Clinical trial results:
An open-label, prospective, single-centre, phase II study to assess dose and dose interval requirements with respect to efficacy and safety of AOP2014, PEG-Proline-Interferon alpha-2b, in patients with primary myelofibrosis (grade MF-0 and MF-1)

Summary

EudraCT number	2014-001367-13
Trial protocol	AT
Global end of trial date	24 April 2019

Results information

Result version number	v1 (current)
This version publication date	16 April 2023
First version publication date	16 April 2023

Trial information

Trial identification

Sponsor protocol code	IASO_MF

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria,
Public contact	Medical University of Vienna, AOP ORPHAN PHARMACEUTICALS AG, sanda.sturlan@aoporphan.com
Scientific contact	Medical University of Vienna, AOP ORPHAN PHARMACEUTICALS AG, sanda.sturlan@aoporphan.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2017
Global end of trial reached?	Yes
Global end of trial date	24 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of novel Pegylated-Pro Interferon α-2b formulation in terms of response rate in both, Interferon naive and pretreated patients with early primary myelofibrosis (MF-0 to MF-1).
The favourable pharmacokinetic profile of AOP2014 suggests possible dose reduction and/or treatment interval prolongation options, which, at preserved efficacy, may improve the tolerability of IFN α treatment.

Protection of trial subjects:

AOP2014 belongs to the interferon substance class that is effectively able to suppress the malignant of myeloid precursor cells and subsequently is expected to possibly adjourn or avoid long term sequel to thrombosis, transformation into overt myelofibrosis and transformation into acute leukemia. The tolerability of peg-IFN-α-2b might potentially have a positive impact on reducing the drop-out rate compared to conventional IFNs. It's expected that the reduced administration frequency of peg-IFN-α-2b will contribute to higher compliance rates.
The safety profile of interferon alpha is well characterised after clinical experience for nearly 20 years. No additional new adverse drug reactions are expected using this third generation of interferon alpha. It is an effective drug for treating PV with acceptable toxicity28. Since the dose is carefully titrated to the optimal effective dose, no additional risks for the patients are expected.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	04 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	7
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients where eligible to enter the study if they had a confirmed diagnosis of primary myelofibrosis (grade MF-0 and MF-1) according to the 2008 WHO criteria. This included either newly diagnosed Interferon naive patients or patients pre-treated with Pegasys® or PegIntron®, who had stable disease for the previous 3 months.

Pre-assignment

Screening details:

Written informed consent; Patients age ≥18 years; Confirmed diagnosis of primary myelofibrosis (grade MF-0 and MF-1) ; patients of childbearing potential need a negative pregnancy test; ECOG ≤ 2

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	pre-treated

Arm description:

The initial dose of AOP2014 applied to Interferon pre-treated patients will be determined for each patient individually and it will depend of his/her current treatment dose of either Pegasys® or PegIntron. The dose of AOP2014 will be calculated according to the formula:

AOP2014 (µg) = Patient's current treatment dose Pegasys® /PegIntron® (µg)* 0.7.

Arm type	Experimental
Investigational medicinal product name	AOP2014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The initial dose of AOP2014 applied to Interferon pre-treated patients will be determined for each patient individually and it will depend of his/her current treatment dose of either Pegasys® or PegIntron. The dose of AOP2014 will be calculated according to the formula:

AOP2014 (µg) = Patient's current treatment dose Pegasys® /PegIntron® (µg)* 0.7.

Arm title	treatment-naive

Arm description:

In Interferon-naïve patients the initial dose will be calculated as follows:
AOP2014 (µg) = Clinically reasoned dose Pegasys® (µg)* 0.7,
where Clinically reasoned dose of Pegasys® will depend on the patient's clinical status and it will be determined individually as if the patient was treated with Pegasys®.

Arm type	Experimental
Investigational medicinal product name	AOP2014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

In Interferon-naïve patients the initial dose will be calculated as follows:
AOP2014 (µg) = Clinically reasoned dose Pegasys® (µg)* 0.7,
where Clinically reasoned dose of Pegasys® will depend on the patient's clinical status and it will be determined individually as if the patient was treated with Pegasys®.

Number of subjects in period 1	pre-treated	treatment-naive
Started	9	16
Completed	9	16

Baseline characteristics

Reporting groups

Reporting group title	pre-treated

Reporting group description:

The initial dose of AOP2014 applied to Interferon pre-treated patients will be determined for each patient individually and it will depend of his/her current treatment dose of either Pegasys® or PegIntron. The dose of AOP2014 will be calculated according to the formula:
AOP2014 (µg) = Patient's current treatment dose Pegasys® /PegIntron® (µg)* 0.7.

Reporting group title	treatment-naive

Reporting group description:

In Interferon-naïve patients the initial dose will be calculated as follows:
AOP2014 (µg) = Clinically reasoned dose Pegasys® (µg)* 0.7,
where Clinically reasoned dose of Pegasys® will depend on the patient's clinical status and it will be determined individually as if the patient was treated with Pegasys®.

Reporting group values	pre-treated	treatment-naive	Total
Number of subjects	9	16	25
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	15	18
From 65-84 years	6	1	7
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	10	14
Male	5	6	11

Subject analysis sets

Subject analysis set title	Erythrocytes, T/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Erythrocytes, T/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Hemoglobin, g/dl; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Hemoglobin, g/dl; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Leukocytes, G/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Leukocytes, G/l; treatment-naive (N=16)
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Thrombocytes, G/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Thrombocytes, G/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics

are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	LDH, U/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	LDH, U/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	ANC, K/µl; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	ANC, K/µl; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Spleen size, cm; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Spleen size, cm; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon

yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Reporting group values	Erythrocytes, T/l; pre-treated	Erythrocytes, T/l; treatment-naive	Hemoglobin, g/dl; pre-treated
Number of subjects	9	16	9
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	15	3
From 65-84 years	6	1	6
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female			
Male			

Reporting group values	Hemoglobin, g/dl; treatment-naive	Leukocytes, G/l; pre-treated	Leukocytes, G/l; treatment-naive (N=16)
Number of subjects	16	9	16
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	3	15
From 65-84 years	1	6	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female			
Male			

Reporting group values	Thrombocytes, G/l; pre-treated	Thrombocytes, G/l; treatment-naive	LDH, U/l; pre-treated
Number of subjects	9	16	9
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0

Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	15	3
From 65-84 years	6	1	6
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female			
Male			

Reporting group values	LDH, U/l; treatment-naive	ANC, K/µl; pre-treated	ANC, K/µl; treatment-naive
Number of subjects	16	9	16
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	3	15
From 65-84 years	1	6	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female			
Male			

Reporting group values	Spleen size, cm; pre-treated	Spleen size, cm; treatment-naive	
Number of subjects	9	16	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	15	
From 65-84 years	6	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	pre-treated

Reporting group description:

The initial dose of AOP2014 applied to Interferon pre-treated patients will be determined for each patient individually and it will depend of his/her current treatment dose of either Pegasys® or PegIntron. The dose of AOP2014 will be calculated according to the formula:
AOP2014 (µg) = Patient's current treatment dose Pegasys® /PegIntron® (µg)* 0.7.

Reporting group title	treatment-naive

Reporting group description:

In Interferon-naïve patients the initial dose will be calculated as follows:
AOP2014 (µg) = Clinically reasoned dose Pegasys® (µg)* 0.7,
where Clinically reasoned dose of Pegasys® will depend on the patient's clinical status and it will be determined individually as if the patient was treated with Pegasys®.

Subject analysis set title	Erythrocytes, T/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Erythrocytes, T/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Hemoglobin, g/dl; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Hemoglobin, g/dl; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Leukocytes, G/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Leukocytes, G/l; treatment-naive (N=16)
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Thrombocytes, G/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Thrombocytes, G/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	LDH, U/l; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	LDH, U/l; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	ANC, K/µl; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics

are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	ANC, K/µl; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Spleen size, cm; pre-treated
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Subject analysis set title	Spleen size, cm; treatment-naive
Subject analysis set type	Per protocol

Subject analysis set description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglobin and LDH values, no statistically significant difference could be found, which can be explained by the cytoreductive effect of previous intereron treatments.

Primary: Patient characteristics after 6 months

End point title	Patient characteristics after 6 months

End point description:

End point type	Primary

End point timeframe:

6 months

End point values	Erythrocytes, T/l; pre-treated	Erythrocytes, T/l; treatment-naive	Hemoglobin, g/dl; pre-treated	Hemoglobin, g/dl; treatment-naive
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	16	9	16
Units: Laboratory parameters; Dose, µg				
median (full range (min-max))	4.2 (3.8 to 5.1)	4.55 (3.6 to 5.6)	11.8 (10.3 to 15.2)	13.25 (9.4 to 14.7)

End point values	Leukocytes, G/l; pre-treated	Leukocytes, G/l; treatment-naive (N=16)	Thrombocytes, G/l; pre-treated	Thrombocytes, G/l; treatment-naive
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	16	9	16
Units: Laboratory parameters; Dose, µg				
median (full range (min-max))	6.48 (4.04 to 13.11)	6.76 (3.43 to 16.93)	375 (211 to 1378)	501 (131 to 1476)

End point values	LDH, U/l; pre-treated	LDH, U/l; treatment-naive	ANC, K/µl; pre-treated	ANC, K/µl; treatment-naive
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	16	9	16
Units: Laboratory parameters; Dose, µg				
median (full range (min-max))	205 (153 to 507)	273.5 (137 to 559)	4.05 (3.5 to 8.2)	4.65 (2.2 to 12.3)

End point values	Spleen size, cm; pre-treated	Spleen size, cm; treatment-naive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	16		
Units: Laboratory parameters; Dose, µg				
median (full range (min-max))	11 (8 to 19.5)	12.7 (9 to 19.2)		

Statistical analyses

Statistical analysis title	Patient characteristics after 6 months

Statistical analysis description:

For this analysis, patient data were evaluated after the first 6 months of therapy. Descriptive statistics are used to present data on clinical parameters. Since the study cohort comprised of patients who were previously treated with an interferon compound as well as patients who had not received an interferon yet, these two groups are used for comparative investigations. Statistically, the two groups did not differ. Although treatment-naive patients tended to present higher thrombocyte, hemoglo

Comparison groups	Erythrocytes, T/l; pre-treated v Erythrocytes, T/l; treatment-naive
Number of subjects included in analysis	25
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0
Method	PEG-P-IFN α-2b

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

No information about AE grading is stated, as the data was insufficient to perform any meaningful evaluation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: All adverse effects which occurred in the first six months of treatment are summarized in table 6. Generally, pre-treated patients suffered from fewer side effects than treatment-naïve patients in every category. This may be due to the fact that pre-treated patients had already been exposed to an interferon in previous treatment regimen whereas treatment-naïve patients had not. No information about AE grading is stated, as the data was insufficient to perform any meaningful evaluation.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported