Study to Explore the Effect of Mefloquine in Participants With Progressive Multifocal Leukoencephalopathy (PML)

This study has been terminated.

(Primary endpoint not achieved)

Sponsor:
Biogen Idec

Collaborator:
Elan Pharmaceuticals

Information provided by (Responsible Party):
Biogen Idec

ClinicalTrials.gov Identifier:
NCT00746941

First received: September 3, 2008
Last updated: July 2, 2014
Last verified: July 2014
History of Changes

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Results First Received: January 3, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Single Blind (Outcomes Assessor); Primary Purpose: Treatment
Condition:	Progressive Multifocal Leukoencephalopathy
Intervention:	Drug: mefloquine

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
Twelve sites enrolled participants prior to study termination.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants were initially randomized in a 1:1 ratio to the local standard of care arm (represented below as 3 treatment arms depending on Week 4 and Week 8 decisions) or the local standard of care plus mefloquine 250 mg arm.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. These participants received only local standard of care throughout the study; they did not choose to add 250 mg mefloquine at Week 4 (Day 28) or Week 8 (Day 56).
Local Standard of Care; Mefloquine at Week 4	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.

	These participants chose to add 250 mg mefloquine by mouth at Week 4 for 3 days and then weekly through Week 24 to their local standard of care treatment.
Local Standard of Care; Mefloquine at Week 8	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. These participants chose to add 250 mg mefloquine by mouth at Week 8 for 3 days and then weekly through Week 24 to their local standard of care treatment.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Participant Flow: Overall Study

	Local Standard of Care	Local Standard of Care; Mefloquine at Week 4	Local Standard of Care; Mefloquine at Week 8	Local Standard of Care Plus Mefloquine 250 mg
STARTED	7	5	5	20
COMPLETED	0	1	3	7
NOT COMPLETED	7	4	2	13
Death	2	0	0	6
Physician Decision	0	0	2	0
Withdrawal by Subject	3	0	0	2
Other, reason not provided	2	4	0	4
Adverse Event	0	0	0	1

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. These participants received only local standard of care throughout the study; they did not choose to add 250 mg mefloquine at Week 4 (Day 28) or Week 8 (Day 56).
Local Standard of Care; Mefloquine at Week 4	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the

	treatment of a PML patient at their study site or hospital. These participants chose to add 250 mg mefloquine by mouth at Week 4 for 3 days and then weekly through Week 24 to their local standard of care treatment.
Local Standard of Care; Mefloquine at Week 8	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. These participants chose to add 250 mg mefloquine by mouth at Week 8 for 3 days and then weekly through Week 24 to their local standard of care treatment.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.
Total	Total of all reporting groups

Baseline Measures

	Local Standard of Care	Local Standard of Care; Mefloquine at Week 4	Local Standard of Care; Mefloquine at Week 8	Local Standard of Care Plus Mefloquine 250 mg	Total
Number of Participants [units: participants]	7	5	5	20	37
Age [units: years] Mean ± Standard Deviation	48.7 ± 20.56	41.6 ± 11.37	47.4 ± 10.06	48.1 ± 9.4	47.2 ± 12.16
Gender [units: participants]					
Female	1	2	2	5	10
Male	6	3	3	15	27
Race (NIH/OMB) [units: participants]					
American Indian or Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	1	2	2	4	9
White	6	3	3	16	28
More than one race	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0
Disease history [1] [units: participants]					
HIV positive: HAART Naive	3	5	3	13	24

HIV positive: History of HAART	1	0	1	3	5
HIV negative	3	0	1	4	8
JVC Titer at Screening [2] [units: participants]					
<= 50 copies/mL	0	0	0	4	4
> 50 copies/mL	7	5	5	15	32
Missing	0	0	0	1	1

[1] Participants were stratified into the following groups

- HAART-naïve stratum: human immunodeficiency virus (HIV) -positive participants who developed PML in the absence of highly active anti-retroviral therapy (HAART) were placed in this stratum.
- History of HAART stratum: HIV-positive participants who developed PML while on HAART were placed in this stratum.
- HIV-negative stratum: All participants who were HIV-negative were placed in this stratum.

[2] JC virus (human polyomavirus) titer prior to study randomization.

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline to Week 4 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF) [Time Frame: Day 0 (baseline), Week 4]

Measure Type	Primary
Measure Title	Change From Baseline to Week 4 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF)
Measure Description	Change from baseline to Week 4 in JC viral load in CSF is expressed as log10 copies/mL. Negative values indicate a reduction in viral load. Only participants with measurable baseline values are included. Post-baseline values of 'Below the Limit of Quantification' or 'Below Limit of Detection' or 'Negative' were set to 50. Log10 (50) = 1.699
Time Frame	Day 0 (baseline), Week 4
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms. Participants with undetectable CSF JCV load at baseline were not included in the efficacy analysis. All other enrolled participants were included in the efficacy analysis if values for Week 4 were available.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	13	14
Change From Baseline to Week 4 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF) [units: log10 copies/mL] Mean ± Standard Deviation	-0.2424 ± 0.83556	-0.0675 ± 1.52685

Statistical Analysis 1 for Change From Baseline to Week 4 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF)

Groups [1]	All groups
Method [2]	Student's t-test
P Value [3]	0.7132

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

2. Primary: Change From Baseline to Week 8 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF) [Time Frame: Day 0 (baseline), Week 8]

Measure Type	Primary
Measure Title	Change From Baseline to Week 8 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF)
Measure Description	Change from baseline to Week 8 in JC viral load in CSF is expressed as log10 copies/mL. Negative values indicate a reduction in viral load. Only participants with measurable baseline values are included. Post-baseline values of 'Below the Limit of Quantification' or 'Below Limit of Detection' or 'Negative' were set to 50. Log10 (50) = 1.699
Time Frame	Day 0 (baseline), Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms. Participants with undetectable CSF JCV load at baseline were not included in the efficacy analysis. All other enrolled participants were included in the efficacy analysis if values for Week 8 were available.

Reporting Groups

	Description

Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	4	10
Change From Baseline to Week 8 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF) [units: log10 copies/mL] Mean ± Standard Deviation	-0.2843 ± 0.68666	-0.3455 ± 0.93960

Statistical Analysis 1 for Change From Baseline to Week 8 in JC Virus (JCV) Load in Cerebrospinal Fluid (CSF)

Groups [1]	All groups
Method [2]	Student's t-test
P Value [3]	0.9086

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

3. Secondary: Change From Baseline to Week 4 and Week 8 in the Expanded Disability Status Scale (EDSS) Score [Time Frame: Day 0 (baseline), Week 4 and 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in the Expanded Disability Status Scale (EDSS) Score
Measure Description	EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death) was calculated. Negative change scores indicate improvement.
Time Frame	Day 0 (baseline), Week 4 and 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. EDSS was not required for participants who had physical or cognitive

impairments that limited their ability to perform the assessment.

Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in the Expanded Disability Status Scale (EDSS) Score [units: units on a scale] Mean ± Standard Deviation		
Week 4 (n=12, 21)	0.79 ± 1.054	0.50 ± 1.129
Week 8 (n=7, 16)	0.71 ± 1.868	0.88 ± 1.360

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in the Expanded Disability Status Scale (EDSS) Score

4. Secondary: Change From Baseline to Week 4 and Week 8 in Karnofsky Performance Status (KPS) Index Score [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in Karnofsky Performance Status (KPS) Index Score
Measure Description	The KPS Index classifies participants' functional impairment. KPS can be used to compare effectiveness of different therapies and to assess the prognosis in individual participants. KPS was recorded on an 11-point scale (0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100.) where '0=Dead' and '100=Normal, no complaints, no evidence of disease'. The lower the KPS score, the worse the survival for most serious illnesses. The KPS index is subdivided into 3 categories: incapacitated (0 to 40), self-care (50 to 70), and normal activity (80 to 100). Negative change from baseline scores indicate improved prognosis.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. Participants with undetectable CSF JCV load at baseline by the central laboratory were not included in the efficacy analysis. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in Karnofsky Performance Status (KPS) Index Score [units: units on a scale] Mean ± Standard Deviation		
Week 4 (n=12, 21)	0.00 ± 14.771	-8.10 ± 12.891
Week 8 (n=7, 16)	-10.0 ± 26.46	-10.6 ± 19.14

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in Karnofsky Performance Status (KPS) Index Score

5. Secondary: Change From Baseline to Week 4 and Week 8 in Symbol Digit Modalities Test (SDMT) [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in Symbol Digit Modalities Test (SDMT)
Measure Description	The SDMT is a simple substitution task. The test gives participants 90 seconds to pair specific numbers with given geometric figures as a measure for screening cognitive impairment. The total score is the total number of correctly completed boxes in the time allowed. The test score range is from 0 (worst outcome) to 110 (best outcome). Negative change from baseline scores indicates a worsening outcome.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. SDMT was not required for participants who had physical or cognitive impairments that limited their ability to perform the assessment. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description

Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in Symbol Digit Modalities Test (SDMT) [units: units on a scale] Mean ± Standard Deviation		
Week 4 (n=6,8)	4.00 ± 6.723	-1.50 ± 3.780
Week 8 (n=3,6)	1.7 ± 10.12	3.8 ± 6.43

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in Symbol Digit Modalities Test (SDMT)

6. Secondary: Change From Baseline to Week 4 and Week 8 in Participants' Neurological Function Using a Visual Analog Scale (VAS) [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in Participants' Neurological Function Using a Visual Analog Scale (VAS)
Measure Description	Participants rate their neurological function on a scale of 100 mm line, where the 0 end of the scale indicates poor neurological function and 100 indicates excellent neurological function. VAS was not required for participants who had physical or cognitive impairments that limited their ability to perform the assessment. Negative change from baseline scores indicates a worsening outcome.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. VAS was not required for participants who had physical or cognitive impairments that limited their ability to perform the assessment. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have

	included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in Participants' Neurological Function Using a Visual Analog Scale (VAS) [units: units on a scale] Mean ± Standard Deviation		
Week 4 (n=9,16)	8.9 ± 29.14	-0.7 ± 33.71
Week 8 (n=4,13)	26.3 ± 49.00	3.5 ± 23.87

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in Participants' Neurological Function Using a Visual Analog Scale (VAS)

7. Secondary: Participants With Gadolinium (Gd)-Enhanced Lesions at Baseline, Week 4 and Week 8 as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Participants With Gadolinium (Gd)-Enhanced Lesions at Baseline, Week 4 and Week 8 as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains
Measure Description	No text entered.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. Participants with undetectable CSF JCV load at baseline by the central laboratory were not included in the efficacy analysis. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Participants With Gadolinium (Gd)-Enhanced Lesions at Baseline, Week 4 and Week 8 as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains [units: participants]		
Week 0 (n=15,21)	8	8
Week 4 (n=12,12)	5	8
Week 8 (n=5,11)	1	7

No statistical analysis provided for Participants With Gadolinium (Gd)-Enhanced Lesions at Baseline, Week 4 and Week 8 as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains

8. Secondary: Change From Baseline to Week 4 and Week 8 in T1 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in T1 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains
Measure Description	No text entered.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. Participants with undetectable CSF JCV load at baseline by the central laboratory were not included in the efficacy analysis. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed		

[units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in T1 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains [units: log10 mm^3] Mean ± Standard Deviation		
Week 4 (n=12,11)	0.1407 ± 0.20345	0.1631 ± 0.22523
Week 8 (n=5,11)	0.0248 ± 0.12425	0.1029 ± 0.26502

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in T1 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains

9. Secondary: Change From Baseline to Week 4 and Week 8 in T2 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains [Time Frame: Day 0 (baseline), Week 4, Week 8]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 4 and Week 8 in T2 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains
Measure Description	No text entered.
Time Frame	Day 0 (baseline), Week 4, Week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants with values at the time frames being measured. Participants with undetectable CSF JCV load at baseline by the central laboratory were not included in the efficacy analysis. Local standard of care participants who added mefloquine at Week 4 or Week 8 were counted as being dosed under both treatment arms.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Change From Baseline to Week 4 and Week 8 in T2 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains		

[units: log10 mm^3] Mean ± Standard Deviation		
Week 4 (n=12,11)	0.1704 ± 0.22012	0.1619 ± 0.17501
Week 8 (n=5,10)	0.1738 ± 0.21454	0.1050 ± 0.23429

No statistical analysis provided for Change From Baseline to Week 4 and Week 8 in T2 Lesion Volume as Seen on Magnetic Resonance Imaging (MRI) Scans of Participants' Brains

10. Secondary: Participants Who Died Within 6 Months [Time Frame: Day 1 up to 6 months]

Measure Type	Secondary
Measure Title	Participants Who Died Within 6 Months
Measure Description	The death event is counted under the treatment arm relative to adding mefloquine to the treatment regimen.
Time Frame	Day 1 up to 6 months
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety population: All participants who enrolled in the study and were dosed, and who have at least 1 post-baseline safety assessment. The death event is counted under the treatment arm relative to adding mefloquine to the treatment regimen.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24. Also includes participants who were randomized to receive local standard of care (only) and added mefloquine at Week 4 or Week 8.

Measured Values

	Local Standard of Care	Local Standard of Care Plus Mefloquine 250 mg
Number of Participants Analyzed [units: participants]	17	30
Participants Who Died Within 6 Months [units: participants]	2	5

No statistical analysis provided for Participants Who Died Within 6 Months

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Day 1 to Month 6
Additional Description	Because participants were primarily patients with HIV/Acquired Immunodeficiency Syndrome (AIDS), SAEs considered to be AIDS-Defining Events (ADEs) were exempt from SAE reporting and were collected on a specific case report form instead of being captured as SAEs. However, any ADE that resulted in death did not qualify for an SAE exemption.

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Weeks 4 or 8 to their standard of care treatment are counted in this treatment arm until the time of switching to mefloquine treatment.
Local Standard of Care; Mefloquine at Week 4	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Week 4 to their standard of care treatment are counted in this treatment arm once mefloquine treatment started.
Local Standard of Care; Mefloquine at Week 8	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Week 8 to their standard of care treatment are counted in this treatment arm once mefloquine treatment started.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Serious Adverse Events

	Local Standard of Care	Local Standard of Care; Mefloquine at Week 4	Local Standard of Care; Mefloquine at Week 8	Local Standard of Care Plus Mefloquine 250 mg
Total, serious adverse events				
# participants affected / at risk	5/17 (29.41%)	1/5 (20.00%)	3/5 (60.00%)	13/20 (65.00%)
Blood and lymphatic system disorders				
Pancytopenia † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
General disorders				
Death † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)

Infections and infestations				
Appendicitis † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Urinary tract infection † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Pneumonia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Periorbital cellulitis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Progressive multifocal leukoencephalopathy † 1				
# participants affected / at risk	2/17 (11.76%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Staphylococcal infection † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Urinary tract infection pseudomonal † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Osteomyelitis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Meningitis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Candida pneumonia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Injury, poisoning and procedural complications				
Narcotic intoxication † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Metabolism and nutrition disorders				
Marasmus † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)

Musculoskeletal and connective tissue disorders				
Pain in extremity † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Muscular weakness † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Nervous system disorders				
Neurological decompensation † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Status epilepticus † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Convulsion † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	3/20 (15.00%)
Psychiatric disorders				
Delirium † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Cough † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Chronic obstructive pulmonary disease † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Pneumonia aspiration † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Dyspnoea † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Asphyxia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)

Respiratory failure † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Respiratory tract congestion † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	Day 1 to Month 6
Additional Description	Because participants were primarily patients with HIV/Acquired Immunodeficiency Syndrome (AIDS), SAEs considered to be AIDS-Defining Events (ADEs) were exempt from SAE reporting and were collected on a specific case report form instead of being captured as SAEs. However, any ADE that resulted in death did not qualify for an SAE exemption.

Frequency Threshold

Threshold above which other adverse events are reported	0%

Reporting Groups

	Description
Local Standard of Care	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Weeks 4 or 8 to their standard of care treatment are counted in this treatment arm until the time of switching to mefloquine treatment.
Local Standard of Care; Mefloquine at Week 4	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Week 4 to their standard of care treatment are counted in this treatment arm once mefloquine treatment started.
Local Standard of Care; Mefloquine at Week 8	Participants were randomized to receive local standard of care, which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital. Participants who chose to add mefloquine at Week 8 to their standard of care treatment are counted in this treatment arm once mefloquine treatment started.
Local Standard of Care Plus Mefloquine 250 mg	Participants were randomized to receive local standard of care (which may have included any treatment or procedure that the Investigator would normally use in the treatment of a PML patient at their study site or hospital) and 250 mg mefloquine by mouth on Days 0, 1, and 2 and then weekly through Week 24.

Other Adverse Events

	Local Standard of Care	Local Standard of Care; Mefloquine at Week 4	Local Standard of Care; Mefloquine at Week 8	Local Standard of Care Plus Mefloquine 250 mg

Total, other (not including serious) adverse events				
# participants affected / at risk	12/17 (70.59%)	4/5 (80.00%)	5/5 (100.00%)	19/20 (95.00%)
Blood and lymphatic system disorders				
Lymphadenopathy † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Pancytopenia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Anaemia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Hilar lymphaedenopathy † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Neutropenia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Splenomegaly † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Cardiac disorders				
Arrhythmia supraventricular † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Tachycardia † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Dilatation ventricular † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Sinus arrhythmia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Sinus bradycardia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Sinus tachycardia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Ear and labyrinth disorders				
Vertigo † 1				

# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Ear pain † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Otorrhoea † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Eye disorders				
Diplopia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Iridocyclitis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Scotoma † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Visual impairment † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Eye discharge † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Eye irritation † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Eye pain † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Inflammation of lacrimal passage † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Periorbital oedema † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Photopsia † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Vision blurred † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Gastrointestinal disorders				
Dysphagia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	3/20 (15.00%)

Nausea † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	3/20 (15.00%)
Constipation † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	2/20 (10.00%)
Abdominal pain † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Ascites † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Gastrooesophageal reflux disease † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Glossitis † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Vomiting † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Abdominal pain upper † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Cheilitis † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Colitis † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Diarrhoea † [1]				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Intestinal mucosal hypertrophy † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Rectal haemorrhage † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Tooth loss † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
General disorders				
Asthenia † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	2/20 (10.00%)

Pyrexia † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	2/20 (10.00%)
Feeling hot † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Injection site reaction † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Irritability † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Local swelling † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Mucosal membrane hyperplasia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Chest pain † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Chills † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Extravasation † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Gait disturbance † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Infusion site haematoma † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Oedema peripheral † 1				
# participants affected / at risk	2/17 (11.76%)	2/5 (40.00%)	0/5 (0.00%)	0/20 (0.00%)
Hepatobiliary disorders				
Hyperbilirubinaemia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Immune system disorders				
Immune reconstitution syndrome † 1				
# participants affected / at risk	2/17 (11.76%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Infections and infestations				

Pneumonia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	3/20 (15.00%)
Progressive multifocal leukoencephalopathy † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	3/20 (15.00%)
Anogenital warts † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Bronchitis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Campylobacter gastroenteritis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Candidiasis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Folliculitis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	1/5 (20.00%)	1/20 (5.00%)
Genital herpes † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Helicobacter gastritis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Herpes simplex † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Oral candidiasis † 1				
# participants affected / at risk	2/17 (11.76%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Sinusitis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Urinary tract infection † 1				
# participants affected / at risk	2/17 (11.76%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Bacillus infection † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Bacterial disease carrier † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Cellulitis † 1				

# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Conjunctivitis infection † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Enterobacter infection † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Escherichia infection † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Klebsiella infection † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Oral herpes † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Pelvic abscess † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Purulent discharge † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Pyomyositis † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Rash pustular † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Sepsis † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Tinea versicolour † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Injury, poisoning and procedural complications				
Contusion † [1]				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	2/20 (10.00%)
Limb injury † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Excoriation † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Fall † [1]				

# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	1/5 (20.00%)	0/20 (0.00%)
Fracture displacement † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Head injury † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Joint dislocation † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Mouth injury † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Investigations				
Aspartate aminotransferase increased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Blood lactate dehydrogenase increased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Liver function test abnormal † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Skin turgor decreased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Weight decreased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Blood bicarbonate decreased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Blood bilirubin increased † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Blood glucose increased † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Blood potassium decreased † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Blood potassium increased † [1]				
# participants affected / at	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)

risk				
Blood pressure increased † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Breath sounds abnormal † 1				
# participants affected / at risk	1/17 (5.88%)	2/5 (40.00%)	0/5 (0.00%)	0/20 (0.00%)
Eosinophil count increased † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Haematocrit decreased † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Haemoglobin decreased † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Neurological examination abnormal † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Prealbumin decreased † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Red blood cell count decreased † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Vitamin D decreased † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
White blood cell count decreased † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Metabolism and nutrition disorders				
Hyponatraemia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Dehydration † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Hypocalcaemia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hypokalaemia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)

Magnesium deficiency † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hyperlipidaemia † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Vitamin D deficiency † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Musculoskeletal and connective tissue disorders				
Pain in extremity † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	2/20 (10.00%)
Back pain † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Mobility decreased † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Muscle spasms † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Arthralgia † [1]				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	1/5 (20.00%)	0/20 (0.00%)
Bursitis † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Coccydynia † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Joint effusion † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Joint swelling † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Muscle atrophy † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Muscular weakness † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	1/5 (20.00%)	0/20 (0.00%)
Musculoskeletal disorder † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)

Musculoskeletal pain † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Musculoskeletal stiffness † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Myalgia † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Myositis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Uterine leiomyoma † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Nervous system disorders				
Headache † 1				
# participants affected / at risk	0/17 (0.00%)	2/5 (40.00%)	1/5 (20.00%)	4/20 (20.00%)
Ataxia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Epilepsy † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Hemianopia homonymous † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	2/20 (10.00%)
Hemiparesis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	2/20 (10.00%)
Apallic syndrome † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Aphasia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Cerebellar syndrome † 1				
# participants affected / at risk	2/17 (11.76%)	0/5 (0.00%)	1/5 (20.00%)	1/20 (5.00%)
Cognitive disorder † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Convulsion † 1				

# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Extensor plantar response † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hemiplegia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hyperreflexia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hypertonia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hypoaesthesia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Hypokinesia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Lethargy † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Memory impairment † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Movement disorder † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Multiple sclerosis relapse † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Muscle spasticity † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Partial seizures † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Syncope † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Visual field defect † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Disarthria † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
† 1				

Nervous system disorder				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Neuropathy peripheral † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Nystagmus † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Sensory loss † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Tremor † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Psychiatric disorders				
Anxiety † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	2/20 (10.00%)
Abnormal behaviour † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Confusional state † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	1/5 (20.00%)	1/20 (5.00%)
Depression † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Insomnia † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Sleep disorder † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Abnormal dreams † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Agitation † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Delusion † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Drug abuse † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Drug dependence † 1				

# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Dysphemia † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Hallucination, auditory † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Renal and urinary disorders				
Pollakiuria † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Renal failure † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Urinary incontinence † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Micturition urgency † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Urinary retention † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Reproductive system and breast disorders				
Cervical dysplasia † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Vaginal discharge † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Pneumothorax † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Acquired diaphragmatic eventration † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Aspiration † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Atelectasis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)

Chronic obstructive pulmonary disease † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Cough † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Dyspnoea † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Dyspnoea exertional † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Hypoventilation † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Hypoxia † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Oropharyngeal pain † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Pleural effusion † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Pneumonitis † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Productive cough † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Respiratory distress † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Respiratory tract congestion † [1]				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	1/5 (20.00%)	0/20 (0.00%)
Tachypnoea † [1]				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Tonsillar hypertrophy † [1]				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Skin and subcutaneous tissue disorders				
Alopecia † [1]				
# participants affected / at				

risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Rash pruritic † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Urticaria † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Blister † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Decubitus ulcer † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Dennie-Morgan fold † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Dry skin † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	1/5 (20.00%)	0/20 (0.00%)
Erythema † 1				
# participants affected / at risk	0/17 (0.00%)	2/5 (40.00%)	0/5 (0.00%)	0/20 (0.00%)
Exfoliative rash † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Petechiae † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Pruritus † 1				
# participants affected / at risk	1/17 (5.88%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Psoriasis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Rash † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	1/5 (20.00%)	0/20 (0.00%)
Rash macular † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Rash papular † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Seborrhoeic dermatitis † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Skin exfoliation † 1				

# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)
Skin hypertrophy † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Skin ulcer † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Vascular disorders				
Hypertension † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	1/20 (5.00%)
Hypotension † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Phlebitis † 1				
# participants affected / at risk	0/17 (0.00%)	0/5 (0.00%)	0/5 (0.00%)	1/20 (5.00%)
Deep vein thrombosis † 1				
# participants affected / at risk	1/17 (5.88%)	0/5 (0.00%)	0/5 (0.00%)	0/20 (0.00%)
Phlebolith † 1				
# participants affected / at risk	0/17 (0.00%)	1/5 (20.00%)	0/5 (0.00%)	0/20 (0.00%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

From ongoing analysis, it became clear, based on conditional power calculations, that the study would not reach its primary endpoint, a decrease of JC viral load in CSF with mefloquine treatment; therefore, the study was terminated early.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days. The sponsor cannot require changes to the communication and cannot extend the embargo.

☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: The PI can publish, for noncommercial purposes only, results and methods of the trial, but no other Sponsor Confidential Information. PI must give Sponsor no less than 45 to 60 days as agreed within their clinical trial agreement to review any manuscript for a proposed publication and must delay publication for up to an additional 60 to 90 days thereafter if Sponsor needs to file any patent application to protect any of Sponsor's intellectual property contained in the proposed publication.

Results Point of Contact:

Name/Title: Biogen Idec Study Medical Director
Organization: Biogen Idec
e-mail: clinicaltrials@biogenidec.com

Publications of Results:

Clifford DB, Nath A, Cinque P, Brew BJ, Zivadinov R, Gorelik L, Zhao Z, Duda P. A study of mefloquine treatment for progressive multifocal leukoencephalopathy: results and exploration of predictors of PML outcomes. J Neurovirol. 2013 Aug;19(4):351-8. doi: 10.1007/s13365-013-0173-y. Epub 2013 Jun 4.

Responsible Party:	Biogen Idec
ClinicalTrials.gov Identifier:	NCT00746941 History of Changes
Other Study ID Numbers:	111JC101
Study First Received:	September 3, 2008
Results First Received:	January 3, 2013
Last Updated:	July 2, 2014
Health Authority:	Brazil: National Health Surveillance Agency Italy: Ministry of Health Spain: Spanish Agency of Medicines Germany: Federal Institute for Drugs and Medical Devices United States: Food and Drug Administration