



Clinical trial results:

An International, Multi-Center, Open-Label, Randomized, Phase III Trial of Sacituzumab Govitecan Versus Treatment of Physician Choice in Patients with Metastatic Triple-Negative Breast Cancer Who Received at Least Two Prior Treatments

Summary

EudraCT number	2017-003019-21
Trial protocol	BE ES DE GB
Global end of trial date	08 December 2020

Results information

Result version number	v1 (current)
This version publication date	17 December 2021
First version publication date	17 December 2021

Trial information

Trial identification

Sponsor protocol code	IMMU-132-05
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02574455
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	08 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2020
Global end of trial reached?	Yes
Global end of trial date	08 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the efficacy of sacituzumab govitecan to the treatment of physician's choice (TPC) as measured by independently-reviewed Independent Review Committee (IRC) progression-free survival (PFS) in participants with locally advanced or metastatic triple-negative breast cancer (TNBC) previously treated with at least two systemic chemotherapy regimens for unresectable, locally advanced or metastatic disease, and without brain metastasis at baseline.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 45
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	France: 62
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Spain: 58
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 342
Worldwide total number of subjects	529
EEA total number of subjects	167

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)	428
From 65 to 84 years	101
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Belgium, Canada, France, Germany, Spain, the United Kingdom, and the United States. The first participant was screened on 07 November 2017. The last study visit occurred on 08 December 2020.

Pre-assignment

Screening details:

730 participants were screened.

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	Sacituzumab govitecan

Arm description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion either by gravity or with an infusion pump on Days 1 and 8 of a 21-day treatment cycle for up to 29.6 months. Infusion rate for the first 15 minutes started with 50 mg/hour or less with a subsequent infusion of 100 to 200 mg/hour up to a maximum recommended rate (advanced every 15 to 30 minutes) of 500 mg/hour with a subsequent infusion of 1000 mg/hour. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable adverse events (AEs).

Arm type	Experimental
Investigational medicinal product name	Sacituzumab govitecan
Investigational medicinal product code	
Other name	IMMU-132, Trodelvy®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg administered as a slow intravenous (IV) infusion either by gravity or with an infusion pump. Infusion rate for the first 15 minutes will start with 50 mg/hour or less with a subsequent infusion of 100 to 200 mg/hour up to a maximum recommended rate (advanced every 15 to 30 minutes) of 500 mg/hour with a subsequent infusion of 1000 mg/hour.

Arm title	Treatment of Physician's Choice (TPC)
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Arm description:

Participants received TPC (ie, eribulin, capecitabine, gemcitabine, or vinorelbine), administered as a single-agent regimen that was selected by the investigator before participant randomization. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable AEs.

Arm type	Active comparator
Investigational medicinal product name	Eribulin
Investigational medicinal product code	
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV over 2 to 5 minutes at a dose 1.4 mg/m² at North American sites and 1.23 mg/m² at European sites on Days 1 and 8 of a 21-day cycle for up to 15.3 months. Lower doses were administered on the same schedule to participants with moderate hepatic impairment (ie, Child-Pugh B;

0.7 mg/m² and 0.67 mg/m² for North American and European sites, respectively).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	Xeloda
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1000 to 1250 mg/m² was administered in a 21-day cycle, with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period for up to 10.6 months.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Gemzar
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

800 to 1200 mg/m² was administered IV over 30 minutes on Days 1, 8, and 15 of a 28-day cycle for up to 8.1 months.

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	Navelbine
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m² was administered as a weekly IV injection over 6-10 minutes for up to 11.5 months. Vinorelbine was not allowed as TPC for any participant with Grade 2 neuropathy.

Number of subjects in period 1	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)
Started	267	262
Completed	0	0
Not completed	267	262
Withdrawal of Consent	11	28
Death	197	210
Sponsor's Decision	55	20
Lost to follow-up	4	4

Baseline characteristics

Reporting groups

Reporting group title	Sacituzumab govitecan
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Reporting group description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion either by gravity or with an infusion pump on Days 1 and 8 of a 21-day treatment cycle for up to 29.6 months. Infusion rate for the first 15 minutes started with 50 mg/hour or less with a subsequent infusion of 100 to 200 mg/hour up to a maximum recommended rate (advanced every 15 to 30 minutes) of 500 mg/hour with a subsequent infusion of 1000 mg/hour. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable adverse events (AEs).

Reporting group title	Treatment of Physician's Choice (TPC)
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Reporting group description:

Participants received TPC (ie, eribulin, capecitabine, gemcitabine, or vinorelbine), administered as a single-agent regimen that was selected by the investigator before participant randomization. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable AEs.

