Clinical trial results:
Phase III, randomized, double-blind, multicentre clinical trial on clinical efficacy and safety of platelet concentrates treated with the THERAFLEX UV-Platelets procedure in comparison to conventional platelet components (Capture).

Summary

EudraCT number	2015-001035-20
Trial protocol	DE
Global end of trial date	11 March 2019

Results information

Result version number	v1 (current)
This version publication date	20 August 2021
First version publication date	20 August 2021

Trial information

Trial identification

Sponsor protocol code	PIPL002a

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	DRK Blood Service NSTOB
Sponsor organisation address	Eldagsener Strasse 38, Springe, Germany, 31832
Public contact	R&D Department, Clinical Trial Group, DRK-Blood Service NSTOB, +49 5041 772 310, SekretariatFuE@bsd-nstob.de
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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	14 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2019
Global end of trial reached?	Yes
Global end of trial date	11 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to demonstrate the non-inferiority of UVC-treated plasma reduced platelet concentrates (synonym: UVC-PLT in comparison to standard untreated plasma reduced platelet concentrates (synonym: Control PLT) stored for up to 5 days in adult patients with hematologic or oncologic diseases and thrombocytopenia. The non-inferiority was met if the mean 1-hour Corrected Count Increment (1-hour CCI) between the control and UVC-PLT group was not more than 30% below the control.

Protection of trial subjects:

The trial was conducted according to ICH-GCP guidelines, the applicable local laws and regulations, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki. Regulatory authorities were notified of the trial as required by national regulations, and where necessary relevant authorization was obtained. An IDMC was involved in order to monitore safety data at regular intervals, making recommendations related to safety relevant issues (i.e. continuing/stopping the trial). In particular, the IDMC assessed and approved the safety data during the stepwise enrolment of patients in terms of increasing risk for the development of TA-GvHD at the beginning of the study. In step 1 only patients not at risk for the development of transfusion associated graft versus host disease (TA-GvHD) were enrolled, in step 2 patients at risk for TA-GvHD exluding patients with allogeneic stem cell transplantation, and in step 3 also patients with allogeneic stem cell transplantation were enrolled into the study.

Background therapy:

There were no prohibited concomitant therapies. The patients received concomitant therapy following medical instructions.

Evidence for comparator: -

Actual start date of recruitment	05 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 175
Worldwide total number of subjects	175
EEA total number of subjects	175

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)	127
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

175 patients were randomized at 10 sites in Germany.

Pre-assignment

Screening details:

177 patients were screened, whereas 175 patients were enrolled. Two patients in each arm were excluded because no PLT transfusion was performed within the specified time period of 6 weeks after randomisation. Hence, a total of 171 patients received as minimum one PLT Transfusion (n=87 in the UVC-PLT arm and n=84 in the Control-PLT arm).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The only health care professionals that knew the treatment that a patient received were the transfusion medicine staff from the manufacturing sites. The IDMC was unblinded when medically indicated.

Arms

Are arms mutually exclusive?	Yes
Arm title	UVC-PLT

Arm description:

Patients received pathogen-reduced platelet concentrates prepared by apheresis or buffy coat procedure (UVC-PLT) stored for up to 5 days before transfusion. Pathogen reduction was performed by UVC-irradiation using the THERAFLEX UV-Platelets procedure. UVC-PLTs were not gamma-irradiated because UVC treament is sufficient to prevent TA-GvHD. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 PLT transfusion episode within 28 days. Baseline characteristics were evaluated for all patients who received at least one UVC-PLT transfusion (ITT-set, n=87). A complete safety follow-up period of 30 days was performed in 71 patients.

Arm type	Experimental
Investigational medicinal product name	THERAFLEX UV-Platelets
Investigational medicinal product code	
Other name	Pathogen-reduced, plasma-reduced platelet concentrates stored in SSP+additive solution
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

After randomisation patients received prophylactic or therapeutic PLT transfusions in accordance to the German cross section guideline for therapy with blood components. Typically, one or more platelet units were transfused when the PLT count was 10E9/L or lower. However, the dose and frequency of administration also depended on the individual decision by the attending physician. In this clinical trial a mean of 3.7 PLT units (about 350 ml, 3.5 x 10E11 PLTs, each) were transfused during the treatment period of 28 days. UVC-PLTs were not gamma-irradiated, because UVC-treatment is sufficient to prevent TA-GvHD.

Arm title	Control-PLT

Arm description:

Patients received standard plasma-reduced platelet concentrates prepared by apheresis or buffy coat procedure (Control-PLT) stored for up to 5 days before transfusion. In contrast to UVC-PLTs, Control-PLTs were gamma-irradiated for TA-GvHD prophylaxis, when medically indicated. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 platelet

transfusion episodes within 28 days. Baseline characteristics were evaluated for all patients who received at least one Control-PLT transfusion (ITT-set, n=84 patients). A complete safety follow-up period of 30 days was performed in 69 patients.

Arm type	Active comparator
Investigational medicinal product name	Untreated plasma reduced platelet concentrates stored in SSP+ additive solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

After randomisation patients received prophylactic or therapeutic PLT transfusions in accordance to the German cross section guideline for therapy with blood components. Typically, one or more platelet units were transfused when the PLT count was 10E9/L or lower. However, the dose and frequency of administration also depended an the individual decision by the attending physician. In this clinical trial a mean of 3.0 PLT units (about 350 ml, 3.5 x 10E11 PLT, each) were transfused during the treatment period of 28 days.

Number of subjects in period 1[1]	UVC-PLT	Control-PLT
Started	87	84
Completed	71	69
Not completed	16	15
Adverse event, serious fatal	2	1
Consent withdrawn by subject	2	-
Exclusion criteria were met	-	2
other reasons	-	1
Transfusion of routine PLT units or from other arm	12	11

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 177 patients were screened, whereas 175 patients were enrolled. Two patients in each arm were excluded because no PLT transfusion was performed within the specified time period of 6 weeks after randomisation. Hence, a total of 171 patients received as minimum one PLT Transfusion (n=87 in the UVC-PLT arm and n=84 in the Controi-PLT arm).

Baseline characteristics

Reporting groups

Reporting group title	UVC-PLT

Reporting group description:

Patients received pathogen-reduced platelet concentrates prepared by apheresis or buffy coat procedure (UVC-PLT) stored for up to 5 days before transfusion. Pathogen reduction was performed by UVC-irradiation using the THERAFLEX UV-Platelets procedure. UVC-PLTs were not gamma-irradiated because UVC treament is sufficient to prevent TA-GvHD. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 PLT transfusion episode within 28 days. Baseline characteristics were evaluated for all patients who received at least one UVC-PLT transfusion (ITT-set, n=87). A complete safety follow-up period of 30 days was performed in 71 patients.

Reporting group title	Control-PLT

Reporting group description:

Patients received standard plasma-reduced platelet concentrates prepared by apheresis or buffy coat procedure (Control-PLT) stored for up to 5 days before transfusion. In contrast to UVC-PLTs, Control-PLTs were gamma-irradiated for TA-GvHD prophylaxis, when medically indicated. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 platelet transfusion episodes within 28 days. Baseline characteristics were evaluated for all patients who received at least one Control-PLT transfusion (ITT-set, n=84 patients). A complete safety follow-up period of 30 days was performed in 69 patients.

Reporting group values	UVC-PLT	Control-PLT	Total
Number of subjects	87	84	171
Age categorical Units: Subjects			
Adults (18 to 80 years)	87	84	171
Age continuous Units: years			
arithmetic mean	57	55	
standard deviation	± 14	± 12	-
Gender categorical Units: Subjects			
Female	32	32	64
Male	55	52	107
Primary diagnosis Units: Subjects			
Acute lymphoblastic leukemia	7	2	9
Acute myeloid leukemia	40	30	70
Chronic leukemia	1	0	1
Multiple myeloma	22	26	48
Non-Hodgkin's Iymphoma	9	16	25
Hodgkin's Iymphoma	0	3	3
Other	8	7	15
Body Surface area Units: qm			
arithmetic mean	1.95	1.97	
standard deviation	± 0.20	± 0.23	-

End points

End points reporting groups

Reporting group title	UVC-PLT

Reporting group description:

Patients received pathogen-reduced platelet concentrates prepared by apheresis or buffy coat procedure (UVC-PLT) stored for up to 5 days before transfusion. Pathogen reduction was performed by UVC-irradiation using the THERAFLEX UV-Platelets procedure. UVC-PLTs were not gamma-irradiated because UVC treament is sufficient to prevent TA-GvHD. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 PLT transfusion episode within 28 days. Baseline characteristics were evaluated for all patients who received at least one UVC-PLT transfusion (ITT-set, n=87). A complete safety follow-up period of 30 days was performed in 71 patients.

Reporting group title	Control-PLT

Reporting group description:

Patients received standard plasma-reduced platelet concentrates prepared by apheresis or buffy coat procedure (Control-PLT) stored for up to 5 days before transfusion. In contrast to UVC-PLTs, Control-PLTs were gamma-irradiated for TA-GvHD prophylaxis, when medically indicated. The treatment period started on the day of the first study PLT transfusion and continued for a maximum of 8 platelet transfusion episodes within 28 days. Baseline characteristics were evaluated for all patients who received at least one Control-PLT transfusion (ITT-set, n=84 patients). A complete safety follow-up period of 30 days was performed in 69 patients.

Primary: Camparison of the mean 1-hour CCI between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Camparison of the mean 1-hour CCI between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

The primary endpoint of PLT therapeutic efficacy was assessed by calculating the post-transfusion 1-hour CCI for the first 8 PLT transfusion episodes. The CCI measures the count increase (CI) of the PLTs after PLT transfusion, corrected for the patients blood volume and number of platelets transfused. Platelet counts were measured max. 24-hours before and 1-hour (10 to 90 min.) after PLT transfusion. The ITT set included 87 patients in the UVC-PLT arm and 84 in the Control-PLT arm. A total of 568 PLT units were transfused (320 in the UVC-PLT arm and, 248 in the Control-PLT arm). Descriptive statistics (mean, 95% Cl of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum) were performed.
Non-inferiority was concluded if the lower Iimit of the 95% CI calculated on the mean CCI of the UVC-PCs group was not below the lower Iimit of the zone of non-inferiority (up to a 30% reduction in CCI was considered as not inferior).

End point type	Primary

End point timeframe:

1-hour CCI (time range: 10 to 90 min.) after each PLT transfusion measured for up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: 1-hour CCI				
arithmetic mean (confidence interval 95%)	12.70 (11.42 to 13.97)	15.53 (14.18 to 16.88)		

Statistical analyses

Statistical analysis title	1-hour CCI non-inferiority analysis

Statistical analysis description:

For analysis the 1-hour CCI, each patient's mean was calculated separately first since the collected data from several measurements can be expected to be linked to the respective individual. Non- inferiority was concluded if the lower limit of the 95% CI calculated on the mean CCI of the UVC-PCs group was not below the lower Iimit of the zone of non-inferiority (up to a 30% reduction in CCI was considered as not inferior).

Comparison groups	UVC-PLT v Control-PLT
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Diff. Mean-Control vs. lower CI UVC (%)
Point estimate	12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.4
upper limit	14
Variability estimate	Standard deviation

Secondary: Comparison of the mean 24-hour CCI between patients transfused with UVC-PLTs and patients transfused with Control--PLTs.

End point title	Comparison of the mean 24-hour CCI between patients transfused with UVC-PLTs and patients transfused with Control--PLTs.

End point description:

For 24-hours CCI evaluation platelet counts were measured 24-hours after PLT transfusion. Descriptive statistics were performed (mean, 95% Cl of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum). In this report the mean and standard deviaton are shown.

End point type	Secondary

End point timeframe:

24-hours (18 to 30 hours) were evaluated after each PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: 24-hours CCI				
arithmetic mean (standard deviation)	8.77 (± 5.52)	10.85 (± 6.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of the mean 1-hour Count Increment (CI) between patients transfused with UVC-PLTs and patients transfused with Control-PLTs.

End point title	Comparison of the mean 1-hour Count Increment (CI) between patients transfused with UVC-PLTs and patients transfused with Control-PLTs.

End point description:

Like the CCI, the Count Increment (CI) measures the response to platelet transfusion but do not "correct" for the patient's blood volume and the number of platelets transfused. For CI-evaluation platelet counts were measured max. 24h before and 1-hour (10 to 90 min.) after PLT transfusion. Descriptive statistics (mean, 95% CI of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum) was performed. In this report the mean and standard deviation are shown.

End point type	Secondary

End point timeframe:

1-hour CI (30 to 90 min.) after each PLT transfusion up to the first 8 PLT transfusion episods within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: 24-hour CCI				
arithmetic mean (standard deviation)	22.05 (± 11.35)	27.06 (± 12.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of the mean 24-hour CI between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the mean 24-hour CI between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

Continuous data were summarized using the number of observations, mean, 95% CI of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum. In this report the mean and standard deviation are shown.

End point type	Secondary

End point timeframe:

24-hours CI (18 to 30 hours) were evaluated after each PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: 24-hour CI				
arithmetic mean (standard deviation)	15.07 (± 9.65)	18.94 (± 11.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of the mean number of PLT transfusions between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the mean number of PLT transfusions between patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

Comparison of the number of PLT transfusions required in both study arms for the treatment of patient´s thrombocytopenia provides evidence of the efficacy of the tested platelets. Descriptive statistics were performed (number of observations, mean, 95% Cl of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum). In this report the mean and standard deviation are shown. Comparisons of both arms were performed using Student's t-test.

End point type	Secondary

End point timeframe:

First PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: Numbers				
arithmetic mean (standard deviation)	3.68 (± 2.38)	2.95 (± 2.22)		

Statistical analyses

Statistical analysis title	p-Value
Comparison groups	UVC-PLT v Control-PLT
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.041
Method	t-test, 2-sided

Secondary: Comparison of the mean interval between PLT transfusions in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the mean interval between PLT transfusions in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

Comparison of the number of PLT transfusions required in both study arms for the treatment of patient´s thrombocytopenia provides evidence of the efficacy of the tested platelets. Descriptive statistics were performed (number of observations, mean, 95% CI of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum). In this report the mean and standard deviation are shown. Comparisons of both arms were performed using Student's t-test.

End point type	Secondary

End point timeframe:

First PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: days				
arithmetic mean (confidence interval 95%)	2.62 (2.20 to 3.04)	2.80 (2.26 to 3.34)		

Statistical analyses

Statistical analysis title	p-Value
Comparison groups	UVC-PLT v Control-PLT
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.59
Method	t-test, 2-sided

Secondary: Comparison of the number of Red Blood Cell (RBC) transfusions in patients transfused with UVC-PLTs and patients transfused with Control-PLTs.

End point title	Comparison of the number of Red Blood Cell (RBC) transfusions in patients transfused with UVC-PLTs and patients transfused with Control-PLTs.

End point description:

Comparison of the number of Red Blood Cells (RBC) transfusion support in both study arms provides evidence for the efficacy of UVC-PLTs.

Descriptive statistics were performed (number of observations, mean, 95% CI of the mean, standard deviation, median, 25% and 75% quartiles, minimum and maximum). In this report, the mean and standard deviation are shown. Comparisons of both arms were performed using Student's t-test.

End point type	Secondary

End point timeframe:

First PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: Number per patient				
arithmetic mean (standard deviation)	2.71 (± 2.39)	2.20 (± 2.37)		

Statistical analyses

Statistical analysis title	p-Value
Comparison groups	UVC-PLT v Control-PLT
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.16
Method	t-test, 2-sided

Secondary: Comparison of the rate of clinical refractoriness in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the rate of clinical refractoriness in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

The number of patients with clinical refractoriness to PLT transfusions in the UVC-arm vs. the number of patients with clinical refractoriness to PLT transfusions in the Control-PLT arm were determined. Comparison between both arms was performed using the Fisher's exact test.

Episodes of "clinical" refractoriness, defined as two consecutive transfusions, each with a 1-hour CCI lower than 7.5.

End point type	Secondary

End point timeframe:

First PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	84		
Units: Number	15	6		

Statistical analyses

Statistical analysis title	p-Value
Comparison groups	UVC-PLT v Control-PLT
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.055
Method	Fisher exact

Secondary: Comparison of the rate of immunologic refractoriness in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the rate of immunologic refractoriness in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

Number of patients with immunologic refractoriness to PLT transfusions in the UVC-PLT arm vs. Control-PLT arm. Comparison between both arms were performed using Fisher's exact test.

Immunologic refractoriness defined as two consecutive transfusions with a CCI lower then 7.5 and serologic conversion to positive tests for HLA and/or allo antibodies or for antibodies to UVC related neoantigens.

End point type	Secondary

End point timeframe:

First PLT transfusion up to the first 8 PLT transfusion episodes within the treatment period of 28 days.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87[1]	84[2]		
Units: Numbers	0	0		

Notes:

[1] - No immunologic refractoriness due to serologic conversion was reported.

[2] - No immunologic refractoriness due to serologic conversion was reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of the number of WHO Grad 3 and 4 bleeding in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point title	Comparison of the number of WHO Grad 3 and 4 bleeding in patients transfused with UVC-PLTs and patients transfused with Control-PLTs

End point description:

The grade of bleeding was determined using the WHO bleeding scale. The number of cases with severe grade 3 and 4 bleeding were recorded for all patients of the ITT set during the treatment period.

Comparison between both arms was performed using either the Chi-Square test or the Fisher's exact test, depending on the data distribution.

End point type	Secondary

End point timeframe:

First PLT transfusion until the end of follow up period.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87[3]	84		
Units: Number	0	1		

Notes:

[3] - No grade 3 or 4 bleeding was recorded.

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of alloimmunisation to UVC-related neoantigens on PLTs

End point title	Comparison of alloimmunisation to UVC-related neoantigens on PLTs

End point description:

The number of patients with alloimmunisation to possible UVC-related neoantigens on PLTs alter transfusion of UVC- PLTs and Control-PLTs, were analyzed. For the evaluation of alloimmunisation blood samples for alloantibody screening were taken before the First PLT transfusion and at the end of the safety follow-up period. Additional samples were taken in case of suspected refractoriness to platelet transfusions.
Comparison between both arms was performed using either the Chi-Squaretest or the Fisher's exact test.

End point type	Secondary

End point timeframe:

Overall study period.

End point values	UVC-PLT	Control-PLT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87[4]	84[5]		
Units: Numbers	0	0		

Notes:

[4] - No alloimmunisation to UVC-related neoantigens was recorded.

[5] - No alloimmunisation to UVC-related neoantigenswas recorded

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First PLT transfusion until 30 days after the last dose of study drug.

Adverse event reporting additional description:

All safety analysiswas based on ITT population who received at least one PLT transfusion.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	UVC-PLT

Reporting group description:

Patients received UVC-irradiated, plasma reduced, platelet concentrates stored in SSP+ additive solution, manufactured with the THERAFLEX UV-Platelets procedure (UVC-PLTs).

Reporting group title	Control-PLT

Reporting group description:

Patients received untreated plasma reduced platelet concentrates stored in SSP+ additive solution. Control-PLTs were gamma-irradiated for TA-GvHD prophylaxis, when medically indicated.

Serious adverse events	UVC-PLT	Control-PLT	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 87 (11.49%)	8 / 84 (9.52%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	1	3	
Investigations			
Sepsis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasma benign, malignant and unspecified,other, Progression of lymphoma			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Paroxysmal atrial tachycardia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 87 (0.00%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 87 (1.15%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
soft tissue infectioncervical with dysphagia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immune system disorders-Other GVHD after allogeneic stem cell transplantation; Diarrhea			

subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and Infestations-other, CMV-infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
resp.failure/pneumonia/lung infection (RSV)			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis with organ involvement (CNC, kidney liver) V.a meninigitis, encephalitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Catheter related infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	2 / 87 (2.30%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestatations-other, Influenca A infection			

subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	UVC-PLT	Control-PLT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 87 (97.70%)	80 / 84 (95.24%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	8 / 87 (9.20%)	2 / 84 (2.38%)	
occurrences (all)	9	2	
Hypertension			
subjects affected / exposed	9 / 87 (10.34%)	4 / 84 (4.76%)	
occurrences (all)	12	6	
Hypotension			
subjects affected / exposed	2 / 87 (2.30%)	5 / 84 (5.95%)	
occurrences (all)	2	5	
General disorders and administration site conditions			
Chilis			
subjects affected / exposed	4 / 87 (4.60%)	5 / 84 (5.95%)	
occurrences (all)	6	5	
Face oedema			
subjects affected / exposed	3 / 87 (3.45%)	1 / 84 (1.19%)	
occurrences (all)	3	1	
Injection site erythema			
subjects affected / exposed	15 / 87 (17.24%)	4 / 84 (4.76%)	
occurrences (all)	17	5	
Oedema peripheral			
subjects affected / exposed	13 / 87 (14.94%)	8 / 84 (9.52%)	
occurrences (all)	13	9	
Pain			
subjects affected / exposed	8 / 87 (9.20%)	3 / 84 (3.57%)	
occurrences (all)	9	5	
Pyrexia			

subjects affected / exposed	47 / 87 (54.02%)	44 / 84 (52.38%)	
occurrences (all)	64	64	
Fatigue			
subjects affected / exposed	3 / 87 (3.45%)	9 / 84 (10.71%)	
occurrences (all)	3	9	
Localised oedema			
subjects affected / exposed	2 / 87 (2.30%)	3 / 84 (3.57%)	
occurrences (all)	3	3	
Non-cardiac ehest pain			
subjects affected / exposed	3 / 87 (3.45%)	1 / 84 (1.19%)	
occurrences (all)	3	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	4 / 87 (4.60%)	2 / 84 (2.38%)	
occurrences (all)	5	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 87 (8.05%)	11 / 84 (13.10%)	
occurrences (all)	7	11	
Dyspnoea			
subjects affected / exposed	9 / 87 (10.34%)	7 / 84 (8.33%)	
occurrences (all)	10	7	
Epistaxis			
subjects affected / exposed	10 / 87 (11.49%)	8 / 84 (9.52%)	
occurrences (all)	14	9	
Oropharyngeal pain			
subjects affected / exposed	6 / 87 (6.90%)	4 / 84 (4.76%)	
occurrences (all)	7	4	
Productive cough			
subjects affected / exposed	3 / 87 (3.45%)	3 / 84 (3.57%)	
occurrences (all)	3	4	
Dysphonia			
subjects affected / exposed	1 / 87 (1.15%)	3 / 84 (3.57%)	
occurrences (all)	10	7	
Pleural effusion			

subjects affected / exposed	2 / 87 (2.30%)	2 / 84 (2.38%)	
occurrences (all)	3	2	
Psychiatric disorders			
Hallucination			
subjects affected / exposed	0 / 87 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	3	
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 87 (4.60%)	4 / 84 (4.76%)	
occurrences (all)	4	4	
C-reactive protein increased			
subjects affected / exposed	9 / 87 (10.34%)	9 / 84 (10.71%)	
occurrences (all)	9	9	
Platelet count decreased			
subjects affected / exposed	7 / 87 (8.05%)	10 / 84 (11.90%)	
occurrences (all)	14	21	
White blood cell count decreased			
subjects affected / exposed	10 / 87 (11.49%)	7 / 84 (8.33%)	
occurrences (all)	10	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 87 (1.15%)	5 / 84 (5.95%)	
occurrences (all)	1	5	
Blood bilirubin increased			
subjects affected / exposed	0 / 87 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	5	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 87 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Refractoriness to platelet transfusion			
subjects affected / exposed	14 / 87 (16.09%)	4 / 84 (4.76%)	
occurrences (all)	14	4	
Cardiac disorders			

Atrial tachycardia			
subjects affected / exposed	3 / 87 (3.45%)	2 / 84 (2.38%)	
occurrences (all)	3	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 87 (5.75%)	3 / 84 (3.57%)	
occurrences (all)	7	3	
Headache			
subjects affected / exposed	17 / 87 (19.54%)	13 / 84 (15.48%)	
occurrences (all)	22	14	
Tremor			
subjects affected / exposed	3 / 87 (3.45%)	1 / 84 (1.19%)	
occurrences (all)	3	1	
Dysgeusia			
subjects affected / exposed	1 / 87 (1.15%)	4 / 84 (4.76%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	29 / 87 (33.33%)	20 / 84 (23.81%)	
occurrences (all)	29	20	
Febrile neutropenia			
subjects affected / exposed	9 / 87 (10.34%)	12 / 84 (14.29%)	
occurrences (all)	11	14	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	4 / 87 (4.60%)	2 / 84 (2.38%)	
occurrences (all)	4	2	
Abdominal pain			
subjects affected / exposed	4 / 87 (4.60%)	2 / 84 (2.38%)	
occurrences (all)	4	5	
Abdominal pain upper			
subjects affected / exposed	5 / 87 (5.75%)	9 / 84 (10.71%)	
occurrences (all)	5	10	
Constipation			
subjects affected / exposed	10 / 87 (11.49%)	3 / 84 (3.57%)	
occurrences (all)	15	4	
Diarrhoea			

subjects affected / exposed	25 / 87 (28.74%)	27 / 84 (32.14%)	
occurrences (all)	28	31	
Dysphagia			
subjects affected / exposed	3 / 87 (3.45%)	2 / 84 (2.38%)	
occurrences (all)	5	2	
Nausea			
subjects affected / exposed	20 / 87 (22.99%)	25 / 84 (29.76%)	
occurrences (all)	24	29	
Stomatitis			
subjects affected / exposed	22 / 87 (25.29%)	22 / 84 (26.19%)	
occurrences (all)	22	22	
Vomiting			
subjects affected / exposed	15 / 87 (17.24%)	12 / 84 (14.29%)	
occurrences (all)	19	13	
Dyspepsia			
subjects affected / exposed	3 / 87 (3.45%)	2 / 84 (2.38%)	
occurrences (all)	3	2	
Enteritis			
subjects affected / exposed	4 / 87 (4.60%)	0 / 84 (0.00%)	
occurrences (all)	4	0	
Haemorrhoids			
subjects affected / exposed	3 / 87 (3.45%)	2 / 84 (2.38%)	
occurrences (all)	3	2	
Asthenia			
subjects affected / exposed	3 / 87 (3.45%)	3 / 84 (3.57%)	
occurrences (all)	3	3	
Proctalgia			
subjects affected / exposed	3 / 87 (3.45%)	0 / 84 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	5 / 87 (5.75%)	1 / 84 (1.19%)	
occurrences (all)	5	1	
Petechia			
subjects affected / exposed	9 / 87 (10.34%)	8 / 84 (9.52%)	
occurrences (all)	9	9	

Pruritus			
subjects affected / exposed	6 / 87 (6.90%)	0 / 84 (0.00%)	
occurrences (all)	6	0	
Rash			
subjects affected / exposed	7 / 87 (8.05%)	7 / 84 (8.33%)	
occurrences (all)	8	7	
Rash maculo-papular			
subjects affected / exposed	5 / 87 (5.75%)	5 / 84 (5.95%)	
occurrences (all)	5	5	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 87 (6.90%)	3 / 84 (3.57%)	
occurrences (all)	6	3	
Bone pain			
subjects affected / exposed	3 / 87 (3.45%)	3 / 84 (3.57%)	
occurrences (all)	3	3	
Myalgia			
subjects affected / exposed	3 / 87 (3.45%)	0 / 84 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	7 / 87 (8.05%)	1 / 84 (1.19%)	
occurrences (all)	7	1	
Infections and infestations			
Device related infection			
subjects affected / exposed	8 / 87 (9.20%)	1 / 84 (1.19%)	
occurrences (all)	8	1	
Enterococcal infection			
subjects affected / exposed	3 / 87 (3.45%)	3 / 84 (3.57%)	
occurrences (all)	3	3	
Nasapharyngitis			
subjects affected / exposed	3 / 87 (3.45%)	4 / 84 (4.76%)	
occurrences (all)	3	4	
Bronchitis			
subjects affected / exposed	3 / 87 (3.45%)	2 / 84 (2.38%)	
occurrences (all)	3	2	
Infection			

subjects affected / exposed	3 / 87 (3.45%)	1 / 84 (1.19%)	
occurrences (all)	4	1	
Injection site infection			
subjects affected / exposed	1 / 87 (1.15%)	3 / 84 (3.57%)	
occurrences (all)	1	3	
Lung infection			
subjects affected / exposed	5 / 87 (5.75%)	5 / 84 (5.95%)	
occurrences (all)	5	5	
Weight increased			
subjects affected / exposed	6 / 87 (6.90%)	2 / 84 (2.38%)	
occurrences (all)	6	2	
Sepsis			
subjects affected / exposed	0 / 87 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	3	
Staphylococcal infection			
subjects affected / exposed	4 / 87 (4.60%)	0 / 84 (0.00%)	
occurrences (all)	4	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 87 (11.49%)	6 / 84 (7.14%)	
occurrences (all)	10	6	
Hypokalaemia			
subjects affected / exposed	8 / 87 (9.20%)	5 / 84 (5.95%)	
occurrences (all)	9	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2016	Study protocol V3, dated 15.06.2016: Personnel-related changes; Further clarification on definitions and handling, Changes in the observation period for the endpoint "clinical refractoriness" and time point for temperature measurements. Patient Information and consent form V3, dated 15.06.2016: Implementation of genetic tests in case of expected TA-GvHD.
22 November 2016	Patient Information and consent form V4, dated 25.10.2016 were updated.
07 December 2016	Study protocol V4, dated 07.11.2016: Addition of new manufacturing site and trial sites. Further clarification on protocol definitions.
12 December 2016	Patient Information and consent form V5, dated 06.12.2016: Reimbursement of travel costs up to 50 €.
23 January 2018	Study protocol V5, dated 02.10.2017: Addition of manufacturing of apheresis derived PC at the manufacturing site in Frankfurt; Patients with planned allogeneic stem cell transplantation could be enrolled and treated with IMP until starting of the conditioning regime (Step 3); Personnel-related changes; Further clarification on study protocol definitions.
19 October 2018	Patient Information and consent form V6, dated 18.07.2018: Update in accordance to the new EU general data protection regulation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported