Clinical trial results:
Randomized, Observational Study of Entecavir to Assess Long-term Outcomes Associated with Nucleoside/Nucleotide Monotherapy for Patients with Chronic HBV Infection: The REALM Study

Summary

EudraCT number	2005-003284-22
Trial protocol	FR DE ES IT PT GR CZ
Global end of trial date	26 October 2016

Results information

Result version number	v1 (current)
This version publication date	04 February 2018
First version publication date	04 February 2018

Trial information

Trial identification

Sponsor protocol code	AI463-080

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00388674
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, EU Study Start-Up Unit, , Bristol-Myers Squibb International, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, EU Study Start-Up Unit, , Bristol-Myers Squibb International, Clinical.Trials@bms.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	26 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2016
Global end of trial reached?	Yes
Global end of trial date	26 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to prospectively assess the long-term outcomes (benefits and risks) associated with entecavir (ETV) therapy as compared to other antivirals approved for the treatment of chronic HBV infection. For the China substudy, patients randomized to entecavir will have safety and efficacy assessments performed during the first year of the study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2006
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	Argentina: 49
Country: Number of subjects enrolled	Brazil: 529
Country: Number of subjects enrolled	Canada: 151
Country: Number of subjects enrolled	China: 5333
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Czech Republic: 58
Country: Number of subjects enrolled	France: 92
Country: Number of subjects enrolled	Germany: 175
Country: Number of subjects enrolled	Greece: 26
Country: Number of subjects enrolled	India: 1016
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Korea, Republic of: 2500
Country: Number of subjects enrolled	Mexico: 114
Country: Number of subjects enrolled	Philippines: 310
Country: Number of subjects enrolled	Poland: 69
Country: Number of subjects enrolled	Portugal: 35
Country: Number of subjects enrolled	Romania: 300
Country: Number of subjects enrolled	Russian Federation: 453
Country: Number of subjects enrolled	Singapore: 139

Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Taiwan: 416
Country: Number of subjects enrolled	Thailand: 309
Country: Number of subjects enrolled	Turkey: 59
Country: Number of subjects enrolled	United States: 318
Worldwide total number of subjects	12522
EEA total number of subjects	816

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)	113
Adults (18-64 years)	12111
From 65 to 84 years	294
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 12,522 subjects were enrolled;12,485 subjects were randomized; and 12,378 randomized subjects received treatment. 107 randomized not treated; 100 subjects were never treated with the study medication; 3 subjects were at subject's request; 2 subjects were not reported; 1 subject was administrative reason by sponsor; and 1 was other.

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	entecavir (ETV)

Arm description:

Tablets / Oral Solution, Oral, ETV = 0.5 mg - 1 mg, once daily.

Arm type	Experimental
Investigational medicinal product name	entecavir (ETV)
Investigational medicinal product code	
Other name	Baraclude
Pharmaceutical forms	Tablet and powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Tablets / Oral Solution, Oral, ETV = 0.5 mg - 1 mg, once daily, Investigator/Patient decision

Arm title	Other anti-HBV medication (Non-ETV)

Arm description:

Standard of care HBV Nucleoside/Nucleotide Monotherapy, specific agent selected at the discretion of the investigator

Arm type	Active comparator
Investigational medicinal product name	Adefovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard of Care dependent on Country

Investigational medicinal product name	Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard of Care dependent on Country

Investigational medicinal product name	Telbivudine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Standard of Care dependent on Country	
Investigational medicinal product name	Tenofovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Standard of Care dependent on Country	

Number of subjects in period 1[1]	entecavir (ETV)	Other anti-HBV medication (Non-ETV)
Started	6216	6162
Completed Treatment	4388 [2]	3576 [3]
Completed	4482	3993
Not completed	1734	2169
Adverse event, serious fatal	239	262
Subject Withdrew Consent	437	673
Not Reported	-	1
Non-Study Related Comorbidities	3	4
Not Defined	135	214
Administrative Reason By Sponsor	299	253
Lost to follow-up	587	715
No Off-Treatment Status Data	22	30
HBV Disease Progression (Non-HCC)	3	9
HCC	8	7
Malignancy (Non-HCC)	1	1

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: 12,522 subjects were enrolled. Baseline Characteristics are shown for the 12,378 randomized and treated subjects.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 6216 subjects started the study. 4388 subjects completed the treatment period. 4482 subjects completed the overall study.
[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 6162 subjects started the study. 3576 subjects completed the treatment period. 3993 subjects completed the overall study.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
All randomized treated subjects	

Reporting group values	Overall Study	Total	
Number of subjects	12378	12378	
Age categorical			
All randomized treated subjects			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	112	112	
Adults (18-64 years)	11973	11973	
From 65-84 years	289	289	
85 years and over	4	4	
Age Continuous			
Units: years			
arithmetic mean	39.7		
standard deviation	± 12.12	-	
Gender, Male/Female			
Units: Subjects			
Female	2993	2993	
Male	9385	9385	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	10422	10422	
Native Hawaiian or Other Pacific Islander	4	4	
Black or African American	127	127	
White	1599	1599	
Other	224	224	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	307	307	
Unknown or Not Reported	12068	12068	

