Clinical trial results: "A national, multicenter, single-blind, parallel-group, controlled study, to evaluate the efficacy and tolerability of the sequential combination of Mitoxantrone and Interferon beta 1a (Rebif 44 mcg 3 times a week) in patients affected by MS, in the initial phase of the disease"

Summary

EudraCT number*	2004-001601-10
Trial protocol	MULTICENTTRIC, NATIONAL, SINGLE BLIND,CONTROLLED IN PARALLEL GROUP TO EVALUATE THE SAFETY AND EFFICACY OF THE SEQUENTIAL COMBINATION OF MITOXANTRONE AND BETA INTERFERON REBIF 44 mcg X 3 TIMES WEEKLY IN PATIENTS AFFECTED BY MULTIPLE SCLEROSIS, IN THE FIRST STEP OF THE DISEASE
Global end of trial date*	03 May 2019

Trial information

Trial identification	
Sponsor protocol code*	MTX10R44
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	Not applicable
WHO universal trial number (UTN)	-

Notes:

Sponsors details*	
Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	Prof. Massimo Filippi, IRCCS Ospedale San Raffaele e-mail: filippi.massimo@hsr.it phone: +39 02 2643 3958
Scientific contact	Prof. Massimo Filippi, IRCCS Ospedale San Raffaele e-mail: filippi.massimo@hsr.it phone: +39 02 2643 3958

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

Results analysis stage	
Analysis stage*	Final
Date of interim/final analysis*	

Is this the analysis of the primary completion data?*	Yes
Global end of trial reached?*	Yes
Global end of trial date*	03 May 2019
Was the trial ended prematurely?	No

General information about the trial

Main objective of the trial*: To evaluate effectiveness and tolerability of the sequential treatment with Mitoxantrone (10mg/m^2 monthly for 6 months) and Interferon beta-1a (Rebif 44mcg 3 times a week) *versus* Interferon beta-1a alone, in multiple sclerosis (MS) patients at high risk of progression at initial stage of the disease.

Actual start date of recruitment*	21 November 2005
Long term follow-up planned*	No
If Yes, rationale:	Not applicable
Duration	Global trial duration ~ 13 years (period of observation: 4 Years per subject)
Independent data monitoring committee(IDMC) involvement?*	No
Protection of trial subjects*:	Study conducted in full compliance with the principles of the "Declaration of Helsinki" (9th revision, Fortaleza), and the International Conference on Harmonization (ICH) guidelines. EU Clinical Trials Directives 2001/20/EC and 2005/28/EC were followed.
Background therapy:	Medications not allowed were: i) previous immunosuppressive and/or immunomodulating treatments; ii) use of steroids within two weeks before treatment; iii) steroid therapy protracted for longer than one month; iv) experimental treatments within 6 months before study start and during the study.
Evidence for comparator:	The traditional escalation strategy consists in treating MS patients at high risk of evolution firstly with immunomodulatory drugs (e.g. Interferon beta-1a) followed by immunosuppressants (e.g. MTX). Instead, the study proposed a therapeutic plan based on induction strategy, i.e. immunosuppressant treatment (i.e. MTX) to stop inflammation, which could maintain the profit through a long-term immunomodulatory treatment (i.e. Interferon beta-1a).

Population of trial subjects

Subjects enrolled per country

Country:	Italy
Planned number of subjects	270
Actual Number of subjects enrolled*	55
Worldwide total number of subjects	55
EEA total number of subjects	55

Subjects enrolled per age group

In utero*	0
Preterm newborn - gestational age < 37wks*	0
Newborns (0-27 days)*	0
Infants and toddlers (28 days-23months)*	0
Children (2-11 years)*	0
Adolescents (12-17 years)*	0
Adults (18-64 years)*	55
From 65 to 84 years*	0
85 years and over*	0

Subject disposition

Recruitment details: *Enter key information relevant to the recruitment process for the trial (eg gates of recruitment period and territories)* *Patients were selected for the study by their referring medical centres. Eligible patients must have a MS diagnosis according to the Mc Donald criteria, with onset of disease within one year from enrolment and with a high short-term evolution risk, as from clinical observation*

Pre-assignment - *Screening details*: *Enter relevant information related to screening (eg screening criteria, significant events and approaches)* *In order to be considered eligible, all the following criteria were to be met:*
1. Patients must show MS symptoms according to Mc Donald criteria:
a. Single episode with temporal dissemination shown in an MRI (performed less than 2 months prior to inclusion) if it satisfies at least one of the following criteria:
i. multifocal presentation
ii. episode determining serious disability (EDSS ≥ 3.5)
iii. 2 or more Gd enhancing lesions at MRI examination
iv. or 9 or more lesions in T2, plus a Gd enhancing lesion
2. Patients must be between 18 and 50 years of age
3. Onset of disease must be within 1 year from enrolment.
4. Women of child-bearing potential must practice an acceptable method of birth control, for the whole duration of the study;
5. Patients must be able to provide their own informed consent before their inclusion in the study.

Period 1

Period title*	*Enter a title describing the stage of the trial. If the only one period is defined, the default title should be "Overall Trial"* *Overall Trial*
Is this the baseline period?	Yes
Allocation method*	Randomised - controlled
Blinding used*	Single blind

Arms

Arm title*	*Enter a title to identify the arm - Add arm and IMP if applicable* ***Group A***
Arm description:	*Interferon beta 1a only group*
Arm type*	Active comparator
Investigational medicinal product name*	Interferon beta-1a (Rebif 44)
Investigational medicinal product code	
Other name	NA
Pharmaceutical forms*	Solution for injection
Routes of administration*	Subcutaneous injection
Dosage and administration details*	44 mcg 3 times per week from baseline to Month 48

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	28	Group A
Completed*	12	Group A
Subject non-completion reason (if applicable)		
AE, non fatal	-	-
AE, fatal	-	-
Consent withdrawn by subject	3	Group A

Lack of efficacy	4	Group A
Lost to follow up	8	Group A
Physician decision	-	-
Pregnancy	-	-
Protocol Deviation	-	-
Other	1	Group A

Arm title*	*Enter a title to identify the arm - Add arm and IMP if applicable* ***Group B***
Arm description:	*Mitoxantrone followed by Interferon beta 1a*
Arm type*	Experimental
Investigational medicinal product name*	Mitoxantrone (Onkotrone)+ Interferon beta-1a (Rebif 44)
Investigational medicinal product code	
Other name	NA
Pharmaceutical forms*	Solution for injection
Routes of administration*	Mitoxantrone: infusion Interferon beta 1-a: subcutaneous injection
Dosage and administration details*	Mitoxantrone: 10mg/m^2 monthly for 6 months Interferon beta-1a: 44 mcg 3 times per week from month 6 to month 48

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	27	Group B
Completed*	11	Group B
Subject non-completion reason (if applicable)		
AE, non fatal	2	Group B
AE, fatal	-	-
Consent withdrawn by subject	-	-
Lack of efficacy	-	-
Lost to follow up	7	Group B
Physician decision	-	-
Pregnancy	-	-
Protocol Deviation	1	Group B
Other	6	Group B

Baseline characteristics

Reporting groups* Overall cohort	
Reporting group title*	Overall cohort
Number of subjects at the baseline*	55

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	Group A
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Enter a clear description which defines this set of subjects* *Interferon beta 1a only group*
Number of subjects in subjects analysis set*	28
Subject analysis set title*	Group B
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Enter a clear description which defines this set of subjects* *Mitoxantrone followed by Interferon beta 1a*
Number of subjects in subjects analysis set*	27

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical	NA	NA	NA

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	Mean age	Years Months Weeks Days	Arithmetic Mean Median least square mean geometric mean log mean	full range (min-max) standard deviation inter quartile range
Overall cohort	N=49 subjects (6 missing)	Years	Mean=33.82	SD=8.51
Group A	N=26 subjects (2 missing)	Years	Mean=33.12	SD=8.62
Group B	N=23 subjects (4 missing)	Years	Mean=34.61	SD=8.51

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	Sex	Number of subjects	Female Male
Overall cohort	N=5 subjects	53	30 Females

	missing		18 Males
Group A	N=2 subjects missing	27	13 Females 12 Males
Group B	N=3 subjects missing	26	17 Females 6 Males

Study specific characteristics

	Characteristic title*	Units *	Categories*	Number of subject for each categories
Study specific categorical	NA	NA	NA	NA
Study specific categorical	NA	NA	NA	NA
Study specific categorical	NA	NA	NA	NA
Study specific categorical	NA	NA	NA	NA
Study specific categorical	NA	NA	NA	NA

End points

Add subject analysis set if you wish to report on groups different form reporting groups defined above

Subject analysis set title*	Group A
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Enter a clear description which defines this set of subjects* *Interferon beta 1a only group*
Number of subjects in subjects analysis set*	27
Subject analysis set title*	Group B
Subject analysis set type*	Intention to treat
Subject analysis set description*	*Enter a clear description which defines this set of subjects* *Mitoxantrone followed by Interferon beta 1a*
Number of subjects in subjects analysis set*	26

End points definitions

End point title*	Rate of patients free from disease at Month 24	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Percentage	Percentage: (number of patients / total number of patients) * 100
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	NA
Precision/dyspersion type*	NA	NA

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 24 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 24	Month 24
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Percentage	59.3 %	80.8%

End points definitions

End point title*	Rate of patients with disease progression at Month 48 (EDSS increase >= 1.0)	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Percentage	Percentage: (number of patients / total number of patients) * 100
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	NA
Precision/dyspersion type*	NA	NA

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 48	Month 48
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Number of subjects	27.3%	0%

End points definitions

End point title*	Time to first relapse	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Measurable
If countable, Countable units*:	Number of subjects	NA
If measurable, Measurable units*	NA	Months
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Artithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Overall trial	Overall trial
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean time to first relapse (SD) [months]	8.27 (7.23)	11.33 (11.78)

End points definitions

End point title*	Number of relapses at Month 24	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Number of patients stratified by number of relapses	Number
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	NA

Precision/dyspersion type*	NA	NA

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 24 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 24	Month 24
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Number of patients showing 0 relapses	16	21
Number of patients showing 1 relapse	8	4
Number of patients showing 2 relapses	2	1
Number of patients showing 3 relapses	1	0

End points definitions

End point title*	Number of relapses at Month 48	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Number of patients stratified by number of relapses	Number
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	NA
Precision/dyspersion type*	NA	NA

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 48	Month 48

Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Number of patients showing 0 relapses	16	20
Number of patients showing 1 relapse	6	5
Number of patients showing 2 relapses	3	1
Number of patients showing 3 relapses	2	0

End points definitions

End point title*	Mean disability (EDSS score) at Month 24	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Measurable
If countable, Countable units*:	NA	NA
If measurable, Measurable units*	NA	Unitless
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Arithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Month 24 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 24	Month 24
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean disability – EDSS score (SD)	2.08 (1.30)	2.07 (1.12)

End points definitions

End point title*	Mean disability (EDSS score) at Month 48	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Measurable
If countable, Countable units*:	NA	NA
If measurable, Measurable units*	NA	Unitless
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Arithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Month 48 visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Month 48	Month 48
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean disability – EDSS score (SD)	2.41 (1.26)	1.85 (1.18)

End points definitions

End point title*	Total number of T1-enhancing lesions	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Number of lesions	NA
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Arithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit, stratified by visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Overall trial	Overall trial
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean number of T1-enhancing lesions, Baseline (SD)	4.54 (7.38)	7.17 (22.71)
Mean number of T1-enhancing lesions, Month 6 (SD)	0	0
Mean number of T1-enhancing lesions, Month 12 (SD)	0	0
Mean number of T1-enhancing lesions, Month 24 (SD)	0	0
Mean number of T1-enhancing lesions, Month 36 (SD)	0	0
Mean number of T1-enhancing lesions, Month 48 (SD)	0	0.60 (0.89)

End points definitions

End point title*	Number of new T2-hyperintense lesions	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Countable
If countable, Countable units*:	Number of lesions	NA
If measurable, Measurable units*	NA	NA
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Artithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Month 6 to Month 48 visit, stratified by visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Overall trial	Overall trial
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean number of new T2-hyperintense lesions, Month 6 (SD)	1.45 (2.58)	0.57 (0.79)
Mean number of new T2-hyperintense lesions, Month 12 (SD)	0.45 (1.51)	0.17 (0.41)
Mean number of new T2-hyperintense lesions, Month 24 (SD)	1.83 (2.64)	1.33 (3.27)
Mean number of new T2-hyperintense lesions, Month 36 (SD)	0.20 (0.45)	0.50 (1.22)
Mean number of new T2-hyperintense lesions, Month 48 (SD)	0	0.60 (0.89)

End points definitions

End point title*	T2-hyperintense lesion volume	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Measurable
If countable, Countable units*:	NA	NA
If measurable, Measurable units*	Cubic mm	Cubic mm
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Artithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit, stratified by visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Overall trial	Overall trial
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Mean T2 lesion volume, Baseline (SD)	14696 (14519)	9657 (11787)
Mean T2 lesion volume, Month 6 (SD)	11009 (6597)	13287 (15034)
Mean T2 lesion volume, Month 12 (SD)	11798 (7017)	13644 (12606)
Mean T2 lesion volume, Month 24 (SD)	12754 (8938)	13511 (12137)
Mean T2 lesion volume, Month 36 (SD)	12080 (9663)	7757 (8854)
Mean T2 lesion volume, Month 48 (SD)	9657 (7302)	9975 (9913)

End points definitions

End point title*	Atrophy (percentage brain volume change)	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	Measurable
If countable, Countable units*:	NA	NA
If measurable, Measurable units*	Percentage brain volume change	%
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	Artithmetic mean
Precision/dyspersion type*	SD	Standard deviation

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*: Period from Baseline to Month 48 visit, stratified by visit

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	Group A	Group B
Period	Overall trial	Overall trial
Arms	Group A	Group B
subject analysis sets	Intention to treat	Intention to treat
Percentage brain volume change, Month 24 (SD)	-2.52 (0.85)	-3.00 (3.51)
Percentage brain volume change, Month 48 (SD)	-1.08*	-0.99 (1.28)

*No SD is reported for Month 48 measurement because just one patient reached this endpoint at Month 48

Adverse events

Adverse events information

Timeframe for reporting adverse events*: *Enter the time point(s) or time period for AE assessment*

First patient first visit: 21 November 2005
Last recruitment date: 07 July 2015
Study closure: 03 May 2019

Adverse event reporting additional description: *Enter information about the AE collection and provide details about the method of assessment and monitoring*

Adverse events were monitored during the clinical visits of the study, scheduled at Baseline, Month 1, Month 3, Month 6 and every three months till Month 48 for Group A, and scheduled at Baseline, Month 1, Month 2, Month 3, Month 4, Month 5, Month 6 and every three months till Month 48 for Group B.

Assessment type*	Systematic or Non Systematic
Frequency threshold for reporting non-serious adverse events*	*Enter the frequency of non SAE that are reported in the results database for all arms or reporting groups* *All non-serious adverse events were reported regardless of frequency*

Dictionary used

Dictionary name*	MedDRA or CTCAE
Dictionary version*	7

Adverse events reporting group definition

Use arms from baseline period as reporting groups
OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	55
Subjects affected by non -SAE*	40
Total number of deaths (all causes)*	0
Total number of deaths resulting from adverse event*	0

Reporting group title*: *Group A*

For this reporting group, provide the following totals:

Subject exposed*	28
Subjects affected by non -SAE*	19
Total number of deaths (all causes)*	0
Total number of deaths resulting from adverse event*	0

Reporting group title*: *Group B*

For this reporting group, provide the following totals:

Subject exposed*	27
Subjects affected by non -SAE*	21
Total number of deaths (all causes)*	0
Total number of deaths resulting from adverse event*	0

Serious adverse event details and values

System organ class*: Pregnancy, puerperium and perinatal conditions

Event term*: Exposure during pregnancy

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number
Group B	1	27	1	1	0	0

Non - Serious adverse event details and values

System organ class*: Reproductive system and breast disorders

Event terms*: Vaginitis, Amenorrhoea, Uterine polyp

System organ class*: General disorders and administration site conditions

Event terms*: Chills, Astenia, Fatigue

System organ class*: Infections and infestations

Event terms*: Influenza, Parainfluenza, Tracheitis, Measles, Urinary tract infection, Herpes infection

System organ class*: Hepatobiliary disorders

Event terms*: Transaminases increased, Hepatic dysfunction

System organ class*: Blood and lymphatic disorders

Event terms*: Lymphopenia, Neutropenia

System organ class*: Nervous system disorders

Event terms*: Syncope, Drowsiness, Insomnia, Paresthesia, Disesthesia, Dizziness, Vertigo, Headache, Spasticity

System organ class*: Gastrointestinal disorders

Event terms*: Nausea, Vomiting, Abdominal colic

System organ class*: Muscoloskeletal and connective tissue disorders

Event terms*: Weakness, Back pain, Muscle pain, Arthralgia, Cramps

System organ class*: Endocrine disorders

Event terms*: Thyroid dysfunction

System organ class*: Renal and urinary disorders

Event terms*: Urinary urgency

System organ class*: Cardiac disorders

Event terms*: Tachycardia

System organ class*: Vascular disorders

Event terms*: Trombophlebitis

System organ class*: Skin and subcutaneous tissue disorders

Event terms*: Dermatitis, Erythema

System organ class*: Psychiatric disorders

Event terms*: Anxiety, Depression

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number
Group A	19	28	72
Group B	21	27	114

Additional note: In Group A 37 of the adverse events were not related to the study treatment and 35 were related; only 1 adverse event led to treatment interruption by 1 patient. In Group B 32 of the adverse events were not related to the study treatment and 79 were considered related; 8 adverse events led to treatment interruption by 6 patients. The majority of the adverse events reported were of mild-moderate severity: only 5 adverse events were severe, 1 in Group A and 4 in Group B. One of the 5 severe adverse events was also evaluated as serious (as reported above, suspected pregnancy during Mitoxantrone treatment)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? No

Date	Amendment
NA	NA

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? No

If Yes, Interruption date

Interruption descrption

Limitations and caveats

The trial enrolled a very low number of patients (55 instead of the planned 242) and data were not always properly collected by clinical sites. This prevented reliable results and the possibility to properly compare the two treatment groups using formal statistical tests. Even if some results were visible, taken in consideration of the poor number of patients enrolled and the low number of data analysed, no reliable efficacy conclusion could be drawn.
From the safety point of view, the typology of recorded adverse events as treatment-related was aligned with the safety profile of Mitoxantrone and Interferon beta-1a reported in the respective summary of product characteristics.

Online references