Reporting group values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)	Total
Number of subjects	267	262	529
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	54.0 ± 11.34	54.0 ± 11.69	-
Gender categorical Units: Subjects			
Female	265	262	527
Male	2	0	2
Race Units: Subjects			
Asian	13	9	22
Black	28	34	62
White	215	203	418
Other	11	16	27
Ethnicity Units: Subjects			
Hispanic or Latino	20	25	45
Not Hispanic or Latino	234	226	460
Unknown or Not Reported	13	11	24

End points

End points reporting groups

Reporting group title	Sacituzumab govitecan
Reporting group description: Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow intravenous (IV) infusion either by gravity or with an infusion pump on Days 1 and 8 of a 21-day treatment cycle for up to 29.6 months. Infusion rate for the first 15 minutes started with 50 mg/hour or less with a subsequent infusion of 100 to 200 mg/hour up to a maximum recommended rate (advanced every 15 to 30 minutes) of 500 mg/hour with a subsequent infusion of 1000 mg/hour. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable adverse events (AEs).	
Reporting group title	Treatment of Physician's Choice (TPC)
Reporting group description: Participants received TPC (ie, eribulin, capecitabine, gemcitabine, or vinorelbine), administered as a single-agent regimen that was selected by the investigator before participant randomization. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable AEs.	

Primary: Progression-Free Survival (PFS) by Independent Review Committee (IRC) Assessment in Brain Metastasis Negative (BM-ve) Population

End point title	Progression-Free Survival (PFS) by Independent Review Committee (IRC) Assessment in Brain Metastasis Negative (BM-ve) Population
End point description: PFS was defined as the time from randomization until objective tumor progression by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or death, whichever came first. The date of progression was date of the last observation or radiological assessment of target lesions that either showed a predefined increase (greater than or equal to $\geq$ 20%) in the sum of the target lesions or the appearance of new non-target lesions. PFS was estimated using Kaplan-Meier estimate. The BM-ve Population included all randomized participants who were randomized to the strata of no baseline brain metastasis at the time of randomization.	
End point type	Primary
End point timeframe: From randomization until objective tumor progression or death (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)	

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: months				
median (confidence interval 95%)	5.6 (4.3 to 6.3)	1.7 (1.5 to 2.6)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.387
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.305
upper limit	0.492

Notes:

[1] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies, presence of known brain metastases at study entry, and region.

Secondary: Progression-Free Survival (PFS) by IRC Assessment in the ITT Population

End point title	Progression-Free Survival (PFS) by IRC Assessment in the ITT Population
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End point description:

PFS was defined as the time from randomization until objective tumor progression by RECIST v1.1 or death, whichever came first. The date of progression was date of the last observation or radiological assessment of target lesions that either showed a predefined increase ($\geq 20\%$) in the sum of the target lesions or the appearance of new non-target lesions. PFS was estimated using Kaplan-Meier estimate. The ITT Population included all randomized participants.

End point type	Secondary
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End point timeframe:

From randomization until objective tumor progression or death (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	262		
Units: months				
median (confidence interval 95%)	4.8 (4.1 to 5.8)	1.7 (1.5 to 2.5)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)

Number of subjects included in analysis	529
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.413
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.517

Notes:

[2] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies, presence of known brain metastases at study entry, and region.

Secondary: Overall Survival (OS) in BM-ve Population

End point title	Overall Survival (OS) in BM-ve Population
End point description:	Overall survival (OS) was defined as the time from the randomization to death from any cause. OS was estimated using Kaplan-Meier estimate. Participants in the BM-ve Population were analyzed.
End point type	Secondary
End point timeframe:	From the randomization to death from any cause (maximum follow-up duration: 30.8 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: months				
median (confidence interval 95%)	12.1 (10.7 to 14.0)	6.7 (5.8 to 7.7)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.481

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.592

Notes:

[3] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies and region.

Secondary: Overall Survival (OS) in ITT Population

End point title	Overall Survival (OS) in ITT Population
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End point description:

Overall survival (OS) was defined as the time from the randomization to death from any cause. OS was estimated using Kaplan-Meier estimate. Participants in the ITT Population were analyzed.

End point type	Secondary
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End point timeframe:

From the randomization to death from any cause (maximum follow-up duration: 30.8 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	262		
Units: months				
median (confidence interval 95%)	11.8 (10.5 to 13.8)	6.9 (5.9 to 7.7)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	529
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.514
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.422
upper limit	0.625

Notes:

[4] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies and region.

Secondary: Objective Response Rate (ORR) by IRC and Investigator Assessment in BM-ve Population

End point title	Objective Response Rate (ORR) by IRC and Investigator Assessment in BM-ve Population
End point description:	
ORR was defined as the percentage of participants who had the overall best response as either a confirmed complete response (CR) or partial response (PR) relative to the size of population under evaluation. CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; and no new lesions. PR: $\geq 30\%$ decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD; and no new lesions. Participants in the BM-ve Population with available data were analyzed.	
End point type	Secondary
End point timeframe:	
From randomization to the date of progression or death (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)	

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: percentage of participants				
number (confidence interval 95%)				
ORR by IRC Assessment N=230,230	34.9 (28.8 to 41.4)	4.7 (2.4 to 8.3)		
ORR by Investigator Assessment	33.2 (27.2 to 39.6)	6.4 (3.6 to 10.4)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description:	
ORR by IRC Assessment	
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	10.859
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.59
upper limit	21.095

Statistical analysis title	Sacituzumab Govitecan vs TPC
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Statistical analysis description: ORR by Investigator Assessment	
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	7.363
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.063
upper limit	13.341

Secondary: Time to Objective Response by the Investigator Assessment in BM-ve Population

End point title	Time to Objective Response by the Investigator Assessment in BM-ve Population
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End point description:

Time to response was defined as the time from randomization to the first recorded objective response (ie, CR or PR). CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; and no new lesions. PR: $\geq 30\%$ decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD; and no new lesions. Participants in the BM-ve Population with objective response were analyzed.

End point type	Secondary
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End point timeframe:

From randomization to the first recorded objective response (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	15		
Units: months				
arithmetic mean (standard deviation)	2.14 ($\pm$ 1.322)	2.72 ($\pm$ 2.933)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Objective Response by the IRC Assessment in BM-ve Population

End point title	Time to Objective Response by the IRC Assessment in BM-ve Population
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End point description:

Time to response was defined as the time from randomization to the first recorded objective response (ie, CR or PR). CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; and no new lesions. PR: $\geq 30\%$ decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD; and no new lesions. Participants in the BM-ve Population with objective response were analyzed.

End point type	Secondary
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End point timeframe:

From randomization to the first recorded objective response (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	11		
Units: months				
arithmetic mean (standard deviation)	2.67 ($\pm$ 1.913)	1.86 ($\pm$ 0.919)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by IRC and Investigator Assessment in BM-ve Population

End point title	Duration of Response (DOR) by IRC and Investigator Assessment in BM-ve Population
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End point description:

DOR was defined as the number of days between the first date showing a documented response of CR or PR and the date of progression or death. CR: Disappearance of all target and non-target lesions; and normalization of tumor marker levels initially above upper limits of normal; and no new lesions. PR: $\geq 30\%$ decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD; and no new lesions. The date of progression was date of the last observation or radiological assessment of target lesions that either showed a predefined increase ($\geq 20\%$) in the sum of the target lesions or the appearance of new non-target lesions. Participants in the BM-ve Population with objective response were analyzed. 9999=Due to smaller number of participants with an event, upper limit of 95% confidence interval (CI) could not be calculated.

End point type	Secondary
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End point timeframe:

From the first date of documented response of CR or PR to the date of progression or death (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	15		
Units: months				
median (confidence interval 95%)				
IRC Assessment N=82,11	6.3 (5.5 to 7.9)	3.6 (2.8 to 9999)		
Investigator Assessment N=78,15	6.9 (5.6 to 7.9)	3.0 (2.8 to 4.3)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: DOR by IRC Assessment	
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0683 ^[5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.407
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	1.107

Notes:

[5] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies, and region.

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: DOR by Investigator Assessment	
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.212
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.103
upper limit	0.435

Notes:

[6] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies, and region.

Secondary: Time to Progression (TTP) by Investigator Assessment in BM-ve Population

End point title	Time to Progression (TTP) by Investigator Assessment in BM-ve Population
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End point description:

Time to Progression (TTP) was defined as the time from the date of randomization to the date of the first evidence of disease progression as assessed using RECIST 1.1 criteria. The date of progression was date of the last observation or radiological assessment of target lesions that either showed a predefined increase ($\geq 20\%$) in the sum of the target lesions or the appearance of new non-target lesions. Participants without progression were censored. Participants in the BM-ve Population were analyzed.

End point type	Secondary
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End point timeframe:

From randomization until disease progression (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: months				
median (confidence interval 95%)	5.7 (5.2 to 6.9)	1.8 (1.5 to 2.6)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
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Statistical analysis description:

TTP by Investigator Assessment

Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [7]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.317
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.248
upper limit	0.404

Notes:

[7] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies and region.

Secondary: Time to Progression (TTP) by IRC Assessment in BM-ve Population

End point title	Time to Progression (TTP) by IRC Assessment in BM-ve Population
End point description: Time to Progression (TTP) was defined as the time from the date of randomization to the date of the first evidence of disease progression as assessed using RECIST 1.1 criteria. The date of progression was date of the last observation or radiological assessment of target lesions that either showed a predefined increase ($\geq 20\%$) in the sum of the target lesions or the appearance of new non-target lesions. Participants without progression were censored. Participants in the BM-ve Population were analyzed.	
End point type	Secondary
End point timeframe: From randomization until disease progression (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)	

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: months				
median (confidence interval 95%)	5.8 (4.8 to 6.9)	2.1 (1.5 to 2.7)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
Statistical analysis description: TTP by IRC Assessment	
Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 ^[8]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.406
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.315
upper limit	0.525

Notes:

[8] - Stratified log-rank test and stratified Cox regression adjusted for stratification factors: number of prior chemotherapies and region.

Secondary: Clinical Benefit Rate (CBR) by IRC and Investigator Assessment in BM-ve Population

End point title	Clinical Benefit Rate (CBR) by IRC and Investigator Assessment in BM-ve Population
End point description: CBR was defined as the percentage of participants with best response as either CR, PR, or stable disease (SD) with a duration of ≥ 6 months. CR: Disappearance of all target and non-target lesions; and	

normalization of tumor marker levels initially above upper limits of normal; and no new lesions. PR: $\geq 30\%$ decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD; and no new lesions. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum LD since the treatment started; and Persistence of one or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits. PD: $\geq 20\%$ increase in the sum of LD of target lesions, taking as reference the smallest sum LD recorded since treatment started/appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions. Participants in the BM-ve Population were analyzed.

End point type	Secondary
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End point timeframe:

From randomization to the date of progression or death (assessed every 6 weeks for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease; maximum exposure: 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	233		
Units: percentage of participants				
number (confidence interval 95%)				
IRC Assessment	44.7 (38.2 to 51.3)	8.6 (5.3 to 12.9)		
Investigator Assessment	45.5 (39.0 to 52.1)	10.3 (6.7 to 14.9)		

Statistical analyses

Statistical analysis title	Sacituzumab Govitecan vs TPC
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Statistical analysis description:

CBR by IRC Assessment

Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	8.543
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.055
upper limit	14.437

Statistical analysis title	Sacituzumab Govitecan vs TPC
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Statistical analysis description:

CBR by Investigator Assessment

Comparison groups	Sacituzumab govitecan v Treatment of Physician's Choice (TPC)
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	7.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.54
upper limit	12.364

Secondary: Percentage of Participants Experiencing Any Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and TEAEs Leading to Discontinuation of Study Drug

End point title	Percentage of Participants Experiencing Any Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and TEAEs Leading to Discontinuation of Study Drug
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End point description:

Treatment-emergent adverse events (TEAEs) were defined as any adverse events (AEs) that begin or worsen on or after the start of study drug through 30 days after the last dose of study drug. The severity was graded based on the National Cancer Institute's Common Terminology Criteria for Adverse Events Version 4.03. An AE that met one or more of the following outcomes was classified as serious:

- Fatal
- Life-threatening
- Disabling/incapacitating
- Results in hospitalization or prolongs a hospital stay
- A congenital abnormality
- Other important medical events may also be considered serious AEs if they may require medical or surgical intervention to prevent one of the outcomes listed above. Safety Population included all participants who received at least one dose of sacituzumab govitecan or TPC.

End point type	Secondary
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End point timeframe:

First dose date up to last follow-up (maximum up to 30.8 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	224		
Units: percentage of participants				
number (not applicable)				
Any TEAEs	99.6	97.8		
SAEs	26.7	28.6		
TEAEs Leading to Discontinuation of Study Drug	4.7	5.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 (EORTC QLQ-C30) Score

End point title	Change From Baseline in European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 (EORTC QLQ-C30) Score
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End point description:

The EORTC QLQ-C30 is a questionnaire to assess quality of life (QoL), it is composed of 30 questions (items) resulting in 5 functional scales (physical functioning [phy fun], role functioning [rol fun], emotional functioning [emo fun], cognitive functioning [cog fun], social functioning [soc fun]), 1 global health status (glo hea sta) scale, 3 symptom scales (fatigue, nausea and vomiting [nau and vom], pain), and 6 single items (dyspnea, insomnia, loss of appetite [app loss], constipation [con], diarrhea, financial difficulties [fin dif]). All of the scales and single-item measures range in score from 0 to 100. Higher score for the functioning scales and global health status indicate a better quality of life; a positive change from baseline indicates improvement. Lower scores on the symptom and single-item scales indicate a better quality of life; a negative change from baseline indicates improvement. Participants in the Safety analysis set with available data were analyzed.

End point type	Secondary
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End point timeframe:

Baseline; End of Treatment (EOT) (up to 29.6 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	224		
Units: score on a scale				
arithmetic mean (standard deviation)				
Global Health Status/QoL: Baseline N=247,217	61.9 (± 21.31)	56.4 (± 22.21)		
Glo Hea Sta Change From Baseline at EOT N=181,147	-5.8 (± 22.71)	-9.4 (± 20.46)		
Physical Functioning: Baseline N=248,217	73.2 (± 21.69)	71.2 (± 21.24)		
Phy Fun Change From Baseline at EOT N=183,147	-4.6 (± 21.07)	-13.5 (± 20.54)		
Role Functioning: Baseline N=248,217	68.1 (± 30.35)	65.1 (± 30.31)		
Rol Fun Change From Baseline at EOT N=183,146	-8.4 (± 32.87)	-18.8 (± 29.83)		
Emotional Functioning: Baseline N=247,217	71.9 (± 22.33)	68.9 (± 23.87)		
Emo Fun Change From Baseline at EOT N=182,147	-3.8 (± 25.02)	-3.5 (± 22.16)		
Cognitive Functioning: Baseline N=247,217	81.7 (± 21.08)	79.5 (± 23.91)		

Cog Fun Change From Baseline at EOT N=182,147	-7.5 (± 22.81)	-6.1 (± 22.92)		
Social Functioning: Baseline N=247,216	69.1 (± 29.96)	69.6 (± 26.88)		
Soc Fun Change From Baseline at EOT N=182,145	-5.9 (± 27.52)	-10.3 (± 29.60)		
Fatigue: Baseline N=248,217	39.4 (± 25.72)	42.1 (± 25.99)		
Fatigue: Change From Baseline at EOT N=183,147	5.1 (± 25.93)	14.0 (± 23.05)		
Nausea and Vomiting: Baseline N=248,217	8.3 (± 16.36)	10.3 (± 18.26)		
Nau and Vom Change From Baseline at EOT N=183,147	5.2 (± 23.93)	7.3 (± 23.33)		
Pain: Baseline N=248,217	37.9 (± 30.54)	42.5 (± 30.38)		
Pain: Change From Baseline at EOT N=183,147	2.8 (± 27.84)	6.8 (± 30.33)		
Dyspnoea: Baseline N=248,217	25.4 (± 30.36)	25.0 (± 29.09)		
Dyspnoea: Change From Baseline at EOT N=180,146	0.7 (± 30.91)	5.9 (± 28.95)		
Insomnia: Baseline N=248,217	33.2 (± 30.95)	35.6 (± 31.42)		
Insomnia: Change From Baseline at EOT N=183,147	4.4 (± 34.67)	-4.3 (± 32.24)		
Appetite Loss: Baseline N=248,217	20.8 (± 27.34)	25.8 (± 28.68)		
App Loss: Change From Baseline at EOT N=183,147	3.1 (± 31.78)	10.0 (± 30.32)		
Constipation: Baseline N=247,217	17.7 (± 27.18)	19.0 (± 26.56)		
Con Change From Baseline at EOT N=182,147	3.3 (± 28.92)	7.0 (± 31.27)		
Diarrhoea: Baseline N=247,217	7.2 (± 17.73)	6.5 (± 15.69)		
Diarrhoea: Change From Baseline at EOT N=182,147	11.4 (± 28.56)	3.6 (± 22.46)		
Financial Difficulties: Baseline N=246,217	27.6 (± 34.39)	22.4 (± 30.91)		
Fin Dif Change From Baseline at EOT N=181,147	0.4 (± 24.09)	1.1 (± 23.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing the Worst Laboratory Abnormalities Grade 3 or 4 Post-Baseline

End point title	Percentage of Participants Experiencing the Worst Laboratory Abnormalities Grade 3 or 4 Post-Baseline
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End point description:

Blood samples were collected for hematology, serum chemistry and the laboratory abnormalities were assessed. The most severe graded abnormality observed post-baseline for each graded test was counted for each participant. Safety as assessed by grading of laboratory values and AEs according to the National Cancer Institutes' Common Terminology Criteria for Adverse Events (NCI CTCAE) covering grades 0-5 (0=Normal, 1=Mild, 2=Moderate, 3=Severe, 4=Life-threatening, 5=Death). The percentage of participants with worst postbaseline grades 3 or 4 are reported. Participants in the Safety analysis set were analyzed.

End point type	Secondary
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End point timeframe:

First dose date up to last follow-up (maximum up to 30.8 months)

End point values	Sacituzumab govitecan	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	224		
Units: percentage of participants				
number (not applicable)				
Anemia	8.9	5.4		
Lymphocyte Count Decreased	33.3	25.0		
Neutrophil Count Decreased	48.8	35.3		
Platelet Count Decreased	1.2	2.7		
White Blood Cell Decreased	41.1	25.4		
Alanine Aminotransferase Increased	1.2	2.2		
Alkaline Phosphatase Increased	3.1	3.6		
Aspartate Aminotransferase Increased	3.5	2.2		
Blood Bilirubin Increased	1.9	2.7		
Creatinine Increased	0.4	0		
Hypercalcemia	0	0.4		
Hyperglycemia	3.1	3.1		
Hyperkalemia	0.8	0		
Hypermagnesemia	0.4	0.4		
Hypernatremia	0	0		
Hypoalbumenemia	0.8	1.3		
Hypocalcemia	1.6	1.3		
Hypoglycemia	0.4	0		
Hypokalemia	4.3	0.9		
Hypomagnesemia	0.8	0		
Hyponatremia	3.9	3.6		
Hypophosphatemia	8.1	3.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to last follow-up (maximum up to 30.8 months);

All-Cause Mortality: From randomization up to 30.8 months

Adverse event reporting additional description:

Serious Adverse Events and Other Adverse Events: Safety Population included all participants who received at least one dose of sacituzumab govitecan or TPC.

All-Cause Mortality: The ITT Population included all randomized participants (i.e. participants exposed, sacituzumab govitecan=267, TPC=262).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Treatment of Physician's Choice (TPC)
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Reporting group description:

Participants received TPC (ie, eribulin, capecitabine, gemcitabine, or vinorelbine), administered as a single-agent regimen that was selected by the investigator before participant randomization. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable AEs.

Reporting group title	Sacituzumab Govitecan
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Reporting group description:

Participants received sacituzumab govitecan 10 mg/kg of body weight, administered as a slow IV infusion either by gravity or with an infusion pump on Days 1 and 8 of a 21-day treatment cycle for up to 29.6 months. Infusion rate for the first 15 minutes started with 50 mg/hour or less with a subsequent infusion of 100 to 200 mg/hour up to a maximum recommended rate (advanced every 15 to 30 minutes) of 500 mg/hour with a subsequent infusion of 1000 mg/hour. Participants continued treatment until progression of disease requiring treatment discontinuation or occurrence of unacceptable AEs.

Serious adverse events	Treatment of Physician's Choice (TPC)	Sacituzumab Govitecan	
Total subjects affected by serious adverse events			
subjects affected / exposed	64 / 224 (28.57%)	69 / 258 (26.74%)	
number of deaths (all causes)	222	201	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 224 (0.45%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pregnancy			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 224 (2.23%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	2 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site extravasation			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast ulceration			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vaginal haemorrhage			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 224 (3.13%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	6 / 224 (2.68%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 224 (0.89%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 224 (0.89%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypoxia			
subjects affected / exposed	1 / 224 (0.45%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 224 (0.45%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactic acid increased			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation necrosis			

subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	2 / 224 (0.89%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 224 (0.00%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	4 / 224 (1.79%)	13 / 258 (5.04%)	
occurrences causally related to treatment / all	4 / 4	15 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 224 (0.45%)	5 / 258 (1.94%)	
occurrences causally related to treatment / all	1 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	2 / 224 (0.89%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 224 (0.00%)	9 / 258 (3.49%)	
occurrences causally related to treatment / all	0 / 0	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 224 (1.34%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 224 (0.00%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 224 (0.00%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 224 (1.79%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 224 (1.79%)	7 / 258 (2.71%)	
occurrences causally related to treatment / all	3 / 4	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis			
subjects affected / exposed	4 / 224 (1.79%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	2 / 4	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 224 (0.89%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	1 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 224 (0.00%)	3 / 258 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 224 (0.45%)	2 / 258 (0.78%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 224 (0.45%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corynebacterium infection			

subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Phlebitis infective			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			

subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 224 (0.00%)	1 / 258 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 258 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment of Physician's Choice (TPC)	Sacituzumab Govitecan	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	213 / 224 (95.09%)	256 / 258 (99.22%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 224 (6.25%)	17 / 258 (6.59%)	
occurrences (all)	21	34	
Lymphoedema			
subjects affected / exposed	7 / 224 (3.13%)	14 / 258 (5.43%)	
occurrences (all)	7	14	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	28 / 224 (12.50%)	39 / 258 (15.12%)	
occurrences (all)	34	57	
Fatigue			
subjects affected / exposed	89 / 224 (39.73%)	133 / 258 (51.55%)	
occurrences (all)	110	181	
Pyrexia			

subjects affected / exposed	27 / 224 (12.05%)	37 / 258 (14.34%)	
occurrences (all)	40	49	
Oedema peripheral			
subjects affected / exposed	24 / 224 (10.71%)	25 / 258 (9.69%)	
occurrences (all)	25	28	
Pain			
subjects affected / exposed	11 / 224 (4.91%)	18 / 258 (6.98%)	
occurrences (all)	12	18	
Mucosal inflammation			
subjects affected / exposed	14 / 224 (6.25%)	20 / 258 (7.75%)	
occurrences (all)	16	23	
Chills			
subjects affected / exposed	6 / 224 (2.68%)	14 / 258 (5.43%)	
occurrences (all)	6	16	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	8 / 224 (3.57%)	14 / 258 (5.43%)	
occurrences (all)	9	15	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	41 / 224 (18.30%)	45 / 258 (17.44%)	
occurrences (all)	46	50	
Cough			
subjects affected / exposed	40 / 224 (17.86%)	61 / 258 (23.64%)	
occurrences (all)	41	75	
Oropharyngeal pain			
subjects affected / exposed	9 / 224 (4.02%)	14 / 258 (5.43%)	
occurrences (all)	10	17	
Dyspnoea exertional			
subjects affected / exposed	3 / 224 (1.34%)	13 / 258 (5.04%)	
occurrences (all)	3	14	
Nasal congestion			
subjects affected / exposed	3 / 224 (1.34%)	13 / 258 (5.04%)	
occurrences (all)	3	14	
Rhinorrhoea			

subjects affected / exposed	1 / 224 (0.45%)	15 / 258 (5.81%)	
occurrences (all)	1	15	
Epistaxis			
subjects affected / exposed	1 / 224 (0.45%)	13 / 258 (5.04%)	
occurrences (all)	1	15	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 224 (4.91%)	30 / 258 (11.63%)	
occurrences (all)	11	33	
Anxiety			
subjects affected / exposed	8 / 224 (3.57%)	17 / 258 (6.59%)	
occurrences (all)	8	18	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	45 / 224 (20.09%)	71 / 258 (27.52%)	
occurrences (all)	97	185	
Aspartate aminotransferase increased			
subjects affected / exposed	27 / 224 (12.05%)	30 / 258 (11.63%)	
occurrences (all)	31	50	
White blood cell count decreased			
subjects affected / exposed	23 / 224 (10.27%)	33 / 258 (12.79%)	
occurrences (all)	37	80	
Alanine aminotransferase increased			
subjects affected / exposed	22 / 224 (9.82%)	28 / 258 (10.85%)	
occurrences (all)	25	43	
Weight decreased			
subjects affected / exposed	15 / 224 (6.70%)	22 / 258 (8.53%)	
occurrences (all)	15	24	
Lymphocyte count decreased			
subjects affected / exposed	13 / 224 (5.80%)	20 / 258 (7.75%)	
occurrences (all)	17	44	
Platelet count decreased			
subjects affected / exposed	15 / 224 (6.70%)	7 / 258 (2.71%)	
occurrences (all)	17	20	
Blood alkaline phosphatase increased			

subjects affected / exposed occurrences (all)	12 / 224 (5.36%) 13	17 / 258 (6.59%) 28	
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 224 (12.50%)	47 / 258 (18.22%)	
occurrences (all)	30	64	
Dizziness			
subjects affected / exposed	16 / 224 (7.14%)	28 / 258 (10.85%)	
occurrences (all)	19	34	
Neuropathy peripheral			
subjects affected / exposed	24 / 224 (10.71%)	9 / 258 (3.49%)	
occurrences (all)	25	10	
Dysgeusia			
subjects affected / exposed	6 / 224 (2.68%)	22 / 258 (8.53%)	
occurrences (all)	11	23	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	56 / 224 (25.00%)	108 / 258 (41.86%)	
occurrences (all)	108	275	
Anaemia			
subjects affected / exposed	61 / 224 (27.23%)	102 / 258 (39.53%)	
occurrences (all)	72	145	
Thrombocytopenia			
subjects affected / exposed	14 / 224 (6.25%)	9 / 258 (3.49%)	
occurrences (all)	18	14	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	68 / 224 (30.36%)	160 / 258 (62.02%)	
occurrences (all)	95	288	
Diarrhoea			
subjects affected / exposed	38 / 224 (16.96%)	168 / 258 (65.12%)	
occurrences (all)	63	403	
Constipation			
subjects affected / exposed	52 / 224 (23.21%)	96 / 258 (37.21%)	
occurrences (all)	68	160	
Vomiting			

subjects affected / exposed	36 / 224 (16.07%)	85 / 258 (32.95%)	
occurrences (all)	51	165	
Stomatitis			
subjects affected / exposed	14 / 224 (6.25%)	27 / 258 (10.47%)	
occurrences (all)	17	36	
Abdominal pain			
subjects affected / exposed	16 / 224 (7.14%)	54 / 258 (20.93%)	
occurrences (all)	20	74	
Abdominal pain upper			
subjects affected / exposed	8 / 224 (3.57%)	23 / 258 (8.91%)	
occurrences (all)	9	24	
Gastrooesophageal reflux disease			
subjects affected / exposed	7 / 224 (3.13%)	14 / 258 (5.43%)	
occurrences (all)	7	14	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	36 / 224 (16.07%)	121 / 258 (46.90%)	
occurrences (all)	36	124	
Rash			
subjects affected / exposed	12 / 224 (5.36%)	32 / 258 (12.40%)	
occurrences (all)	15	44	
Pruritus			
subjects affected / exposed	7 / 224 (3.13%)	26 / 258 (10.08%)	
occurrences (all)	7	34	
Rash maculo-papular			
subjects affected / exposed	3 / 224 (1.34%)	18 / 258 (6.98%)	
occurrences (all)	3	25	
Dry skin			
subjects affected / exposed	3 / 224 (1.34%)	17 / 258 (6.59%)	
occurrences (all)	3	18	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	30 / 224 (13.39%)	44 / 258 (17.05%)	
occurrences (all)	31	51	
Arthralgia			

subjects affected / exposed	16 / 224 (7.14%)	33 / 258 (12.79%)	
occurrences (all)	18	39	
Pain in extremity			
subjects affected / exposed	17 / 224 (7.59%)	21 / 258 (8.14%)	
occurrences (all)	19	28	
Bone pain			
subjects affected / exposed	14 / 224 (6.25%)	21 / 258 (8.14%)	
occurrences (all)	18	26	
Myalgia			
subjects affected / exposed	19 / 224 (8.48%)	12 / 258 (4.65%)	
occurrences (all)	22	13	
Musculoskeletal chest pain			
subjects affected / exposed	6 / 224 (2.68%)	17 / 258 (6.59%)	
occurrences (all)	6	21	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	17 / 224 (7.59%)	35 / 258 (13.57%)	
occurrences (all)	19	47	
Upper respiratory tract infection			
subjects affected / exposed	7 / 224 (3.13%)	32 / 258 (12.40%)	
occurrences (all)	8	44	
Nasopharyngitis			
subjects affected / exposed	5 / 224 (2.23%)	18 / 258 (6.98%)	
occurrences (all)	5	23	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	46 / 224 (20.54%)	71 / 258 (27.52%)	
occurrences (all)	56	75	
Hypokalaemia			
subjects affected / exposed	29 / 224 (12.95%)	46 / 258 (17.83%)	
occurrences (all)	30	72	
Hyperglycaemia			
subjects affected / exposed	12 / 224 (5.36%)	18 / 258 (6.98%)	
occurrences (all)	17	38	
Hypomagnesaemia			

subjects affected / exposed	13 / 224 (5.80%)	32 / 258 (12.40%)	
occurrences (all)	16	42	
Hypophosphataemia			
subjects affected / exposed	9 / 224 (4.02%)	15 / 258 (5.81%)	
occurrences (all)	18	20	
Hypocalcaemia			
subjects affected / exposed	5 / 224 (2.23%)	17 / 258 (6.59%)	
occurrences (all)	6	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 May 2017	• Added guidelines for infusion reactions, dose delay, dose reduction and treatment discontinuation • Added the inclusion criterion that all participants should have been previously treated with taxane regardless of disease stage (adjuvant, neoadjuvant or advanced) when it was given • Revised the inclusion criterion that participants with treated, non-progressive brain metastases must have stable magnetic resonance imaging (MRI) scans for at least 3 months, including within 4 weeks of study entry • Added collection of breast cancer susceptibility gene (BRCA) 1 and BRCA2 mutational status, if known • Removed baseline brain imaging requirement to rule out brain metastases • Removed the CTCAE patient-reported outcome (PRO) questionnaire.
31 July 2017	• Revised the computed tomography (CT)/MRI scans from every 6 weeks for 24 weeks to every 6 weeks for 36 weeks.
22 February 2018	• Allowed participants with locally advanced TNBC to be enrolled • Sample size increased from 328 to 488 participants • Defined as <10% expression for estrogen receptor (ER) and progesterone receptor (PR) and negative for human epidermal growth factor receptor 2 (HER2) by in-situ hybridization • Added the secondary objective and secondary efficacy endpoint of PFS in the ITT Population • Added that ORR and PFS would also be determined by the investigator • Added PFS and OS in the ITT Population • Added an exploratory analysis of Trop-2 tumor expression and efficacy • Increased the sample size and number of participating sites • Limited the number of participants with brain metastasis at 15% • Added eligibility requirements for participants who had either a contraindication or were intolerant to taxanes • Excluded participants who had received >5 prior standard of care chemotherapies for locally advanced or metastatic disease • Excluded participants with active chronic inflammatory bowel disease (ulcerative colitis, Crohn disease) and participants with a history of bowel obstruction • Excluded participants who had received a live vaccine within 30 days of randomization.
14 May 2018	• Removed secondary objective and secondary efficacy endpoint of PFS by investigator assessment • Added inclusion criteria that defined stable CNS disease for participants with brain metastasis • Removed the exclusion of participants who had received >5 prior standard of care chemotherapies for locally advanced or metastatic disease • Excluded participants who had previously received irinotecan • Excluded participants with rapid deterioration during screening • Added a hierarchical testing strategy for efficacy.

14 June 2019	• Removed assessment of other tumor markers • Clarified that both total and free SN-38 (a camptothecin-derived agent) would be assessed • Added that participants who were receiving clinical benefit from sacituzumab govitecan (SG) at the end of the study would be enrolled in a rollover study to ensure continued access to SG • Added that disease progression was not to be reported as an AE • Removed the interim futility analysis for PFS • Added that the significance level for the final analysis of OS in the ITT population would be determined by the Lan-DeMets spending function to ensure alpha was controlled at a 2-sided alpha of 0.05 which was subsequently changed to a 2-sided alpha of 0.0443.
26 August 2019	• Clarified PK sampling time points.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30786188>