End points

End points reporting groups	
Reporting group title	entecavir (ETV)
Reporting group description:	
Tablets / Oral Solution, Oral, ETV = 0.5 mg - 1 mg, once daily.	
Reporting group title	Other anti-HBV medication (Non-ETV)
Reporting group description:	
Standard of care HBV Nucleoside/Nucleotide Monotherapy, specific agent selected at the discretion of the investigator	

Primary: Number of subjects with Adjudicated Overall Malignant Neoplasms	
End point title	Number of subjects with Adjudicated Overall Malignant Neoplasms
End point description:	
The number of subjects with Overall Malignant Neoplasm, as adjudicated by Events Adjudication Committee (EAC)	
End point type	Primary
End point timeframe:	
10 years	

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: Subjects	331	337		

Statistical analyses

Statistical analysis title	Adjudicated Overall Malignant Neoplasms
Statistical analysis description:	
ETV : Non-ETV Hazard Ratio	
Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3553
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93

Confidence interval	
level	95.03 %
sides	2-sided
lower limit	0.8
upper limit	1.084

Primary: Number of Adjudicated Deaths

End point title	Number of Adjudicated Deaths
End point description:	
The number of deaths, as adjudicated by Events Adjudication Committee (EAC)	
End point type	Primary
End point timeframe:	
10 years	

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: Subjects	238	264		

Statistical analyses

Statistical analysis title	Adjudicated Deaths
Statistical analysis description:	
ETV : Non-ETV Hazard Ratio	
Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0676
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95.03 %
sides	2-sided
lower limit	0.713
upper limit	1.012

Primary: Number of subjects with Adjudicated Liver-related HBV disease progression

End point title	Number of subjects with Adjudicated Liver-related HBV disease progression

End point description:

The number of subjects with Liver-related hepatitis B virus (HBV) disease progression, as adjudicated by Events Adjudication Committee (EAC)

End point type	Primary

End point timeframe:

10 years

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: Subjects	350	375		

Statistical analyses

Statistical analysis title	Adjudicated Liver-related HBV disease progression

Statistical analysis description:

ETV : Non-ETV Hazard Ratio

Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1182
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95.03 %
sides	2-sided
lower limit	0.769
upper limit	1.03

Secondary: Number of subjects with Adjudicated non-HCC malignant neoplasm

End point title	Number of subjects with Adjudicated non-HCC malignant neoplasm

End point description:

The number of subjects with non-hepatocellular carcinoma (non-HCC) malignant neoplasm, as adjudicated by Events Adjudication Committee (EAC)

End point type	Secondary

End point timeframe:

10 years

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: subjects	95	81		

Statistical analyses

Statistical analysis title	Adjudicated Non-HCC malignant neoplasms
Statistical analysis description: ETV : Non-ETV Hazard Ratio	
Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.817
upper limit	1.478

Secondary: Number of subjects with Adjudicated HCC malignant neoplasm

End point title	Number of subjects with Adjudicated HCC malignant neoplasm
End point description: The number of subjects with hepatocellular carcinoma (HCC) malignant neoplasm, as adjudicated by Events Adjudication Committee (EAC)	
End point type	Secondary
End point timeframe: 10 years	

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: subjects	240	263		

Statistical analyses

Statistical analysis title	Adjudicated HCC malignant neoplasm
Statistical analysis description: ETV : Non-ETV Hazard Ratio	
Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.727
upper limit	1.032

Secondary: Number of subjects with Adjudicated Liver-related death	
End point title	Number of subjects with Adjudicated Liver-related death
End point description: The number of subjects with Liver-related death, as adjudicated by Events Adjudication Committee (EAC)	
End point type	Secondary
End point timeframe: 10 years	

End point values	entecavir (ETV)	Other anti-HBV medication (Non-ETV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6216	6162		
Units: Subjects	46	48		

Statistical analyses

Statistical analysis title	Adjudicated Liver-related deaths
Statistical analysis description: ETV : Non-ETV Hazard Ratio	

Comparison groups	entecavir (ETV) v Other anti-HBV medication (Non-ETV)
Number of subjects included in analysis	12378
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.608
upper limit	1.365

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From first dose until end of study (10 years)

Adverse event reporting additional description:

Mandatory reporting of non-serious AEs was not required. Reporting of serious adverse events (SAEs) which are considered unrelated (i.e. not likely or not related) to study drug was also not required.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Naive ETV

Reporting group description:

Treatment naïve subjects with CHB received ETV either as the 0.5 mg or 1.0 mg tablet or 0.05 mg/mL oral solution (in countries where the oral solution was approved) up to 10 years and continued on study until the study ended or they died, were lost to follow-up, withdrew informed consent, or discontinued treatment for other reasons.

Reporting group title	Experienced ETV

Reporting group description:

Subjects with CHB received ETV either as the 0.5 mg or 1.0 mg tablet or 0.05 mg/mL oral solution (in countries where the oral solution was approved) up to 10 years and continued on study until the study ended or they died, were lost to follow-up, withdrew informed consent, or discontinued treatment for other reasons.

Reporting group title	Experienced Non-ETV

Reporting group description:

Subjects with CHB received non-ETV standard of care HBV therapies up to 10 years and continued on study until the study ended or they died, were lost to follow-up, withdrew informed consent, or discontinued treatment for other reasons.

Reporting group title	Naive Non-ETV

Reporting group description:

Treatment naïve subjects with CHB received non-ETV standard of care HBV therapies up to 10 years and continued on study until the study ended or they died, were lost to follow-up, withdrew informed consent, or discontinued treatment for other reasons.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Mandatory reporting of non-serious AEs was not required. Reporting of serious adverse events (SAEs) which are considered unrelated (i.e. not likely or not related) to study drug was also not required.

Serious adverse events	Naive ETV	Experienced ETV	Experienced Non-ETV
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 4016 (0.87%)	21 / 2200 (0.95%)	15 / 2178 (0.69%)
number of deaths (all causes)	156	84	90
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			

subjects affected / exposed	4 / 4016 (0.10%)	4 / 2200 (0.18%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Death			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Electrocution			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Oedema peripheral			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic mass			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 4016 (0.05%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 4016 (0.05%)	2 / 2200 (0.09%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	2 / 4016 (0.05%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Atypical femur fracture			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			

subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
Multiple fractures			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Overdose			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Road traffic accident			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Toxicity to various agents			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coma hepatic			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Hepatic encephalopathy			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypoaesthesia			

subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mononeuropathy			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mononeuropathy multiplex			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	2 / 4016 (0.05%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
Enteritis			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
Pancreatitis			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	4 / 4016 (0.10%)	2 / 2200 (0.09%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	1 / 4016 (0.02%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (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
Chronic hepatitis			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Gallbladder polyp			

subjects affected / exposed	2 / 4016 (0.05%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			
subjects affected / exposed	2 / 4016 (0.05%)	2 / 2200 (0.09%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic fibrosis			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic function abnormal			
subjects affected / exposed	2 / 4016 (0.05%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Urethral stenosis			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myopathy			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	4 / 2178 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyositis			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 4016 (0.05%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic hepatitis b			
subjects affected / exposed	0 / 4016 (0.00%)	1 / 2200 (0.05%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis b			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	1 / 2178 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis b reactivation			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Tuberculous pleurisy			
subjects affected / exposed	1 / 4016 (0.02%)	0 / 2200 (0.00%)	0 / 2178 (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
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	3 / 2178 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Naive Non-ETV		
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 3984 (0.88%)		
number of deaths (all causes)	174		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			

subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Papillary cystadenoma lymphomatosum				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest discomfort				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Electrocution				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic mass				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				

Insomnia				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatine phosphokinase increased				
subjects affected / exposed	2 / 3984 (0.05%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Atypical femur fracture				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				

subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral infarction				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coma hepatic				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic encephalopathy				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia				

subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mononeuropathy			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mononeuropathy multiplex			
subjects affected / exposed	1 / 3984 (0.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	2 / 3984 (0.05%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varices oesophageal				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic hepatitis				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gallbladder polyp				

subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic fibrosis				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	0 / 3984 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 3984 (0.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nephropathy				
subjects affected / exposed	2 / 3984 (0.05%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Nephropathy toxic				
subjects affected / exposed	2 / 3984 (0.05%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal impairment				

subjects affected / exposed	1 / 3984 (0.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urethral stenosis			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	4 / 3984 (0.10%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	1 / 3984 (0.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myopathy			
subjects affected / exposed	11 / 3984 (0.28%)		
occurrences causally related to treatment / all	11 / 11		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polymyositis			
subjects affected / exposed	2 / 3984 (0.05%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Chronic hepatitis b			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis b			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis b reactivation			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculous pleurisy			
subjects affected / exposed	0 / 3984 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	1 / 3984 (0.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lactic acidosis			
subjects affected / exposed	1 / 3984 (0.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Naive ETV	Experienced ETV	Experienced Non-ETV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4016 (0.00%)	0 / 2200 (0.00%)	0 / 2178 (0.00%)

Non-serious adverse events	Naive Non-ETV		

Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 3984 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2006	Global Amendment 02: Pharmacogenetics Buccal Sample Amendment
25 June 2007	Global Amendment Number 03: ETV dose reduction options, updated exclusion criterion, COE Reporting clarifications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

1. No baseline or on-treatment HBV-related surrogate markers were collected.
2. BMS supplied only the initial therapy, not any subsequent therapies.

Notes: