作成日：2025 年 10 月 10 日

ルクスターナ注特定使用成績調査（CLTW888A12401，遺伝性網膜ジストロフィー）の中間集計結果

最新情報に基づき，薬剤を適正かつ安全にご使用いただくために，ルクスターナ注特定使用成績調査（CLTW888A12401，遺伝性網膜ジストロフィー）の中間集計結果を，ノバルティスファーマ株式会社 医療関係者向け情報サイトに掲載致しました。

＜留意点＞

- 2023 年 7 月～2025 年 7 月の間で収集された情報です
- 中間の結果であるため，今後，結果は更新されます
- 安全性情報を掲載しています

添付文書 2023 年 6 月作成（第 1 版）※　抜粋

【効能又は効果】

両アレル性 *RPE65* 遺伝子変異による遺伝性網膜ジストロフィー

【用法及び用量】

通常、1.5×10^{11} ベクターゲノム（vg）/0.3mL を各眼の網膜下に単回投与する。各眼への網膜下投与は、短い投与間隔で実施するが、6 日以上あけること。同一眼への本品の再投与はしないこと。

※本剤の使用に際しては，最新の添付文書をご参照ください。

当該調査単位期間終了日：2025 年 7 月 23 日

結果の概要

製造販売後調査の標題	ルクスターナ注　特定使用成績調査 Voretigene Neparvovec 投与患者を対象とした市販後，多施設共同，国際共同，縦断的，安全性観察登録調査（遺伝性網膜ジストロフィー，CLTW888A12401）
調査の課題及び目的	登録式の非介入試験である本調査の目的は，voretigene neparvovec 投与後 5 年間の，実臨床下での長期安全性プロファイルを評価することである。
調査デザイン	市販後，多施設共同，国際共同，縦断的，安全性観察登録調査
主要目的	すべての特に注目すべき有害事象，並びにその他の有害事象及び重篤な有害事象を収集すること
結果	当該調査開始日（2023 年 7 月 27 日）からデータカットオフ日（2025 年 3 月 31 日）までに，国内の調査実施施設で 4 例が登録され，かつ調査票データが収集された。適応外症例はなく（Listing 1-2.3），4 例すべてを安全性解析対象症例とした。データカットオフ時点で，4 例すべてが調査を継続していた（Table 1-1.1b）。 同意取得時点の年齢の範囲は[redacted]歳～3[redacted]歳であり，4 例すべてが女性であった（Listing 1-2.1）。 4 例のうち，本品が両眼に投与された症例は 3 例，片眼に投与された症例は 1 例であった。投与量 450 μL が投与された 1 例 1 眼を除き，添付文書に従った投与量 300 μL で本品が投与された（Listing 1-3.1，Listing 3-1.1）。本品投与前後で，4 例すべてにプレドニゾロンが投与された（Listing 1-3.3）。 有害事象は 4 例中 3 例に発現した（Listing 3-1.1）。 眼の有害事象は，75.0%（3 例）に認められた。最も発現割合が高かった PT 別の有害事象は，嚢下白内障［50.0%（2 例）］であり，次いで結膜充血，眼痛，網膜変性，視力低下，及び偶発的過量投与［各 25.0%（1 例）］であった（Table 3-1.1_jpn）。このうち投与手技に関連すると判断された事象では，最も発現割合が高かった事象は嚢下白内障［50.0%（2 例）］であり，次いで結膜充血，眼痛，網膜変性，及び視力低下［各 25.0%（1 例）］であった（Table 3-1.5_jpn）。Voretigene neparvovec 又は本品投与前後のプレドニゾロン投与に関連すると判断された眼の有害事象は認められなかった（Table 3-1.4_jpn，Table 3-1.6_jpn）。 眼以外の有害事象は，75%（3 例）に認められた。最も発現割合が高かった PT 別の有害事象は，便秘及び不眠症［各 50.0%（2 例）］であり，次いで嘔吐，末梢性浮腫，背部痛，月経困難症，及び皮膚乾燥［各 25.0%（1 例）］であった（Table 3-2.1_jpn）。このうち本品投与前後のプレドニゾロン投与に関連すると判断された事象は，末梢性浮腫及び皮膚乾燥［各 25.0%（1 例）］であった（Table 3-2.6_jpn）。Voretigene neparvovec 又は投与手技に関連すると判断された眼以外の有害事象は認められなかった（Table 3-2.4_jpn，Table 3-2.5_jpn）。 重篤な有害事象は認められなかった（Table 3-1.2_jpn，Table 3-2.2_jpn）。 特に注目すべき有害事象 [1]はいずれも眼の事象であった（Table 3-1.3_jpn，Table 3-2.3_jpn）。50.0%（2 例）に「投与手技に関連する眼内炎症及び／又は眼内感染症」［嚢下白内障（PT）2 例］が，25.0%（1 例）にそれぞれ「網脈絡膜萎縮」［網膜変性（PT）1 例］及び「中心窩機能の喪失」［視力低下（PT）1 例］が認められ（Table 3-1.3_jpn），いずれも投与手技との関連ありと判断された（Listing 3-3.1）。データカットオフ日までの転帰は，網膜変性（1 例）が不明，視力低下（1 例）が未回復として報告されたが，嚢下白内障（2 例）は回復した。
結論	本調査は実施中であり，得られた結果は限定的であるものの，報告された有害事象は承認時の安全性プロファイルと同様であり，データカットオフ日までに安全性検討事項を含め新たに懸念される事象はなかった。 今後も本品の安全性情報を収集し，新たな懸念事項が認められた場合には適切な措置を講じることとする。

備考	添付資料：解析結果

1) 特に注目すべき有害事象は，標準化した安全性に関する質問票（製造販売後調査実施計画書 12.1 項）に基づいて調査責任／分担医師が評価し，有害事象としてデータ収集された。

NOVARTIS

Clinical Development

LTW888 / Voretigene neparvovec

Study No. CLTW888A12401

Non-Interventional Study Interim Report 6 (Japan)

A Post-Authorization, Multicenter, Multinational, Longitudinal Observational Safety Registry Study for Patients Treated with Voretigene Neparvovec

Document type: Clinical Study Report Supplement

Table of Contents

1 Introduction

The purpose of this supplement CSR is to provide statistical outputs for the Japan periodic safety report.

2 Data displays

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Table 1-1.1b (Page 35 of 62)
Patient disposition by country (or subdivision) and center
All enrolled patients

Country or subdivision, center: Japan, 6001

Disposition/reason	n (%)	Voretigene Neparvovec n (%)
Number in the Enrolled Set	2	
Number in the Full Analysis Set		2 (100)
Completed the study		0
Ongoing at the cut-off date		2 (100)
Discontinued the study		0

- The Enrolled Set includes all patients who signed the informed consent.
- The Full Analysis Set (FAS) includes all patients in the Enrolled Set who received at least one injection of voretigene neparvovec.
- Percentages are computed using the number in the preceding analysis set and country, center combination as the denominator.
- Reasons for discontinuation are sorted by descending frequency within each country or subdivision, center.
- Country represents the country of study enrollment. Note, that the country of study enrollment can be different from the country of treatment.
- Center represents the study enrollment center. Note, that the study enrollment center can be different from the center of treatment.

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Table 1-1.1b (Page 36 of 62)
Patient disposition by country (or subdivision) and center
All enrolled patients

Country or subdivision, center: Japan, 6002

Disposition/reason	n (%)	Voretigene Neparvovec n (%)
Number in the Enrolled Set	2	
Number in the Full Analysis Set		2 (100)
Completed the study		0
Ongoing at the cut-off date		2 (100)
Discontinued the study		0

- The Enrolled Set includes all patients who signed the informed consent.
- The Full Analysis Set (FAS) includes all patients in the Enrolled Set who received at least one injection of voretigene neparvovec.
- Percentages are computed using the number in the preceding analysis set and country, center combination as the denominator.
- Reasons for discontinuation are sorted by descending frequency within each country or subdivision, center.
- Country represents the country of study enrollment. Note, that the country of study enrollment can be different from the country of treatment.
- Center represents the study enrollment center. Note, that the study enrollment center can be different from the center of treatment.

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Table 1-3.1b (Page 35 of 62)
Treatment status at study enrollment by country (or subdivision) and center
Full Analysis Set

Country or subdivision, Center: Japan, 6001

Status	Voretigene Neparvovec N=369 n (%)
Total subject number	2
Not treated before study enrollment	2 (100)
Treated before study enrollment	0
Treated in one eye only	0
Treated in both eyes	0

- N = Number of patients in the Full Analysis Set.
- The date of study enrollment is defined as the date of signing informed consent.
- Patients who receive their first injection of voretigene neparvovec on the day of study enrollment are reported as 'Not treated before study enrollment'.
- Patients who receive the injection of voretigene neparvovec in the second eye on the day of study enrollment are reported as 'Treated in one eye only'.
- Country represents the country of study enrollment. Note, that the country of study enrollment can be different from the country of treatment.
- Center represents the study enrollment center. Note, that the study enrollment center can be different from the center of treatment.
- Percentages are computed using Total subject number for the country and center as the denominator.

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Table 1-3.1b (Page 36 of 62)
Treatment status at study enrollment by country (or subdivision) and center
Full Analysis Set

Country or subdivision, Center: Japan, 6002

Status	Voretigene Neparvovec N=369 n (%)
Total subject number	2
Not treated before study enrollment	2 (100)
Treated before study enrollment	0
Treated in one eye only	0
Treated in both eyes	0

- N = Number of patients in the Full Analysis Set.
- The date of study enrollment is defined as the date of signing informed consent.
- Patients who receive their first injection of voretigene neparvovec on the day of study enrollment are reported as 'Not treated before study enrollment'.
- Patients who receive the injection of voretigene neparvovec in the second eye on the day of study enrollment are reported as 'Treated in one eye only'.
- Country represents the country of study enrollment. Note, that the country of study enrollment can be different from the country of treatment.
- Center represents the study enrollment center. Note, that the study enrollment center can be different from the center of treatment.
- Percentages are computed using Total subject number for the country and center as the denominator.

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Table 3-1.1 (Page 1 of 2)
Ocular treatment-emergent adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec					
	Patients			Treated eyes		
Primary system organ class Preferred term	Total N=4 n(%) [E]	< 18 years N=1 n(%) [E]	>= 18 years N=3 n(%) [E]	Total M=7 m(%) [E]	< 18 years M=2 m(%) [E]	>= 18 years M=5 m(%) [E]
Number with at least one event	3 (75.0) [13]	1 (100) [3]	2 (66.7) [10]	6 (85.7) [13]	2 (100) [3]	4 (80.0) [10]
Eye disorders	3 (75.0) [12]	1 (100) [2]	2 (66.7) [10]	6 (85.7) [12]	2 (100) [2]	4 (80.0) [10]
Cataract subcapsular	2 (50.0) [4]	0	2 (66.7) [4]	4 (57.1) [4]	0	4 (80.0) [4]
Conjunctival hyperaemia	1 (25.0) [2]	0	1 (33.3) [2]	2 (28.6) [2]	0	2 (40.0) [2]
Eye pain	1 (25.0) [2]	0	1 (33.3) [2]	2 (28.6) [2]	0	2 (40.0) [2]
Retinal degeneration	1 (25.0) [2]	1 (100) [2]	0	2 (28.6) [2]	2 (100) [2]	0
Visual acuity reduced	1 (25.0) [2]	0	1 (33.3) [2]	2 (28.6) [2]	0	2 (40.0) [2]
Injury, poisoning and procedural complications	1 (25.0) [1]	1 (100) [1]	0	1 (14.3) [1]	1 (50.0) [1]	0

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- Each eye treated with voretigene neparvovec is included in the “Treated eyes” columns.
- SOCs are presented in alphabetical order; PTs are sorted within each SOC by descending frequency in the “Total” patients column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.1 (Page 2 of 2)
Ocular treatment-emergent adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec					
	Patients			Treated eyes		
Primary system organ class Preferred term	Total N=4 n(%) [E]	< 18 years N=1 n(%) [E]	>= 18 years N=3 n(%) [E]	Total M=7 m(%) [E]	< 18 years M=2 m(%) [E]	>= 18 years M=5 m(%) [E]
Accidental overdose	1 (25.0) [1]	1 (100) [1]	0	1 (14.3) [1]	1 (50.0) [1]	0

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- Each eye treated with voretigene neparvovec is included in the “Treated eyes” columns.
- SOCs are presented in alphabetical order; PTs are sorted within each SOC by descending frequency in the “Total” patients column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.2 (Page 1 of 1)
Ocular treatment-emergent serious adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent SAE for a patient is any SAE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent SAE for a treated eye is any SAE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of a SAE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- Each eye treated with voretigene neparvovec is included in the “Treated eyes” columns.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the 'Total' patients column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.3 (Page 1 of 2)
Ocular treatment-emergent adverse events of special interest (AESIs) by term of interest and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec					
	Patients			Treated eyes		
Term of interest Preferred term	Total N=4 n(%) [E]	< 18 years N=1 n(%) [E]	>= 18 years N=3 n(%) [E]	Total M=7 m(%) [E]	< 18 years M=2 m(%) [E]	>= 18 years M=5 m(%) [E]
Number with at least one event	3 (75.0) [8]	1 (100) [2]	2 (66.7) [6]	6 (85.7) [8]	2 (100) [2]	4 (80.0) [6]
CHORIORETINAL ATROPHY	1 (25.0) [2]	1 (100) [2]	0	2 (28.6) [2]	2 (100) [2]	0
Retinal degeneration	1 (25.0) [2]	1 (100) [2]	0	2 (28.6) [2]	2 (100) [2]	0
INTRAOCULAR INFLAMMATION AND OR INFECTION RELATED TO PROCEDURE	2 (50.0) [4]	0	2 (66.7) [4]	4 (57.1) [4]	0	4 (80.0) [4]
Cataract subcapsular	2 (50.0) [4]	0	2 (66.7) [4]	4 (57.1) [4]	0	4 (80.0) [4]

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE term of interest (AESI) or preferred term (PT) is counted only once for each AESI, PT in column n/m. All events are counted in column E.
- Each eye treated with voretigene neparvovec is included in the “Treated eyes” columns.
- AESIs are presented in alphabetical order; PTs are sorted within each AESI by descending frequency in the 'Total' patients column.
- AESIs are collected through a standardized safety questionnaire.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.3 (Page 2 of 2)
Ocular treatment-emergent adverse events of special interest (AESIs) by term of interest and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec					
	Patients			Treated eyes		
Term of interest Preferred term	Total N=4 n(%) [E]	< 18 years N=1 n(%) [E]	>= 18 years N=3 n(%) [E]	Total M=7 m(%) [E]	< 18 years M=2 m(%) [E]	>= 18 years M=5 m(%) [E]
LOSS OF FOVEAL FUNCTION	1 (25.0) [2]	0	1 (33.3) [2]	2 (28.6) [2]	0	2 (40.0) [2]
Visual acuity reduced	1 (25.0) [2]	0	1 (33.3) [2]	2 (28.6) [2]	0	2 (40.0) [2]

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE term of interest (AESI) or preferred term (PT) is counted only once for each AESI, PT in column n/m. All events are counted in column E.
- Each eye treated with voretigene neparvovec is included in the “Treated eyes” columns.
- AESIs are presented in alphabetical order; PTs are sorted within each AESI by descending frequency in the 'Total' patients column.
- AESIs are collected through a standardized safety questionnaire.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.4 (Page 1 of 1)
Ocular treatment-emergent adverse events suspected to be related to voretigene neparvovec by primary system organ class and preferred term
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the patients column.
- Each eye treated with voretigene neparvovec is included in the analysis of Treated eyes.
- Causality reflects the investigator's assessment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.5 (Page 1 of 1)
Ocular treatment-emergent adverse events suspected to be related to the subretinal administration procedure by primary system organ class and preferred term
Full Analysis Set_JAPAN

	Voretigene Neparvovec	
Primary system organ class **Preferred term**	**Patients** **N=4** **n (%) [E]**	**Treated eyes** **M=7** **m (%) [E]**
Number with at least one event	3 (75.0) [12]	6 (85.7) [12]
Eye disorders	3 (75.0) [12]	6 (85.7) [12]
Cataract subcapsular	2 (50.0) [4]	4 (57.1) [4]
Conjunctival hyperaemia	1 (25.0) [2]	2 (28.6) [2]
Eye pain	1 (25.0) [2]	2 (28.6) [2]
Retinal degeneration	1 (25.0) [2]	2 (28.6) [2]
Visual acuity reduced	1 (25.0) [2]	2 (28.6) [2]

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the patients column.
- Each eye treated with voretigene neparvovec is included in the analysis of Treated eyes.
- Causality reflects the investigator’s assessment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-1.6 (Page 1 of 1)
Ocular treatment-emergent adverse events suspected to be related to perioperative corticosteroids by primary system organ class and preferred term
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye. A treatment-emergent AE for a treated eye is any AE that starts on or after the date of the injection of voretigene neparvovec in the respective eye.
- E = Number of events. A patient/treated eye with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n/m. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the patients column.
- Each eye treated with voretigene neparvovec is included in the analysis of Treated eyes.
- Causality reflects the investigator's assessment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

CLTW888A12401(Japan) - Interim Analysis 6 - data cut-off 31Mar2025

Table 3-2.1 (Page 1 of 2)
Non-ocular treatment-emergent adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec		
	Patients		
Primary system organ class **Preferred term**	**Total** **N=4** **n(%) [E]**	**< 18 years** **N=1** **n(%) [E]**	**>= 18 years** **N=3** **n(%) [E]**
Number of patients with at least one event	3 (75.0) [9]	1 (100) [1]	2 (66.7) [8]
Gastrointestinal disorders	3 (75.0) [3]	1 (100) [1]	2 (66.7) [2]
Constipation	2 (50.0) [2]	0	2 (66.7) [2]
Vomiting	1 (25.0) [1]	1 (100) [1]	0
General disorders and administration site conditions	1 (25.0) [1]	0	1 (33.3) [1]
Oedema peripheral	1 (25.0) [1]	0	1 (33.3) [1]
Musculoskeletal and connective tissue disorders	1 (25.0) [1]	0	1 (33.3) [1]
Back pain	1 (25.0) [1]	0	1 (33.3) [1]

- A treatment-emergent AE is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the “Total” column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.1 (Page 2 of 2)
Non-ocular treatment-emergent adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

	Voretigene Neparvovec		
	Patients		
Primary system organ class Preferred term	**Total N=4 n(%) [E]**	**< 18 years N=1 n(%) [E]**	**>= 18 years N=3 n(%) [E]**
Psychiatric disorders	2 (50.0) [2]	0	2 (66.7) [2]
Insomnia	2 (50.0) [2]	0	2 (66.7) [2]
Reproductive system and breast disorders	1 (25.0) [1]	0	1 (33.3) [1]
Dysmenorrhoea	1 (25.0) [1]	0	1 (33.3) [1]
Skin and subcutaneous tissue disorders	1 (25.0) [1]	0	1 (33.3) [1]
Dry skin	1 (25.0) [1]	0	1 (33.3) [1]

- A treatment-emergent AE is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the “Total” column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.2 (Page 1 of 1)
Non-ocular treatment-emergent serious adverse events by primary system organ class and preferred term, overall and by age
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent SAE is any SAE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of a SAE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency in the 'Total' column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.3 (Page 1 of 1)
Non-ocular treatment-emergent adverse events of special interest (AESIs) by term of interest and preferred term, overall and by age
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE term of interest (AESI) or preferred term (PT) is counted only once for each AESI, PT in column n. All events are counted in column E.
- AESIs are presented in alphabetical order; PTs are sorted within each AESI by descending frequency in the “Total” column.
- Age is defined as age at time of study enrollment.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.4 (Page 1 of 1)
Non-ocular treatment-emergent adverse events suspected to be related to voretigene neparvovec by primary system organ class and preferred term
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- Causality reflects the investigator's assessment.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.5 (Page 1 of 1)
Non-ocular treatment-emergent adverse events suspected to be related to the subretinal administration procedure by primary system organ class and preferred term
Full Analysis Set_JAPAN

There were no observations which met the report criteria

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- Causality reflects the investigator's assessment.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Table 3-2.6 (Page 1 of 1)
Non-ocular treatment-emergent adverse events suspected to be related to perioperative corticosteroids by primary system organ class and preferred term
Full Analysis Set_JAPAN

Primary system organ class Preferred term	Voretigene Neparvovec Patients N=4 n (%) [E]
Number of patients with at least one event	1 (25.0) [2]
General disorders and administration site conditions	1 (25.0) [1]
Oedema peripheral	1 (25.0) [1]
Skin and subcutaneous tissue disorders	1 (25.0) [1]
Dry skin	1 (25.0) [1]

- A treatment-emergent AE for a patient is any AE that starts on or after the date of the injection of voretigene neparvovec in the first eye.
- E = Number of events. A patient with multiple occurrences of an AE for a system organ class (SOC) or preferred term (PT) is counted only once for each SOC, PT in column n. All events are counted in column E.
- Causality reflects the investigator's assessment.
- SOCs are presented in alphabetical order; PTs are sorted within SOC by descending frequency.
- MedDRA Version 28.0 has been used for the reporting of adverse events.

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Listing 1-2.1 (Page 14 of 17)
Demographics
All enrolled patients

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Race, further details	Ethnicity	Number of days between date of study enrollment and date of study treatment in the first eye
[redacted]				
JPN/[redacted]	[redacted]/F/AS	JAPANESE	NOT HISPANIC OR LATINO	32
JPN/[redacted]	3[redacted]/F/AS	JAPANESE	NOT HISPANIC OR LATINO	87
JPN/[redacted]	3[redacted]/F/AS	JAPANESE	NOT HISPANIC OR LATINO	1
JPN/[redacted]	3[redacted]/F/AS	JAPANESE	NOT HISPANIC OR LATINO	1
[redacted]				

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- Number of days between date of study enrollment and date of study treatment in the first eye = study treatment date in the first eye – study enrollment date.

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Listing 1-2.3 (Page 15 of 18)
Clinical diagnosis
All enrolled patients

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/Sex/Race	Clinical diagnosis
[redacted]		
JPN/[redacted]	[redacted]/F/AS	
JPN/[redacted]	3[redacted]/F/AS	
JPN/[redacted]	3[redacted]/F/AS	
JPN/[redacted]	3[redacted]/F/AS	
[redacted]		

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.

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Listing 1-2.4 (Page 140 of 166)
Genetic diagnosis
All enrolled patients

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Test	Date of test	Genetic diagnosis	Segregation analysis performed?	Gene mutation number	Gene mutation	Gene mutation classification	Is Gene mutation 1 the same as Gene mutation 2?	Other IRD related mutations present?
[redacted]										
JPN/[redacted]	[redacted]/F/AS	GENE PANEL								
JPN/[redacted]	3[redacted]/F/AS	GENE PANEL								
JPN/[redacted]	3[redacted]/F/AS	GENE PANEL								
JPN/[redacted]	3[redacted]/F/AS	GENE PANEL								

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- IRD=Inherited retinal dystrophy.

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Listing 1-3.1 (Page 59 of 69)
Treatment administration
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Eye treated prior to study enrollment?	Date of surgery	Surgery performed at this site	Surgical center	Lot number	Total number of injection retinotomy sites	Total volume injected (ul)	Number of blebs raised
[redacted]										
JPN/[redacted]	[redacted]/F/AS	FTE/OD	No	[redacted]				1	300	1
		STE/OS	No					1	450	1
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	No					1	300	1

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple,UK=Unknown.
- FTE=First treated eye, STE=Second treated eye, OD=Right eye, OS=Left eye.
- Surgery performed at this site = Yes indicates the site where the data is being collected is the same as the treatment site where the surgery was performed.If surgery performed at this site = No then the center where surgery was performed is specified in the surgical center column.

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Listing 1-3.1 (Page 60 of 69)
Treatment administration
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Eye treated prior to study enrollment?	Date of surgery	Surgery performed at this site	Surgical center	Lot number	Total number of injection retinotomy sites	Total volume injected (ul)	Number of blebs raised
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	No	[redacted]				1	300	1
		STE/OD	No					1	300	1
JPN/[redacted]	3[redacted]/F/AS	FTE/OD	No					1	300	1
		STE/OS	No					1	300	1
[redacted]										

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple,UK=Unknown.
- FTE=First treated eye, STE=Second treated eye, OD=Right eye, OS=Left eye.
- Surgery performed at this site = Yes indicates the site where the data is being collected is the same as the treatment site where the surgery was performed.If surgery performed at this site = No then the center where surgery was performed is specified in the surgical center column.

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Listing 1-3.2 (Page 84 of 92)
Surgical details
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Eye treated prior to study enrollment?	Date of surgery	Surgery performed at this site	Surgical center	Intra-operative OCT used?	Injection technique or materials different from that described in manual
JPN/[redacted]	[redacted]/F/AS	FTE/OD	No	[redacted]	Yes		Yes	No
		STE/OS	No		Yes		Yes	No
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	No		Yes		Yes	No
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	No		Yes		No	No
		STE/OD	No		Yes		No	No
JPN/[redacted]	3[redacted]/F/AS	FTE/OD	No		Yes		No	No
		STE/OS	No		Yes		No	No
[redacted]								

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- FTE=First treated eye, STE=Second treated eye, OD=Right eye, OS=Left eye.
- Surgery performed at this site = Yes indicates the site where the data is being collected is the same as the treatment site where the surgery was performed. If surgery performed at this site = No then the center where surgery was performed is specified in the surgical center column.

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Listing 1-3.3 (Page 173 of 198)
Perioperative steroid use
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Name of medication (Reported Term/ Preferred Term)	Dose	Dose units	Frequency	Route	Start date/ Day	End date/ Day
JPN/[redacted]	[redacted]/F/AS	FTE/OD	PREDONISOLONE/ PREDNISOLONE	25	mg	QD	ORAL	[redacted]	
			PREDONISOLONE/ PREDNISOLONE	12.5	mg	QD	ORAL		
			PREDONISOLONE/ PREDNISOLONE	12.5	mg	QOD	ORAL		
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	PREDNISOLONE/ PREDNISOLONE	20	mg	BID	ORAL		
			PREDNISOLONE/ PREDNISOLONE	20	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	20	mg	QOD	ORAL		
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	PREDNISOLONE/ PREDNISOLONE	40	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	40	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	30	mg	QD	ORAL		

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- OD=Right eye, OS=Left eye, FTE=First treated eye, STE=Second treated eye, NT=Not treated.
- Day is relative to the date of the injection of voretigene neparvovec in that eye. Missing dates are based on imputed dates.
- # Imputed date.
- Medications marked as ongoing: end date=ongoing, end day=missing. Medications not marked as ongoing and with no end date: end date=missing, end day=missing.

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Listing 1-3.3 (Page 174 of 198)
Perioperative steroid use
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Name of medication (Reported Term/ Preferred Term)	Dose	Dose units	Frequency	Route	Start date/ Day	End date/ Day
JPN/[redacted]	3[redacted]/F/AS	FTE/OS	PREDNISOLONE/ PREDNISOLONE	25	mg	QD	ORAL	[redacted]	
			PREDNISOLONE/ PREDNISOLONE	20	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	15	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	10	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	5	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	5	mg	QOD	ORAL		
JPN/[redacted]	3[redacted]/F/AS	FTE/OD	PREDNISOLONE/ PREDNISOLONE	40	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	40	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	30	mg	QD	ORAL		

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- OD=Right eye, OS=Left eye, FTE=First treated eye, STE=Second treated eye, NT=Not treated.
- Day is relative to the date of the injection of voretigene neparvovec in that eye. Missing dates are based on imputed dates.
- # Imputed date.
- Medications marked as ongoing: end date=ongoing, end day=missing. Medications not marked as ongoing and with no end date: end date=missing, end day=missing.

