 6 (50.00%)	4 / 7 (57.14%)	1 / 5 (20.00%)
occurrences (all)	5	7	3
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Accessory nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Facial nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Auditory nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Hypoglossal nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Depressed level of consciousness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dysmetria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Glossopharyngeal nerve disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hemiparesis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hydrocephalus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Central nervous system necrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
IIIrd nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Nystagmus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
VIth nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Trigeminal nerve disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Eosinophilia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutrophilia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
External ear pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Optic atrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Pupillary reflex impaired			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Photophobia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Papilloedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eyelid function disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Visual impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed	3 / 6 (50.00%)	1 / 7 (14.29%)	5 / 5 (100.00%)
occurrences (all)	5	1	6
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	2 / 7 (28.57%)	4 / 5 (80.00%)
occurrences (all)	2	2	8
Dysphagia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Anal incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry mouth			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 7 (71.43%)	3 / 5 (60.00%)
occurrences (all)	0	6	3
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	3
Skin exfoliation			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin atrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Rash macular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	2
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Decubitus ulcer			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Urinary incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Adrenal insufficiency			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hyperthyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	4
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arthralgia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Costochondritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Vaginal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0

COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Skin infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	3	1	3
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 7 (42.86%)	1 / 5 (20.00%)
occurrences (all)	1	4	2
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dehydration			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Alkalosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Hyperphosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Hypoglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	rHGG: REGN2810 + CRT/HYRT (Efficacy Phase)		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	9 / 9 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tumour pseudoprogression			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Catheter site pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pain			

subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Gait disturbance subjects affected / exposed occurrences (all) Non-cardiac chest pain subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Peripheral swelling subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 7 / 9 (77.78%) 10 0 / 9 (0.00%) 0 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Social circumstances Family stress subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Reproductive system and breast disorders Heavy menstrual bleeding subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			

Cough				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Epistaxis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Nasal congestion				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Oropharyngeal pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Rhinorrhoea				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Tachypnoea				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Apnoea				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Aspiration				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Dyspnoea				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Dyspnoea exertional				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Haemoptysis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Laryngeal inflammation				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			

Rhinitis allergic			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory tract congestion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiration abnormal			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pharyngeal ulceration			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Laryngeal oedema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Libido decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Restlessness			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Personality change			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	8		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Blood bilirubin increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	4		
Lymphocyte count decreased			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	7		
Weight decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Amylase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Neutrophil count decreased subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 4		
Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 5		
Blood thyroid stimulating hormone decreased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Haemoglobin increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Blood bicarbonate decreased subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 3		
Protein total decreased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
White blood cell count decreased subjects affected / exposed occurrences (all)	4 / 9 (44.44%) 5		
Injury, poisoning and procedural complications			

Procedural pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Wound dehiscence			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Stoma site pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Radiation skin injury			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Procedural site reaction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Abdominal wound dehiscence			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Incision site erythema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pseudomeningocele			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cardiac disorders			
Sinus tachycardia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Diastolic dysfunction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	4		
Seizure			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Accessory nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dysarthria			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Facial nerve disorder			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Somnolence				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	2			
Tremor				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Aphasia				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Ataxia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Auditory nerve disorder				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Autonomic nervous system imbalance				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Hypoglossal nerve disorder				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Depressed level of consciousness				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Dysmetria				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Glossopharyngeal nerve disorder				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Hemiparesis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Hydrocephalus				

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Central nervous system necrosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
IIIrd nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Muscle spasticity			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nystagmus			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
VIth nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Trigeminal nerve disorder			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Eosinophilia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Neutrophilia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Thrombocytosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
External ear pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dry eye			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Optic atrophy			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Pupillary reflex impaired			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Photophobia			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Papilloedema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	4		
Eyelid function disorder			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Conjunctival hyperaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	5 / 9 (55.56%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	6		
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Abdominal pain				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	2			
Abdominal pain upper				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Anal incontinence				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Cheilitis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Colitis				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Abdominal distension				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Gastrointestinal pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Stomatitis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			

Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dermatitis acneiform			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin exfoliation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin atrophy			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rash macular			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Erythema			

subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Decubitus ulcer subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all) Urinary incontinence subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 1 / 9 (11.11%) 2 1 / 9 (11.11%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all) Adrenal insufficiency subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism	1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1		

subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Costochondritis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Muscle tightness			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Vaginal infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin candida			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Mucosal infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Conjunctivitis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Decreased appetite subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 4		
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 3		
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 4		
Hypermagnesaemia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Dehydration subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Increased appetite subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Alkalosis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3		
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Hyponatraemia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Hyperphosphataemia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	5		
Hypocalcaemia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	6		
Hypoglycaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypernatraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2018	Amendment 1: Revised study design; Added assessments; Added randomization to rHGG cohort; Updated safety information/oversight; Added a global stopping rule; Clarified how disease response will be determined in patients with neuroblastoma with both Metaiodobenzylguanidine (MIBG) avid disease and bone marrow involvement; Added International Neuroblastoma Response Criteria; Excluded urinary catecholamine levels from response assessment for participants with neuroblastoma; Clarified Immunotherapy Response Assessment in Neuro-Oncology (iRANO) criteria; Corrected definition of progressive disease per RANO; Added treatment criteria; Added replacement criteria for non-evaluable participants
04 June 2018	Amendment 2: The primary objective of this amendment was to improve the applicability of our adverse event management guidelines to a pediatric population.
19 March 2020	Amendment 3: The aim of this amendment was to streamline the structure and language of the protocol, to improve the clarity of the study design, and consistency of study conduct. Additionally, changes that impact the design of the study have been made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 May 2023	As all efficacy cohorts for this study have now been closed due to the futility criteria, Regeneron as Sponsor in collaboration PNOC have made a decision to close the study to further enrollment.	-

Notes:

Limitations and caveats

None reported