Clinical trial results:
Phase 3b Study for Management of Ocular Side Effects in Subjects with EGFR-amplified Glioblastoma Receiving Depatuxizumab Mafodotin (ABT-414)

Summary

EudraCT number	2017-003171-64
Trial protocol	GB NL DE
Global end of trial date	03 March 2020

Results information

Result version number	v2 (current)
This version publication date	07 May 2021
First version publication date	04 March 2021
Version creation reason	• Correction of full data set Edited time frame for one outcome measure and adjusted the number of participants per group in another outcome measure.

Trial information

Trial identification

Sponsor protocol code	M16-534

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03419403
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	AbbVie, Global Medical Services, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	AbbVie, Global Medical Services, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 March 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this Phase 3b open-label, randomized, exploratory study was to evaluate the effect of several ophthalmologic prophylactic treatment strategies for the management of ocular side effects (OSEs) in subjects with epidermal growth factor receptor (EGFR)-amplified glioblastoma (GBM) treated with depatuxizumab mafodotin (ABT-414). All subjects received ABT-414 during both phases of the treatment period plus 1 of 3 prophylactic ophthalmologic treatments (standard steroids; standard steroids with vasoconstrictors and cold compress; and enhanced steroids with vasoconstrictors and cold compress. The study had a screening period of up to 7 weeks after surgery, a 6-week concomitant Chemoradiation Phase (radiation plus temozolomide [RT/TMZ]), an Adjuvant Phase (TMZ) beginning approximately 4 weeks after completion of chemoradiation, and a Follow-Up Phase. The study was terminated because clinical development of ABT-414 in glioblastoma was stopped due to lack of survival benefit.

Protection of trial subjects:

Subjects must have voluntarily signed and dated an informed consent form, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any screening or study-specific procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 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	Australia: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	40
EEA total number of subjects	1

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	33
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All randomized subjects; two subjects were randomized to the study but received no doses of depatuxizumab mafodotin or prophylactic eye treatments.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard Steroids

Arm description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days

Arm type	Experimental
Investigational medicinal product name	Steroid eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Intraocular use

Dosage and administration details:

1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days;

Investigational medicinal product name	Depatuxizumab mafodotin
Investigational medicinal product code	
Other name	ABT-414
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, participants were to receive depatuxizumab mafodotin at 2.0 mg/kg IV infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). During the Adjuvant Therapy Phase, participants were to receive depatuxizumab mafodotin at 1.25 mg/kg on Day 1 (± 2 days) and Day 15 (± 2 days) of each 28-day cycle as a 30 – 40 minute infusion for 12 cycles.

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Temozolomide was to be administered according to the local standard of care. Duration of treatment was to be 6 – 12 cycles in the adjuvant phase and at the discretion of the investigator as supported by local standard of care.

Arm title	Standard Steroids + Vasoconstrictor + Cold Compress

Arm description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin

infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. The cold compress should be applied in increments no longer than 30 min (could be shorter if the participant was uncomfortable).

Arm type	Experimental
Investigational medicinal product name	Steroid eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Intraocular use

Dosage and administration details:

1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days;

Investigational medicinal product name	Vasoconstrictor eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Intraocular use

Dosage and administration details:

1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion;

Investigational medicinal product name	Depatuxizumab mafodotin
Investigational medicinal product code	
Other name	ABT-414
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, participants were to receive depatuxizumab mafodotin at 2.0 mg/kg IV infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). During the Adjuvant Therapy Phase, participants were to receive depatuxizumab mafodotin at 1.25 mg/kg on Day 1 (± 2 days) and Day 15 (± 2 days) of each 28-day cycle as a 30 – 40 minute infusion for 12 cycles.

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Temozolomide was to be administered according to the local standard of care. Duration of treatment was to be 6 – 12 cycles in the adjuvant phase and at the discretion of the investigator as supported by local standard of care.

Arm title	Enhanced Steroids + Vasoconstrictor + Cold Compress

Arm description:

Enhanced steroid eye drops: 1 drop each eye, 6 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Ophthalmic Steroid Ointment; applied to each eye once daily before sleep, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. Cold compress was to be applied

in increments no longer than 30 min (could be shorter if the patient is uncomfortable).

Arm type	Experimental
Investigational medicinal product name	Steroid eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Intraocular use

Dosage and administration details:

1 drop each eye, 6 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days;

Investigational medicinal product name	Vasoconstrictor eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Intraocular use

Dosage and administration details:

1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion;

Investigational medicinal product name	Ophthalmic steroid ointment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Ocular use

Dosage and administration details:

Applied to each eye once daily before sleep, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days;

Investigational medicinal product name	Depatuxizumab mafodotin
Investigational medicinal product code	
Other name	ABT-414
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

During the Chemoradiation Phase, participants were to receive depatuxizumab mafodotin at 2.0 mg/kg IV infusion over 30 – 40 minutes once every 2 weeks (Day 1 of Weeks 1, 3, and 5 of the 6-week regimen). During the Adjuvant Therapy Phase, participants were to receive depatuxizumab mafodotin at 1.25 mg/kg on Day 1 (± 2 days) and Day 15 (± 2 days) of each 28-day cycle as a 30 – 40 minute infusion for 12 cycles.

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Temozolomide was to be administered according to the local standard of care. Duration of treatment was to be 6 – 12 cycles in the adjuvant phase and at the discretion of the investigator as supported by local standard of care.

Number of subjects in period 1[1]	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress
Started	14	12	12
Completed	2	3	0
Not completed	12	9	12
Left study due to COVID-19 restrictions	1	1	-
Progressive disease (per protocol)	-	2	2
Other, not specified	6	4	5
Withdrawal by subject	5	2	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Two subjects were randomized to the study but received no doses of depatuxizumab mafodotin or prophylactic eye treatments and are not included in any treatment group.

Baseline characteristics

Reporting groups	
Reporting group title	Standard Steroids
Reporting group description:	
Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days	
Reporting group title	Standard Steroids + Vasoconstrictor + Cold Compress
Reporting group description:	
Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. The cold compress should be applied in increments no longer than 30 min (could be shorter if the participant was uncomfortable).	
Reporting group title	Enhanced Steroids + Vasoconstrictor + Cold Compress
Reporting group description:	
Enhanced steroid eye drops: 1 drop each eye, 6 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Ophthalmic Steroid Ointment; applied to each eye once daily before sleep, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. Cold compress was to be applied in increments no longer than 30 min (could be shorter if the patient is uncomfortable).	

Reporting group values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress
Number of subjects	14	12	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47.6	55.2	57.3
standard deviation	± 9.85	± 10.53	± 8.69
Gender categorical Units: Subjects			
Female	3	4	1
Male	11	8	11

Reporting group values	Total		
Number of subjects	38		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	8		
Male	30		

End points

End points reporting groups

Reporting group title	Standard Steroids

Reporting group description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days

Reporting group title	Standard Steroids + Vasoconstrictor + Cold Compress

Reporting group description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. The cold compress should be applied in increments no longer than 30 min (could be shorter if the participant was uncomfortable).

Reporting group title	Enhanced Steroids + Vasoconstrictor + Cold Compress

Reporting group description:

Enhanced steroid eye drops: 1 drop each eye, 6 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Ophthalmic Steroid Ointment; applied to each eye once daily before sleep, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. Cold compress was to be applied in increments no longer than 30 min (could be shorter if the patient is uncomfortable).

Primary: Percentage of Participants Who Required a Change in Ocular Side Effect (OSE) Management

End point title	Percentage of Participants Who Required a Change in Ocular Side Effect (OSE) Management[1]

End point description:

Inadequate control of ocular side effects (OSE) was defined as either a ≥ 3-line decline from baseline (≥ +0.3 on LogMAR scale) in visual acuity (with baseline correction determined at the screening ophthalmology visit)) or ≥ Grade 3 OSE severity on the Corneal Epithelial Adverse Event (CEAE) scale.

End point type	Primary

End point timeframe:

Within 8 weeks after the initial dose of depatuxizumab mafodotin

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: Treatment differences were not evaluated due to small sample size.