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Listing 1-3.3 (Page 175 of 198)
Perioperative steroid use
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Treated eye/ Laterality	Name of medication (Reported Term/ Preferred Term)	Dose	Dose units	Frequency	Route	Start date/ Day	End date/ Day
JPN/[redacted]	3[redacted]/F/AS	FTE/OD	PREDNISOLONE/ PREDNISOLONE	25	mg	QD	ORAL	[redacted]	
			PREDNISOLONE/ PREDNISOLONE	20	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	15	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	10	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	5	mg	QD	ORAL		
			PREDNISOLONE/ PREDNISOLONE	5	mg	QOD	ORAL		
[redacted]									

- Age in years and defined as age at time of study enrollment; M=Male, F=Female, WH=White, BLAA=Black or African American, AS=Asian, AIAN=American Indian or Alaska native, NHOPI=Native Hawaiian or Other Pacific Islander, ML=Multiple, UK=Unknown.
- OD=Right eye, OS=Left eye, FTE=First treated eye, STE=Second treated eye, NT=Not treated.
- Day is relative to the date of the injection of voretigene neparvovec in that eye. Missing dates are based on imputed dates.
- # Imputed date.
- Medications marked as ongoing: end date=ongoing, end day=missing. Medications not marked as ongoing and with no end date: end date=missing, end day=missing.

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Listing 3-1.1 (Page 228 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
[redacted]														
JPN/ [redacted]	[redacted]/ F/ AS	NO	N	N	VOMITTING/ Vomiting/ Gastrointestinal disorders /669422215	[redacted]		3	MILD	N	N	N	2	2
		O/FTE/OD	N	Y	CHORIORETINAL ATROPHY/ Retinal degeneration/ Eye disorders /761663829				MILD	N	Y	N	6	6

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Listing 3-1.1 (Page 229 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
JPN/ [redacted]	[redacted]/ F/ AS	O/STE/OS	N	N	ACCIDENTAL OVER DOSE DUE TO THE TECHNICAL DIFF ICULTY, WITHOUT CLINICAL SYMPT OMS./ Accidenta l overdose/ Inj ury, poisoning and procedural complications /736103556	[redacted]	[redacted]	1	MILD	N	N	N	6	6
			N	Y	CHORIORETINAL A TROPHY/ Retinal degeneration/ Eye disorders /761663829				MILD	N	Y	N	6	6
JPN/ [redacted]	3[redacted]/ F/ AS	NO	N	N	INSOMNIA/ Insom nia/ Psychiatri c disorders /719429182			1	MILD	N	N	N	2	6

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Listing 3-1.1 (Page 230 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	NO	N	N	LUMBAGO/ Back pain/ Musculoskeletal and connective tissue disorders /671206483	[redacted]		2	MILD	N	N	N	2	6
			N	N	MENSTRUAL CRAMPS/ Dysmenorrhoea/ Reproductive system and breast disorders /718687578			3	MILD	N	N	N	2	6
			N	N	CONSTIPATION/ Constipation/ Gastrointestinal disorders /718687752			8	MILD	N	N	N	2	6
			N	N	DRY SKIN/ Dry skin/ Skin and subcutaneous tissue disorders /718687791			24	MILD	N	N	Y	2	6

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Listing 3-1.1 (Page 231 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	NO	N	N	LOWER LIMBS EDEMA/ Oedema peripheral/ General disorders and administration site conditions /718687823	[redacted]		24	MILD	N	N	Y	2	6
		O/FTE/OS	N	N	OCULAR PAIN/ Eye pain/ Eye disorders /718687508			7	MILD	N	Y	N	2	6
			N	Y	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders /718687531			67	MILD	N	Y	N	2	6
		O/STE/OD	N	N	OCULAR PAIN/ Eye pain/ Eye disorders /718687528			2	MILD	N	Y	N	2	6

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Listing 3-1.1 (Page 232 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdivision/ Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	AESI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/STE/OD	N	Y	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders /718687539	[redacted]		5	MILD	N	Y	N	2	6
JPN/ [redacted]	3[redacted]/ F/ AS	NO	N	N	CONSTIPATION/ Constipation/ Gastrointestinal disorders /733154076			4	MILD	N	N	N	2	6
			N	N	INSOMNIA/ Insomnia/ Psychiatric disorders /733154454			70	MILD	N	N	N	2	6
		O/FTE/OD	N	N	INJECTION OF CONJUNCTIVA/ Conjunctival hyperaemia/ Eye disorders /671206502			7	MILD	N	Y	N	2	6

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Listing 3-1.1 (Page 233 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/FTE/OD	N	Y	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders /733138351	[redacted]	[redacted]	4	MILD	N	Y	N	2	6
			N	Y	VISUAL ACUITY LOSS/ Visual acuity reduced/ Eye disorders /748041410				SEV	N	Y	N	1	6
		O/STE/OS	N	N	INJECTION OF CONJUNCTIVA/ Conjunctival hyperaemia/ Eye disorders /733147045			19	MILD	N	Y	N	2	6

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Listing 3-1.1 (Page 234 of 276)
Adverse events
Full Analysis Set

Treatment: Voretigene Neparvovec

Country or Subdi -vision/ Subject ID	Age/ Sex/ Race	Cate- gory/ Treated eye/ Later- ality	SAE	AE- SI	Adverse Event (Reported Term/ Preferred Term/ System Organ Class) /AE number	Start date/Day	End date/Day	Dura- tion (days)	Sever- ity	Related to VN	Related to SAP	Related to PC	Out- come	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/STE/OS	N	Y	TRANSIENT SUBCA PSULAR OPACIFIC ATION SECONDARY TO VITRECTOMY/ Cataract subca psular/ Eye dis orders /733153190	[redacted]	[redacted]	4	MILD	N	Y	N	2	6
			N	Y	VISUAL ACUITY L OSS/ Visual acu ity reduced/ Ey e disorders /748041529				SEV	N	Y	N	1	6

[redacted]

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Listing 3-3.1 (Page 91 of 215)
Adverse events of special interest (AESI)
Full Analysis Set

Treatment: Voretigene Neparvovec
Adverse of special interest: CHORIORETINAL ATROPHY

Country or Subdivision /Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	Adverse Event (Reported Term/ Preferred Term/ System Organ Class)	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
JPN/ [redacted]	[redacted]/ F/ AS	O/FTE/OD	N	CHORIORETINAL ATROPHY/ Retinal degeneration/ Eye disorders	[redacted]			MILD	N	Y	N	6	6
		O/STE/OS	N	CHORIORETINAL ATROPHY/ Retinal degeneration/ Eye disorders				MILD	N	Y	N	6	6

[redacted]

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Listing 3-3.1 (Page 184 of 215)
Adverse events of special interest (AESI)
Full Analysis Set

Treatment: Voretigene Neparvovec
Adverse of special interest: INTRAOCULAR INFLAMMATION AND OR INFECTION RELATED TO PROCEDURE

Country or Subdivision /Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	Adverse Event (Reported Term/ Preferred Term/ System Organ Class)	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
[redacted]													
JPN/ [redacted]	3[redacted]/ F/ AS	O/FTE/OS	N	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders	[redacted]		67	MILD	N	Y	N	2	6

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Listing 3-3.1 (Page 185 of 215)
Adverse events of special interest (AESI)
Full Analysis Set

Treatment: Voretigene Neparvovec
Adverse of special interest: INTRAOCULAR INFLAMMATION AND OR INFECTION RELATED TO PROCEDURE

Country or Subdivision /Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	Adverse Event (Reported Term/ Preferred Term/ System Organ Class)	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/STE/OD	N	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders	[redacted]		5	MILD	N	Y	N	2	6
JPN/ [redacted]	3[redacted]/ F/ AS	O/FTE/OD	N	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders	[redacted]		4	MILD	N	Y	N	2	6

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Listing 3-3.1 (Page 186 of 215)
Adverse events of special interest (AESI)
Full Analysis Set

Treatment: Voretigene Neparvovec
Adverse of special interest: INTRAOCULAR INFLAMMATION AND OR INFECTION RELATED TO PROCEDURE

Country or Subdivision /Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	Adverse Event (Reported Term/ Preferred Term/ System Organ Class)	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/STE/OS	N	TRANSIENT SUBCAPSULAR OPACIFICATION SECONDARY TO VITRECTOMY/ Cataract subcapsular/ Eye disorders	[redacted]		4	MILD	N	Y	N	2	6

[redacted]

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Listing 3-3.1 (Page 196 of 215)
Adverse events of special interest (AESI)
Full Analysis Set

Treatment: Voretigene Neparvovec
Adverse of special interest: LOSS OF FOVEAL FUNCTION

Country or Subdivision /Subject ID	Age/ Sex/ Race	Category/ Treated eye/ Laterality	SAE	Adverse Event (Reported Term/ Preferred Term/ System Organ Class)	Start date/Day	End date/Day	Duration (days)	Severity	Related to VN	Related to SAP	Related to PC	Outcome	Action taken with VN
JPN/ [redacted]	3[redacted]/ F/ AS	O/FTE/OD	N	VISUAL ACUITY LOSS/ Visual acuity reduced/ Eye disorders	[redacted]			SEV	N	Y	N	1	6
		O/STE/OS	N	VISUAL ACUITY LOSS/ Visual acuity reduced/ Eye disorders				SEV	N	Y	N	1	6

[redacted]