Clinical trial results:
Phase II multicenter study of extracorporeal photopheresis with UvadexTM plus standard steroid treatment for high risk acute Graft-versus-Host Disease

Summary

EudraCT number	2019-000894-22
Trial protocol	DE AT
Global end of trial date	24 June 2024

Results information

Result version number	v1 (current)
This version publication date	19 June 2026
First version publication date	19 June 2026
Summary attachment (see zip file)	MAGIC-HR-ECP-CSR Synopsis (MAGIC-HR-ECP_CSR_Synopsis_Final_31_Mar_2026.pdf)

Trial information

Trial identification

Sponsor protocol code	MAGIC-HR-ECP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04291261
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Hamburg-Eppendorf
Sponsor organisation address	Martinistrasse 52, Hamburg, Germany, 20246
Public contact	Francis A. Ayuk, Department of Stem Cell Transplantation - University Medical Center Hamburg-Eppendorf, 0049 40741055250, ayuketan@uke.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	03 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2024
Global end of trial reached?	Yes
Global end of trial date	24 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to improve Day 28 GvHD complete response rate for Ann Arbor score 2 or 3 GvHD patients from the historical rate of 37% to 52% by treatment with ECP and high dose methylprednisolone (2 mg/kg) or equivalent dose prednisolone.

Protection of trial subjects:

This study was conducted in accordance with applicable ICH/GCP regulations and guidelines, the general principles set forth in the Declaration of Helsinki, and all applicable regulatory requirements. Prior to the start of the study, the study protocol was reviewed and approved by an independent ethics committee (IEC).
Prior to any study-related procedures, subjects were informed by a principal investigator about all procedures and counseled regarding the risks and benefits of the study. Patients were always given sufficient time to ask questions and decide whether they wished to participate in the study. Prior to any study-related procedures, written informed consent was obtained from the patients and the approving investigators.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2020
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	Austria: 1
Country: Number of subjects enrolled	Germany: 23
Worldwide total number of subjects	24
EEA total number of subjects	24

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	19
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 3 sites in Germany and 1 site in Austria. The sites were located at university hospitals with a focus on stem cell transplantation .

Pre-assignment

Screening details:

The screening process started after the patient was diagnosed with aGvHD (Glucksberg grade IIIV) following allogeneic SCT and after Informed Consent was collected. Sceening period time was Day -5 to Day 0. Patient eligibility was determined locally, except Ann Arbor scoring was measured centrally using standard technical procedures.

Pre-assignment period milestones

Number of subjects started	52[1]
Number of subjects completed	24

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening failures: 27
Reason: Number of subjects	Consent withdrawn by subject: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number started pre-assignment period are all screened patients. Number of worldwide enrolled are the patients who entered the trial for treatment (without screening failures).

Period 1

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

Arms

Arm title	ECP plus standard steroid treatment

Arm description:

Days 0-56: ECP 3x/week in Week 1 and Week 2. 2x/week in Week 3 and Week 4, then once weekly until Day 56.
Protocol treatment with ECP had to start within 5 working days (=7 days) after initiation of systemic steroid treatment for aGvHD. Dose of methylprednisolon 2 mg/kg/day orally or i.v. (or prednisone equivalent). The dose of steroids could not be tapered before 3 days of initiation of study therapy (=first ECP, defined as Day 0), but afterwards local institutional tapering practices could be followed.
Weeks 10, 12 and Months 6, 9, 12: Follow-up Period. Patients were followed 1 year after removal from treatment or intil death, whichever accures first.

Arm type	Experimental
Investigational medicinal product name	UVADEX
Investigational medicinal product code	
Other name	methoxsalen, 8-methoxypsoralen
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Extracorporeal use

Dosage and administration details:

UVADEX™ was supplied as a sterile solution containing methoxsalen 20 mcg, propylene glycol 50 mg, sodium chloride 8 mg, sodium acetate 1.75 mg, ethanol 40.550 mg, glacial acetic acid 1.260 mg, and water for injection q.s. to 1.0 mL. Glacial acetic acid and sodium hydroxide were used to adjust the pH of the solution if necessary.
UVADEX™ was provided and distributed to the individual sites by Therakos (Mallinckrodt).

The ECP procedure was be performed according to manufacturer’s guidelines.
For the treatment, photopheresis consisted of removing a portion of the patient's blood and separating the red blood cells from the white cell layer (buffy coat) by centrifugation. The red cells were returned to the patient and the UVADEX™ sterile solution was then injected into the photopheresis system and mixed with the buffy coat. The instrument then irradiated this drug-cell mixture with ultraviolet light (UVA light, 320-400 nm) and returned the treated cells to the patient.

Number of subjects in period 1	ECP plus standard steroid treatment
Started	24
Completed	21
Not completed	3
Adverse event, serious fatal	3

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	24	24	
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)	19	19	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	10	10	
Male	14	14	
GvHD staging Units: Subjects			
Grade II	17	17	
Grade III	6	6	
Grade IV	1	1	
Skin stages Units: Subjects			
No rash	4	4	
Rash <25% BSA	2	2	
Rash 25-50% BSA	4	4	
> 50% generalized erythroderma	14	14	
Liver stages Units: Subjects			
Bilirubin <2 mg/dl	21	21	
Bilirubin 2.1-3 mg/dl	2	2	
Bilirubin 3.1-6 mg/dl	1	1	
Gastrointestinal tract Units: Subjects			
Diarrhea <500 ml/day	10	10	
Diarrhea 500-1000 ml/day or severe nausea/vomiting	8	8	
Diarrhea 1001-1500 ml/day	4	4	
Diarrhea >1500 ml/day	1	1	
severe abdominal pain with/without ileus, grossly	1	1	

Diagnosis for transplantation Units: Subjects			
ALL	2	2	
AML	10	10	
CLL	1	1	
CML	1	1	
CMML	1	1	
CMML-2	1	1	
DLCL	1	1	
Hodgkin's disease	1	1	
MDS	4	4	
MDS/MPN Overlap	1	1	
OMF	1	1	
Remission status at transplant Units: Subjects			
Aplasia	1	1	
CR	12	12	
PD	2	2	
PR	1	1	
Primary refractory	1	1	
Relapse (after CR)	1	1	
Untreated	6	6	
Donor type Units: Subjects			
Related	1	1	
Related (10/10)	1	1	
Related (Haplo)	2	2	
Related sibling (10/10)	1	1	
Unrelated (10/10)	14	14	
Unrelated (8/10)	1	1	
Unrelated (8/8)	1	1	
Unrelated (9/10)	3	3	
Donor/recipient HLA-matching Units: Subjects			
Halfmatch	1	1	
Match	17	17	
Mismatch	6	6	
GvHD prophylaxis (condensed) Units: Subjects			
CNI + MMF	19	19	
CNI + MMF + PTCy	5	5	
Ann Arbor Score Units: none			
median	2.0		
inter-quartile range (Q1-Q3)	2.0 to 3.0	-	
Days since transplantation at enrollment Units: none			
median	20.0		
inter-quartile range (Q1-Q3)	13.5 to 22.5	-	
HCT-CI score at transplant Units: none			

median	3.0		
inter-quartile range (Q1-Q3)	3.0 to 6.0	-	

End points

End points reporting groups

Reporting group title	ECP plus standard steroid treatment

Reporting group description:

Days 0-56: ECP 3x/week in Week 1 and Week 2. 2x/week in Week 3 and Week 4, then once weekly until Day 56.
Protocol treatment with ECP had to start within 5 working days (=7 days) after initiation of systemic steroid treatment for aGvHD. Dose of methylprednisolon 2 mg/kg/day orally or i.v. (or prednisone equivalent). The dose of steroids could not be tapered before 3 days of initiation of study therapy (=first ECP, defined as Day 0), but afterwards local institutional tapering practices could be followed.
Weeks 10, 12 and Months 6, 9, 12: Follow-up Period. Patients were followed 1 year after removal from treatment or intil death, whichever accures first.

Primary: Complete response at Day 28 of study treatment

End point title	Complete response at Day 28 of study treatment[1]

End point description:

The primary endpoint was the proportion of CR at Day 28 of study treatment. Death, lack of CR at Day 28, or initiation of additional immunosuppressive therapy were considered failures for this endpoint. The following values show the proportion of CR together with a two-sided 90% exact Clopper-Pearson confidence interval (CI) and the p-value for the comparison with the historical rate of 0.37.
p-value < 0.001: for testing the null hypothesis that the CR rate is smaller or equal to the historical rate a binomial test with a one-sided type I error rate of 5% was used.

End point type	Primary

End point timeframe:

28 days after first ECP treatment (Day 0).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Details are given in the description.

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	24[2]			
Units: proportion				
number (confidence interval 90%)				
proportion of complete response (CR)	0.8750 (0.7077 to 0.9650)			

Notes:

[2] - Full Analysis Set (FAS)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response at Day 28

End point title	Overall Response at Day 28

End point description:

Pre-defined binary secondary endpoints were overall response at day 28 and 56, defined as CR or PR at

day 28 and 56. Death, lack of CR/PR at the respective day or initiation of additional immunosuppressive therapy are considered as failures for this endpoint. The following values show the proportion of overall response at day 28 consisting of patients who
achieved partial or complete response together with a two-sided 95% exact Wilson-Score CI.

End point type	Secondary

End point timeframe:

Day 28 after first ECP treatment (Day 0)

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	24[3]			
Units: proportion				
number (confidence interval 95%)				
Overall response at Day 28	0.9167 (0.7415 to 0.9768)			

Notes:

[3] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response at Day 56

End point title	Overall Response at Day 56

End point description:

Pre-defined binary secondary endpoints were overall response at day 28 and 56, defined as CR or PR at day 28 and 56. Death, lack of CR/PR at the respective day or initiation of additional immunosuppressive therapy are considered as failures for this endpoint. The following values show the proportion of overall response at day 56 consisting of patients who
achieved partial or complete response together with a two-sided 95% exact Wilson-Score CI.

End point type	Secondary

End point timeframe:

Day 56 after first ECP treatment (Day 0)

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	23[4]			
Units: proportion				
number (confidence interval 95%)				
Overall response at Day 56	0.7826 (0.5810 to 0.9034)			

Notes:

[4] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival at 1 year

End point title	Overall survival at 1 year

End point description:

For the secondary endpoint overall survival (OS) at 1 year, an administrative censoring was applied at 1 year after enrollment, if patients are observed longer. The following table shows the estimates for 1-year OS together with the 95%-CI using Kaplan-Meier estimation.

End point type	Secondary

End point timeframe:

1 year after enrollment

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	24[5]			
Units: proportion				
number (confidence interval 95%)				
1-year OS	0.875 (0.661 to 0.958)			

Notes:

[5] - Full analyis set

Statistical analyses

No statistical analyses for this end point

Secondary: Further time-to-event endpoints

End point title	Further time-to-event endpoints

End point description:

For all further time-to-event endpoints death (from any cause) was treated as competing event. The cumulative incidence at the respective timepoints was estimated using Aalen-Johansen estimators together with its 95%-CI. The following table shows the respective results.

End point type	Secondary

End point timeframe:

6 months / 12 months /Visit Day 28 (visit window until 33 days) / Visit Days 56 (window until 66 days)

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Incidence				
number (confidence interval 95%)				
NRM (6 months)	0.083 (0.014 to 0.233)			
NRM (12 months)	0.083 (0.014 to 0.233)			
Chronic GvHD (12 months)	0.5 (0.291 to 0.678)			
Severe GI aGvHD (6 months)	0.083 (0.014 to 0.233)			
Treatment-refractory GvHD (Visit Day 28)	0.042 (0.003 to 0.176)			
Treatment-refractory GvHD (Visit Day 56)	0.219 (0.062 to 0.436)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety endpoint - Relapse

End point title	Safety endpoint - Relapse

End point description:

The safety endpoints were analysed within the EFS population, which is equivalent to the FAS population. The following table shows the safety endpoint analysis for the endpoint "relapse" in the EFS/FAS population (Aalen-Johansen estimator).

End point type	Secondary

End point timeframe:

12 months

End point values	ECP plus standard steroid treatment			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Incidence				
number (confidence interval 95%)				
Relapse	0.042 (0.003 to 0.176)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Data on all events meeting the criteria and defintion of an AE with CTCAE grade 3 or higher or SAE were collected from the time of consenting until the patient's follow-up phase .

Adverse event reporting additional description:

For the Safety evaluation, AEs during treatment (defined at time of ECP treatment + 28 days) were used.
Only events with CTCAE grade 3 , 4 and 5 (severe AEs and SAEs) were analysed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28

Reporting groups

Reporting group title	Adverse events - Safety population

Reporting group description:

Subjects affected during treatment (defined as time of ECP treatment + 28 days) and with CTCAE grade ≥3.

Serious adverse events	Adverse events - Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 24 (58.33%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Acute graft versus host disease			

subjects affected / exposed	2 / 24 (8.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Myopathy				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Infection	Additional description: unclear focus			
subjects affected / exposed	3 / 24 (12.50%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalivirus infection reactivation				

subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes simplex			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Steroid diabetes			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adverse events - Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 24 (54.17%)		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Anaemia			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Infections and infestations			
Infections			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	4		
Sepsis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		

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