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[2]	12[3]	12[4]	
Units: percentage of participants				
number (not applicable)				

Bilateral vision	50.0	27.3	41.7	
Vision in worst eye	64.3	72.7	50.0	

Notes:

[2] - Subjects rcvd ≥1 ABT-414 dose + ≥1 post-baseline value w/in 8 wks after 1st dose for LogMAR or CEAE

[3] - Subjects rcvd ≥1 ABT-414 dose + ≥1 post-baseline value w/in 8 wks after 1st dose for LogMAR or CEAE

[4] - Subjects rcvd ≥1 ABT-414 dose + ≥1 post-baseline value w/in 8 wks after 1st dose for LogMAR or CEAE

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Dose of Depatuxizumab Mafodotin Received During Chemoradiation and During Adjuvant Treatment

End point title	Cumulative Dose of Depatuxizumab Mafodotin Received During Chemoradiation and During Adjuvant Treatment

End point description:

The cumulative dose of depatuxizumab mafodotin administered was tabulated.

End point type	Secondary

End point timeframe:

Up to 9 months

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[5]	12[6]	12[7]	
Units: mg/kg				
arithmetic mean (standard deviation)	8.5 (± 5.86)	10.5 (± 7.35)	7.0 (± 3.67)	

Notes:

[5] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[6] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[7] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Logarithm of the Minimum Angle of Resolution (LogMAR) Scale After Bandage Contact Lens (BCL) Intervention

End point title	Change From Baseline In Logarithm of the Minimum Angle of Resolution (LogMAR) Scale After Bandage Contact Lens (BCL) Intervention

End point description:

The change on the LogMAR Scale from last assessment prior to BCL intervention to 2 weeks after BCL intervention was calculated. The LogMAR scale measures visual acuity on a continuous scale, with a LogMAR value of 0 equivalent to 20/20 visual acuity. Normal vision is considered to be from -0.2 - 0.1; higher values indicate visual impairment. In the table below, a value of 999 indicates not calculable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to approximately 18 weeks after initial dose of depatuxizumab mafodotin

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4[8]	2[9]	3[10]	
Units: units on a scale				
arithmetic mean (standard deviation)				
W/in 8 wks of 1st dose:Bilateral vision (n= 4,2,3)	0.325 (± 0.1248)	0.13 (± 0.099)	0.54 (± 0.1442)	
W/in 8 wks of 1st dose:Worst eye (n= 4,2,3)	0.435 (± 0.0574)	0.52 (± 0.3111)	0.867 (± 0.2914)	
W/in 8 wks of 1st adj dose:Bil vision (n= 1,2,0)	-0.1 (± 999)	0.41 (± 0.2404)	999 (± 999)	
W/in 8 wks of 1st adj dose:Worst eye (n= 1,2,0)	-0.1 (± 999)	0.33 (± 0.0141)	999 (± 999)	

Notes:

[8] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[9] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[10] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Ocular Side Effect (OSE) Symptom Resolution After Drug Discontinuation (Reversibility)

End point title	Time to Ocular Side Effect (OSE) Symptom Resolution After Drug Discontinuation (Reversibility)

End point description:

The time from discontinuation of depatuxizumab mafodotin to OSE symptom resolution (reversibility) was to be recorded.

End point type	Secondary

End point timeframe:

From the first dose of study drug until 49 days after last depatuxizumab mafodotin administration, up to 47 weeks

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: weeks				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[11] - Data were not collected for this outcome (due to early termination of the study)

[12] - Data were not collected for this outcome (due to early termination of the study)

[13] - Data were not collected for this outcome (due to early termination of the study)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Bandage Contact Lens (BCL) Intervention

End point title	Time to Bandage Contact Lens (BCL) Intervention

End point description:

The time to initiation of bandage contact lenses for those participants who required intervention due to inadequate control of ocular side effects (OSE) was calculated. In the table below, a value of 999 indicates not calculable due to insufficient number of participants with events

End point type	Secondary

End point timeframe:

Up to 9 months after the first dose of depatuxizumab mafodotin

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[14]	12[15]	12[16]	
Units: months				
median (confidence interval 95%)	999 (1.1 to 999)	3.6 (1.1 to 999)	2.1 (1.1 to 999)	

Notes:

[14] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[15] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[16] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants That Recovered to <3-line Decline From Baseline (≤ +0.3 LogMAR) in Visual Acuity After Bandage Contact Lens (BCL) Intervention

End point title	Percentage of Participants That Recovered to <3-line Decline From Baseline (≤ +0.3 LogMAR) in Visual Acuity After Bandage Contact Lens (BCL) Intervention

End point description:

Recovery was defined as return to <3-line decline from baseline (≤ +0.3 LogMAR) in visual acuity after BCL intervention.

End point type	Secondary

End point timeframe:

From the last assessment prior to BCL intervention to the end of BCL intervention

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[17]	0[18]	0[19]	
Units: percentage of participants				
number (not applicable)				

Notes:

[17] - Data were not collected for this outcome (due to early termination of the study)

[18] - Data were not collected for this outcome (due to early termination of the study)

[19] - Data were not collected for this outcome (due to early termination of the study)

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-Emergent Corneal Epithelial Adverse Event (CEAE) Grade at Each Visit

End point title	Treatment-Emergent Corneal Epithelial Adverse Event (CEAE) Grade at Each Visit

End point description:

The corneal epithelial adverse event (CEAE) rating scale is designed to record symptoms associated with corneal epitheliopathy caused by antibody-drug conjugates and to grade the severity of findings. The overall CEAE grade is measured on a scale of 0 to 5, with higher values being more severe, reflecting the impact of corneal abnormalities on visual activities of daily living (ADLs). Additional detailed information is collected for specific domains that are commonly affected, with the following ranges (each in order of increasing severity): ocular discomfort (0 - 4), photophobia (0 - 3), and reading (1 - 3).

End point type	Secondary

End point timeframe:

Up to 47 weeks

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[20]	12[21]	12[22]	
Units: participants				
Week 1: Grade 0	10	8	5	
Week 1: Grade 1	1	3	1	
Week 3: Grade 0	4	5	7	
Week 3: Grade 1	10	6	3	
Week 3: Grade 2	0	0	1	
Week 5: Grade 0	1	0	2	
Week 5: Grade 1	7	5	6	
Week 5: Grade 2	1	3	2	

Week 5: Grade 3	4	2	2	
Week 7: Grade 0	0	0	2	
Week 7: Grade 1	3	4	0	
Week 7: Grade 2	4	6	5	
Week 7: Grade 3	2	0	2	
Week 9: Grade 0	1	0	1	
Week 9: Grade 1	1	2	0	
Week 9: Grade 2	3	5	4	
Week 9: Grade 3	2	0	1	
Week 11: Grade 0	0	0	1	
Week 11: Grade 1	2	1	0	
Week 11: Grade 2	2	0	3	
Week 11: Grade 3	1	0	1	
Week 11: Grade 4	1	0	0	
Week 13: Grade 1	1	0	1	
Adj Week 1: Grade 0	0	1	0	
Adj Week 1: Grade 1	1	3	2	
Adj Week 1: Grade 2	3	2	2	
Adj Week 1: Grade 3	1	0	0	
Adj Week 5: Grade 0	0	2	2	
Adj Week 5: Grade 1	1	3	0	
Adj Week 5: Grade 2	4	0	1	
Adj Week 5: Grade 3	1	1	0	
Adj Week 9: Grade 0	0	1	0	
Adj Week 9: Grade 1	0	2	1	
Adj Week 9: Grade 2	2	2	2	
Adj Week 9: Grade 3	1	1	0	
Adj Week 13: Grade 0	0	1	0	
Adj Week 13: Grade 1	0	2	0	
Adj Week 13: Grade 2	2	2	2	
Adj Week 13: Grade 3	1	0	0	
Adj Week 17: Grade 0	0	0	1	
Adj Week 17: Grade 1	0	1	0	
Adj Week 17: Grade 2	2	3	0	
Adj Week 21: Grade 1	0	0	1	
Adj Week 21: Grade 2	2	3	0	
Adj Week 25: Grade 1	0	2	0	
Adj Week 25: Grade 2	1	1	0	
Adj Week 29: Grade 2	1	0	0	
Adj Week 29: Grade 4	0	1	0	

Notes:

[20] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[21] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[22] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Restart Depatuxizumab Mafodotin if Interrupted Due to Ocular

Side Effects After Bandage Contact Lens (BCL) Intervention

End point title	Time to Restart Depatuxizumab Mafodotin if Interrupted Due to Ocular Side Effects After Bandage Contact Lens (BCL) Intervention

End point description:

The time to restart depatuxizumab mafodotin treatment if it was interrupted due to ocular side effects after BCL Intervention was tabulated.

End point type	Secondary

End point timeframe:

From the last assessment prior to BCL intervention to the end of BCL intervention

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[23]	0[24]	0[25]	
Units: weeks				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[23] - Data were not collected for this outcome (due to early termination of the study)

[24] - Data were not collected for this outcome (due to early termination of the study)

[25] - Data were not collected for this outcome (due to early termination of the study)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Depatuxizumab Mafodotin Dose Modifications to Ocular Side Effects After Bandage Contact Lens (BCL) Intervention

End point title	Number of Participants With Depatuxizumab Mafodotin Dose Modifications to Ocular Side Effects After Bandage Contact Lens (BCL) Intervention

End point description:

Dose modifications included depatuxizumab mafodotin withdrawal, interruption, and reductions in dose initiated due to OSEs after BCL intervention.

End point type	Secondary

End point timeframe:

From the last assessment prior to BCL intervention to the end of BCL intervention, up to 38 weeks

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[26]	12[27]	12[28]	
Units: participants	2	1	0	

Notes:

[26] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[27] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[28] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Depatuxizumab Mafodotin Dose Modifications Due to Ocular Side Effects (OSE)

End point title	Number of Participants With Depatuxizumab Mafodotin Dose Modifications Due to Ocular Side Effects (OSE)

End point description:

Dose modifications included depatuxizumab mafodotin withdrawal, interruption, and reductions in dose initiated due to OSEs.

End point type	Secondary

End point timeframe:

From the first dose of study drug until 49 days after last depatuxizumab mafodotin administration, up to 47 weeks

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14[29]	12[30]	12[31]	
Units: participants	2	3	2	

Notes:

[29] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[30] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[31] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Change From Baseline on the Logarithm of the Minimum Angle of Resolution (LogMAR) Scale

End point title	Maximum Change From Baseline on the Logarithm of the Minimum Angle of Resolution (LogMAR) Scale

End point description:

The LogMAR scale measures visual acuity on a continuous scale, with a LogMAR value of 0 equivalent to 20/20 visual acuity. Normal vision is considered to be from -0.2 - 0.1; higher values indicate visual impairment. The baseline observation is defined as the last non-missing measurement collected prior to the first dose of depatuxizumab mafodotin.

End point type	Secondary

End point timeframe:

Within 8 weeks after the initial dose of depatuxizumab mafodotin

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12[32]	10[33]	9[34]	
Units: units on a scale				
arithmetic mean (standard deviation)				
Bilateral vision	0.353 (± 0.1888)	0.402 (± 0.1985)	0.272 (± 0.3888)	
Vision in worst eye	0.482 (± 0.2028)	0.528 (± 0.3073)	0.430 (± 0.5120)	

Notes:

[32] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[33] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[34] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Emergent Corneal Epithelial Adverse Event (CEAE) Grade at Each Visit After Bandage Contact Lens (BCL) Intervention

End point title	Treatment Emergent Corneal Epithelial Adverse Event (CEAE) Grade at Each Visit After Bandage Contact Lens (BCL) Intervention

End point description:

The corneal epithelial adverse event (CEAE) rating scale is designed to record symptoms associated with corneal epitheliopathy caused by antibody-drug conjugates and to grade the severity of findings. The overall CEAE grade is measured on a scale of 0 to 5, with higher values being more severe, reflecting the impact of corneal abnormalities on visual activities of daily living (ADLs). Additional detailed information is collected for specific domains that are commonly affected, with the following ranges (each in order of increasing severity): ocular discomfort (0 - 4), photophobia (0 - 3), and reading (1 - 3).

End point type	Secondary

End point timeframe:

From the last assessment prior to BCL intervention to the end of BCL intervention, up to 38 weeks

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[35]	4[36]	4[37]	
Units: participants				
Week 5: Grade 1	2	0	0	
Week 7: Grade 2	1	1	0	

Week 9: Grade 2	1	1	1	
Week 11: Grade 2	0	0	2	
Week 11: Grade 3	1	0	0	
Week 13: Grade 1	1	0	0	
Adj Week 1: Grade 1	0	0	1	
Adj Week 1: Grade 2	0	0	1	
Adj Week 5: Grade 0	0	1	1	
Adj Week 5: Grade 1	0	1	0	
Adj Week 5: Grade 2	1	0	1	
Adj Week 5: Grade 3	1	0	0	
Adj Week 9: Grade 0	0	1	0	
Adj Week 9: Grade 1	0	0	1	
Adj Week 9: Grade 2	0	0	1	
Adj Week 9: Grade 3	1	0	0	
Adj Week 13: Grade 0	0	2	0	
Adj Week 13: Grade 1	0	1	0	
Adj Week 13: Grade 2	1	0	1	
Adj Week 13: Grade 3	1	0	0	
Adj Week 17: Grade 1	0	1	0	
Adj Week 17: Grade 2	1	1	0	
Adj Week 21: Grade 2	2	1	0	
Adj Week 25: Grade 1	0	1	0	
Adj Week 25: Grade 2	1	0	0	
Adj Week 29: Grade 2	1	0	0	

Notes:

[35] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[36] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

[37] - Safety population: randomized subjects who rcvd ≥1 dose of ABT-414 with available data

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Re-initiation of Depatuxizumab Mafodotin After Dose Interruption

End point title	Time to Re-initiation of Depatuxizumab Mafodotin After Dose Interruption

End point description:

The time from dose interruption until re-initiation or permanent discontinuation of depatuxizumab mafodotin was to be recorded.

End point type	Secondary

End point timeframe:

Up to 9 months

End point values	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[38]	0[39]	0[40]	
Units: weeks				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[38] - Data were not collected for this outcome (due to early termination of the study)

[39] - Data were not collected for this outcome (due to early termination of the study)

[40] - Data were not collected for this outcome (due to early termination of the study)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) collected from 1st dose of ABT-414 until 49 d after last dose, up to 47 wks. SAEs and protocol-related nonserious AEs were collected from the time the subject signed consent.

Adverse event reporting additional description:

TEAEs and SAEs are defined as any AE or SAE with onset or worsening reported by a participant from the time that the first dose of depatuxizumab mafodotin is administered until 49 days have elapsed following discontinuation of study drug. TEAEs were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Standard Steroids

Reporting group description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days

Reporting group title	Standard Steroids + Vasoconstrictor + Cold Compress

Reporting group description:

Steroid eye drops: 1 drop each eye, 3 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4– 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. The cold compress was to be applied in increments no longer than 30 min (could be shorter if the participant was uncomfortable).

Reporting group title	Enhanced Steroids + Vasoconstrictor + Cold Compress

Reporting group description:

Enhanced steroid eye drops: 1 drop each eye, 6 times/day, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Ophthalmic Steroid Ointment; applied to each eye once daily before sleep, starting 2 days prior to depatuxizumab mafodotin infusion and continuing until 4 days after infusion, for a total of 7 days; Vasoconstrictor Eye Drops: 1 drop each eye 4 – 6 times on day of infusion in total (5 – 10 minutes before infusion; at end of infusion; and 2 – 4 times during the remainder of the infusion day). Continuing 4 – 6 times/day on Day 1 and Day 2 after each depatuxizumab mafodotin infusion; Cold Compress: Starting 5 minutes prior to start of infusion and continuing for 30 minutes past end of infusion, and then use at least 2 hours total/day on Days 1 – 3 with each depatuxizumab mafodotin infusion. Cold compress was to be applied in increments no longer than 30 min (could be shorter if the patient is uncomfortable).

Serious adverse events	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 14 (42.86%)	4 / 12 (33.33%)	4 / 12 (33.33%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	1	0	0

Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
TUMOUR PSEUDOPROGRESSION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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
HAEMATOMA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			

subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STATUS EPILEPTICUS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (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
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
ULCERATIVE KERATITIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (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
Gastrointestinal disorders			
VOMITING			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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			
PULMONARY EMBOLISM			

subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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
Infections and infestations			
CELLULITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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
EYE INFECTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (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
PNEUMONIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (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

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

Non-serious adverse events	Standard Steroids	Standard Steroids + Vasoconstrictor + Cold Compress	Enhanced Steroids + Vasoconstrictor + Cold Compress
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	12 / 12 (100.00%)	12 / 12 (100.00%)
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
HYPOTENSION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
General disorders and administration			

site conditions			
ASTHENIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
FATIGUE			
subjects affected / exposed	6 / 14 (42.86%)	9 / 12 (75.00%)	7 / 12 (58.33%)
occurrences (all)	10	10	8
CHEST PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
MENSTRUATION IRREGULAR			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
PROSTATIC OBSTRUCTION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	4	0
DYSPNOEA EXERTIONAL			

subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
EPISTAXIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
PLEURITIC PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
ANXIETY			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
CONFUSIONAL STATE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
DEPRESSION			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
INSOMNIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	4 / 14 (28.57%)	2 / 12 (16.67%)	2 / 12 (16.67%)
occurrences (all)	4	2	3
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 14 (14.29%)	5 / 12 (41.67%)	3 / 12 (25.00%)
occurrences (all)	2	7	4
BLOOD BILIRUBIN ABNORMAL			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BLOOD CALCIUM INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BLOOD PHOSPHORUS DECREASED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
INTRAOCULAR PRESSURE INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	3 / 12 (25.00%)
occurrences (all)	1	0	7
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
NEUTROPHIL COUNT INCREASED			

subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
CORNEAL ABRASION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
FALL			
subjects affected / exposed	2 / 14 (14.29%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
INCISION SITE PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
RADIATION NECROSIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
RADIATION SKIN INJURY			
subjects affected / exposed	2 / 14 (14.29%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
SKIN ABRASION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

CARDIOMEGALY			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
TACHYCARDIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Nervous system disorders			
APHASIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
APRAXIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BALANCE DISORDER			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
BRAIN OEDEMA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DIZZINESS			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
HEADACHE			
subjects affected / exposed	5 / 14 (35.71%)	3 / 12 (25.00%)	4 / 12 (33.33%)
occurrences (all)	5	3	5
DYSGEUSIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
HEMIPARESIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
MEMORY IMPAIRMENT			

subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
SEIZURE			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	2 / 12 (16.67%)
occurrences (all)	1	1	3
SYNCOPE			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
TREMOR			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
VASOGENIC CEREBRAL OEDEMA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
LEUKOPENIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
LYMPHOPENIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NEUTROPENIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	2	2
THROMBOCYTOPENIA			
subjects affected / exposed	3 / 14 (21.43%)	5 / 12 (41.67%)	3 / 12 (25.00%)
occurrences (all)	4	7	7
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
HYPOACUSIS			

subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
CONJUNCTIVITIS ALLERGIC			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
ACQUIRED EPIBLEPHARON			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
DIPLOPIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DRY EYE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
EYELID PTOSIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
FOREIGN BODY SENSATION IN EYES			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
VISION BLURRED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
CONSTIPATION			
subjects affected / exposed	5 / 14 (35.71%)	4 / 12 (33.33%)	2 / 12 (16.67%)
occurrences (all)	5	4	2
DIARRHOEA			

subjects affected / exposed	1 / 14 (7.14%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
DRY MOUTH			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DUODENAL ULCER			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
DYSPHAGIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
MOUTH ULCERATION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	6 / 14 (42.86%)	6 / 12 (50.00%)	3 / 12 (25.00%)
occurrences (all)	7	7	3
STOMATITIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	5 / 14 (35.71%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	5	1	1
Hepatobiliary disorders			
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	3	0

Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
ALOPECIA			
subjects affected / exposed	2 / 14 (14.29%)	2 / 12 (16.67%)	5 / 12 (41.67%)
occurrences (all)	2	2	7
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
DRY SKIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ERYTHEMA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
PETECHIAE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
RASH			
subjects affected / exposed	3 / 14 (21.43%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	4	1	0
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
RASH PRURITIC			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
SCAR PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
NOCTURIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
URINARY INCONTINENCE			

subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BACK PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 14 (14.29%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	5	0	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
NECK PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
BALANITIS CANDIDA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ORAL HERPES			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
SINUSITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	3 / 14 (21.43%)	3 / 12 (25.00%)	3 / 12 (25.00%)
occurrences (all)	4	5	3
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
DEHYDRATION			
subjects affected / exposed	0 / 14 (0.00%)	2 / 12 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
HYPONATRAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
MALNUTRITION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2018	Version 2.0 •Implemented safety measures for subjects with hepatic laboratory abnormalities due to a Grade 5 acute liver injury in a patient receiving depatuxizumab mafodotin in an ongoing study •Provided guidelines for depatuxizumab mafodotin dose modifications due to hepatic laboratory abnormalities •Provided guidelines for management and evaluation of severe hepatic laboratory abnormalities and for data collection •Provided clarification on measurements of visual acuity (VA) •Primary measure of interest, used for assessing the VA component of primary endpoint and other changes from baseline in VA, defined as VA with baseline correction, to be determined at the initial ophthalmology examination and used throughout the study •Provided additional flexibility in OSE management once endpoints for study objectives were assessed •Allowed subjects to transition to the Investigator Discretion Phase once key period of interest for OSE observation has ended (after 8 wks of adjuvant therapy) regardless of CEAE grade or prior intervention with BCLs •Increased frequency of vasoconstrictor eye drop administration, as consistent with labeling information •Clarified sequence of steroid eye drop substitution: initial eye drop is Prednisolone acetate 1% suspension and substitution with 0.1% dexamethasone phosphate is allowed after emergency of ocular side effects, if deemed necessary •Provided clarification on supportive care measures allowed or prohibited during Initial Prophylaxis and BCL Intervention phases of OSE management •Clarified language describing optional biomarker study •Clarified purpose of optional cornea collection: histopathologic evaluation of the post-mortem corneal tissue will be assessed to further characterize histopathologic features of OSEs •Specified that non-corrective (plano) bandage contact lenses are to be used in the study •Provided clarification on adverse event reporting by following current template language

14 December 2018	Version 3.0 •Updated Benefits and Risks to patients to reflect clinical study data reported in current Investigator Brochure and updated Reference for IB •Added active infection with hepatitis B virus, hepatitis C virus, or HIV as exclusion criteria •Provided updated contraception language to be consistent with AbbVie protocol template •Prohibited use of live attenuated vaccines during study and for 49 days after end of study drug administration •Clarified instructions for withdrawal of subjects and discontinuation of study •Clarified use of vasoconstrictor eye drops 4 - 6 times in total on day of infusion, including 2-4 times during remainder of infusion day, and 4 - 6 times/day in total on Day 1 - Day 2 after infusion •Clarified that all adverse events reported will be collected from the time of study drug administration until 49 days after last depatuxizumab mafodotin administration; clarified that administration of depatuxizumab mafodotin must be discontinued immediately in the event that a subject becomes pregnant during the study •Included instructions for Toxicity Management in Protocol; moved from Operations Manual. •Updated CTCAE to version 5.0 for grading of clinical toxicity in order to use most recent version. •Specified that study drug should be permanently discontinued if subject develops corneal ulceration with impending perforation (CU) or corneal perforation (CP) •Clarified end of study as the date of subject's last visit •Added time points for collection of visual quality of life questionnaire and visual symptoms questionnaire; added time points for collection of perception of treatment value question; provided clarification on timing and type of pregnancy tests; added randomization visit with prophylactic treatment for OSE; clarified timing of central lab tests during Follow Up 35 Day visit and not at Follow Up 49 Day visit; added Post-Treatment Follow Up visit at 49 Day
28 May 2019	Version 4.0 •Added brief summary of results for the protocol-specified interim efficacy analysis for INTELLANCE-1 in the Introduction •Provided modified study procedures and instructions for depatuxizumab mafodotin dosing in for those subjects who were currently receiving depatuxizumab mafodotin and who choose to continue depatuxizumab mafodotin. No additional efficacy data was to be collected, and procedures were minimized to include those necessary for study drug dosing, safety monitoring and collection of safety data related to adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported