Clinical trial results:
Prospective donor-specific Cellular alloresponse assessment for Immunosuppression Minimization in de novo renal transplantation

Summary

EudraCT number	2014-001325-33
Trial protocol	DE ES CZ NL
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	09 July 2022
First version publication date	09 July 2022
Summary attachment (see zip file)	Preformed T cell alloimmunity and HLA eplet mismatch to guide immunosuppression minimization with tacrolimus monotherapy in kidney transplantation: Results of the CELLIMIN trial (ajt.16563.pdf)

Trial information

Trial identification

Sponsor protocol code	CELLIMIN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02540395
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department Nephrology and BCRT, Charité Universitätsmedizin Berlin
Sponsor organisation address	Augustenburger Pl. 1, Berlin, Germany, 13353
Public contact	Project manager, Charité - Universitätsmedizin Berlin, +34 932607385, petra.reinke@charite.de
Scientific contact	Project manager, Charité - Universitätsmedizin Berlin, +34 932607385, petra.reinke@charite.de

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	Interim
Date of interim/final analysis	31 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to demonstrate the utility and safety of the IFN-? ELISPOT marker for the stratification of kidney transplant recipients into low and high IS regimens. The enrichment study will test non-inferiority of low IS regimen compared to high IS regimen, assuming 10% of BPAR at 6-months in the control group, and allowing a non-inferiority limit of maximum 15%.

Protection of trial subjects:

An external Data Safety Monitoring Board (DSMB) was responsible for periodic safety review and guided by predetermined protocol–defined stopping criteria.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 March 2015
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	Netherlands: 42
Country: Number of subjects enrolled	Spain: 52
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 50
Worldwide total number of subjects	167
EEA total number of subjects	167

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)	167

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Low immunological risk subjects were eligible to participate
if >18 years of age and receiving a primary single kidney transplant.
Enrolment was targeted to 673 patients, with 302 E− transplant
patients randomized to low or SOC immunosuppression. the trial was terminated when 167
were recruited. In all, 101 patients were randomized and followed

Pre-assignment

Screening details:

All subjects freely gave written informed consent prior to participation, including informed consent for the screening procedures to establish subject eligibility.
Screened Patients: 186
Screening failure: 19 (10 Invalid ELISPOT; 1 Pre transplant DSA; 1 Early graft loss; 7 Consent withdrawal)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	E−/SOC Group

Arm description:

Standard of care immunosuppression (SOC)

Arm type	Experimental
Investigational medicinal product name	TACROLIMUS
Investigational medicinal product code	Tacrolimus
Other name	Tacrolimus
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Based on current standard of care therapy consisting in TAC to achieve a 4–8ng/ml plasma trough levels.

Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	mycophenolate mofetil
Other name	MYCOPHENOLATE MOFETIL
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

mycophenolate mofetil (MMF) initially 1gr bid and subsequently adjusted according to the subjects tolerance.

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	Prednisolone
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intraarticular use, Intramuscular use, Oral use

Dosage and administration details:

500 mg methylprednisolone perioperatively to continue with oral prednisone (20 mg/day the first 2 weeks and tapered not less than 5 mg/day at 4 weeks posttransplant).

Arm title	E−/LI Group
Arm description:	
Low immunosuppression (LI)	
Arm type	Experimental
Investigational medicinal product name	TACROLIMUS
Investigational medicinal product code	Tacrolimus
Other name	Tacrolimus
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Based on TAC monotherapy to achieve TAC 8–10 ng/ml plasma trough levels during the first 4 weeks and 6–8ng/ml thereafter.	
Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	mycophenolate mofetil
Other name	MYCOPHENOLATE MOFETIL
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
MMF (1 g bid) during the first week	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	Prednisolone
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intraarticular use, Intramuscular use, Oral use
Dosage and administration details:	
500 mg methylprednisolone perioperatively to continue with oral prednisone 20 mg/day the first 2 weeks and tapered to 5 mg/day from month 1 to month 2 when finally discontinued.	
Arm title	E+ Group
Arm description:	
Group II. ELISPOT positive (E+) transplant candidates received the same current standard of care immunosuppressive regimen than group E−/SOC.	
Arm type	Experimental
Investigational medicinal product name	TACROLIMUS
Investigational medicinal product code	Tacrolimus
Other name	Tacrolimus
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Based on current standard of care therapy consisting in TAC to achieve a 4–8ng/ml plasma trough levels.	
Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	mycophenolate mofetil
Other name	MYCOPHENOLATE MOFETIL
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
mycophenolate mofetil (MMF) initially 1gr bid and subsequently adjusted according to the subjects tolerance.	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	Prednisolone
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intraarticular use, Intramuscular use, Oral use

Dosage and administration details:

500 mg methylprednisolone perioperatively to continue with oral prednisone (20 mg/day the first 2 weeks and tapered not less than 5 mg/day at 4 weeks posttransplant).

Number of subjects in period 1	E−/SOC Group	E−/LI Group	E+ Group
Started	53	48	66
Completed	41	35	55
Not completed	12	13	11
rATG	1	-	-
Belatacept	1	-	-
TAC/mTori	-	-	8
MMF withdrawal	2	-	-
CsA	4	-	-
triple therapy	-	2	-
TAC+ steroids	-	5	-
rescue therapy for sc-BPAR	-	3	-
Lost to follow-up	2	2	3
mTORI	1	-	-
low TAC levels	-	1	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	E−/SOC Group
Reporting group description:	
Standard of care immunosuppression (SOC)	
Reporting group title	E−/LI Group
Reporting group description:	
Low immunosuppression (LI)	
Reporting group title	E+ Group
Reporting group description:	
Group II. ELISPOT positive (E+) transplant candidates received the same current standard of care immunosuppressive regimen than group E−/SOC.	

Reporting group values	E−/SOC Group	E−/LI Group	E+ Group
Number of subjects	53	48	66
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.51	54.68	53.88
standard deviation	± 12.81	± 14.11	± 13.97
Gender categorical Units: Subjects			
Female	12	16	19
Male	41	32	46
N/A	0	0	1
Recipient ethnicity Units: Subjects			
Caucasian	50	45	46
No Caucasian	3	3	1
N/A	0	0	19
Cause of end-stage renal disease Units: Subjects			
Glomerulonephritis	10	15	17
Vascular	3	3	8
Diabetes Mellitus	12	4	7
Polycystic kidney disease	12	10	13
Unknown	9	10	15
Others	7	5	5
N/A	0	1	1
Time on dialysis (months) Units: monthths			
arithmetic mean	41.20	34.50	23.06
standard deviation	± 50.44	± 51.06	± 28.30
Baseline Panel Reactive Antibodies Units: Levels			
arithmetic mean	0.45	0	0.23

standard deviation	± 2.43	± 0	± 1.14
HLA allelic MM			
Units: Count?			
arithmetic mean	5.58	6.77	7.24
standard deviation	± 2.59	± 1.77	± 2.30
HLA Class I			
Units: Count			
arithmetic mean	3.57	4.33	4.24
standard deviation	± 1.69	± 1.19	± 1.59
HLA Class II			
Units: Count			
arithmetic mean	2.02	2.44	3.00
standard deviation	± 1.29	± 1.09	± 1.07
Pretransplant donor-specific IFN-γ ELISpots			
Units: Count			
arithmetic mean	7.75	7.67	80.02
standard deviation	± 6.82	± 7.03	± 83.14

Reporting group values	Total		
Number of subjects	167		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	47		
Male	119		
N/A	1		
Recipient ethnicity			
Units: Subjects			
Caucasian	141		
No Caucasian	7		
N/A	19		
Cause of end-stage renal disease			
Units: Subjects			
Glomerulonephritis	42		
Vascular	14		
Diabetes Mellitus	23		
Polycystic kidney disease	35		
Unknown	34		
Others	17		
N/A	2		
Time on dialysis (months)			
Units: monthths			
arithmetic mean			
standard deviation	-		
Baseline Panel Reactive Antibodies			

Units: Levels arithmetic mean standard deviation	-		
HLA allelic MM Units: Count? arithmetic mean standard deviation	-		
HLA Class I Units: Count arithmetic mean standard deviation	-		
HLA Class II Units: Count arithmetic mean standard deviation	-		
Pretransplant donor-specific IFN-γ ELISpots Units: Count arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	E−/SOC Group
Reporting group description: Standard of care immunosuppression (SOC)	
Reporting group title	E−/LI Group
Reporting group description: Low immunosuppression (LI)	
Reporting group title	E+ Group
Reporting group description: Group II. ELISPOT positive (E+) transplant candidates received the same current standard of care immunosuppressive regimen than group E−/SOC.	
Subject analysis set title	E+ with low eplet risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups	
Subject analysis set title	E+ with high risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups	
Subject analysis set title	E-/SOC low eplet risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups	
Subject analysis set title	E-/SOC high risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups	
Subject analysis set title	E-/LI low risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups.	
Subject analysis set title	E-/LI high risk
Subject analysis set type	Sub-group analysis
Subject analysis set description: Donor/recipient HLA DQ eplet MM risk score for clinical and subclinical BPAR between study groups.	

Primary: Evaluation of the BPAR between E-/Soc vs E-/LI

End point title	Evaluation of the BPAR between E-/Soc vs E-/LI
End point description: BPAR, biopsy-proven acute rejection; BL, borderline lesions;	
End point type	Primary
End point timeframe: 6 months	

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	35	55	
Units: Subjects				
BPAR (excluding BL)	1	4	12	

Attachments (see zip file)	BPAR between the study groups in all patients/BPAR.pdf

Statistical analyses

Statistical analysis title	The time-dependent association of BPAR

Statistical analysis description:

Since the primary study endpoint could not be achieved, a number of clinically relevant outcomes were analyzed as a post-hoc analysis.

Comparison groups	E−/SOC Group v E−/LI Group
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	non-inferiority
P-value	< 0.05 [1]
Method	Logrank

Notes:

[1] - excluding BL lesions, showed no statistically significant differences between groups (1/43 [2%] vs. 4/35 [13%], p = .16, respectively)

Primary: Evaluation BPAR ITT

End point title	Evaluation BPAR ITT

End point description:

End point type	Primary

End point timeframe:

6 months

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	48	66	
Units: Subjects				
6-mo BPAR	5	11	12	

Statistical analyses

Statistical analysis title	BPAR ITT after six months
Comparison groups	E−/SOC Group v E−/LI Group v E+ Group

Number of subjects included in analysis	167
Analysis specification	Post-hoc
Analysis type	non-inferiority
P-value	< 0.05
Method	Logrank

Secondary: eGFR progression

End point title	eGFR progression

End point description:

Twelve-month eGFR progression between study groups in all patients (intention to treat)

End point type	Secondary

End point timeframe:

untill 12 months

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	48	66	
Units: ml/min				
arithmetic mean (standard deviation)				
at 15 days	40.88 (± 19.88)	42.26 (± 16.36)	38.21 (± 17.74)	
at 1 month	47.66 (± 18.71)	43.46 (± 15.69)	42.93 (± 14.70)	
at 2 months	48.72 (± 19.98)	42.62 (± 15.51)	46.00 (± 13.79)	
at 3 months	49.95 (± 22.27)	39.97 (± 16.41)	47.20 (± 13.03)	
at 6 months	53.95 (± 21.16)	45.31 (± 15.44)	4991 (± 14.41)	
at 12 months	55.44 (± 18.21)	46.25 (± 13.29)	51.36 (± 15.81)	

Attachments (see zip file)	eGFR over 12 months/eGFR.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: De novo DSA at 12 months

End point title	De novo DSA at 12 months

End point description:

dnDSA, de novo donor-specific antibodies;
At 12 months, 149 (89%) patients were tested for anti-HLA antibodies; 47 (88%) among E−/SOC, 43 (89%) within E−/LI and 59(89%) among E+ patients (Table S4). In all, 17 dnDSA were detected among 11 (7.4%) patients, 6 class I (3 anti-A and 3 anti-B), and 11 class II (7 anti-DQ and 4 anti-DR). no differences were observed regarding total dnDSA between the

three groups, E+ patients displayed higher class-II dnDSA than the other groups.

End point type	Secondary

End point timeframe:

12 months

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	43	53	
Units: Subjects				
Total dnDSA	1	3	7	
Class-I dnDSA	1	3	2	
Class-II dnDSA	0	1	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of clinical and subclinical BPAR

End point title	Incidence of clinical and subclinical BPAR

End point description:

When E+ patients were also analyzed, at 6 months, E+ showed significantly higher BPAR (both with and without BL lesions) than E−/SOC patients. Similarly, at 12 months, BPAR rates were significantly higher within E+ and E−/LI patients as compared to E−/SOC, especially in patients remaining on protocol. 12-month cumulative BPAR between the three groups showed the same differences both when assessed PP or ITT (Figure 2C-D). Likewise clinical BPAR, both E+ and E−/LI groups developed significantly higher incidence of sc-BPAR than E−/SOC.

End point type	Secondary

End point timeframe:

Baseline to 12 months

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	48	66	
Units: Subjects				
6-mo BPAR	5	11	12	
12-mo BPAR	6	12	13	
Sc-BPAR	1	10	6	
Sc-BL	4	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: HLA eplet mismatching and de novo alloimmune activation

End point title	HLA eplet mismatching and de novo alloimmune activation

End point description:

We next assessed the impact of donor/recipient HLAMatchmaker eplet mismatches on main immune-mediated events between the distinct study groups. Similar to HLA allele mismatches, E− patients showed lower eplet mismatches as compared to E+

End point type	Secondary

End point timeframe:

From Baseline to 12 months

End point values	E−/SOC Group	E−/LI Group	E+ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	48	66	
Units: Mismatch				
arithmetic mean (standard deviation)				
Global HLA Eplet MM	28.24 (± 17.10)	33.33 (± 11.81)	36.15 (± 15.19)	
HLA class I eplet MM	12.94 (± 7.56)	16.0 (± 5.84)	15.62 (± 7.12)	
HLA class II eplet MM	15.30 (± 11.81)	17.33 (± 10.30)	20.54 (± 10.93)	
HLA class II eplet MM: DRB1	7.83 (± 6.20)	8.50 (± 5.32)	9.87 (± 5.44)	
HLA class II eplet MM: DQB1	5.64 (± 5.53)	6.69 (± 5.33)	8.07 (± 5.43)	
HLA class II eplet MM:DQA1	1.83 (± 1.95)	2.15 (± 1.99)	2.59 (± 1.98)	
HLA class II eplet MM: DQ(A1+B1)	7.47 (± 6.73)	8.83 (± 6.37)	10.67 (± 6.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: HLA DQ eplet MM risk score for clinical BPAR between study groups

End point title	HLA DQ eplet MM risk score for clinical BPAR between study groups

End point description:

Mean class-II eplet mismatches (MM) (DRB1+DQ), and particularly at DQ locus, were significantly higher in patients developing BPAR than in those that did not.However, these differences were only observed among the two E− study groups. A threshold o f DQ (A1/B1) e plet m ismatches ≥10 defined high eplet risk for BPAR with the highest accuracy within all E−patients.
See attachment for more details: Donor/recipient HLA DQ eplet MM risk score

End point type	Secondary

End point timeframe:

Baseline to 12months

End point values	E+ with low eplet risk	E+ with high risk	E-/SOC low eplet risk	E-/SOC high risk
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	38	28	25
Units: Subjects				
at risk	6	7	1	5

End point values	E-/LI low risk	E-/LI high risk		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28	20		
Units: Subjects				
at risk	4	8		

Attachments (see zip file)	Donor/recipient HLA DQ eplet MM risk score/Subgroup.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months

Adverse event reporting additional description:

Please see publication

Assessment type	Systematic

Dictionary used

Dictionary name	own
Dictionary version	1

Reporting groups

Reporting group title	Total cohort

Reporting group description:

No distinguish between the Groups

Serious adverse events	Total cohort		
Total subjects affected by serious adverse events			
subjects affected / exposed	60 / 167 (35.93%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Cardiac disorders			
Angina Pectoris	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
atrial fibrillation	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cardiac decompensation	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
cardiogenic shock	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		

subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoe déffort				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
mitralvalveinsufficiency				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NSTEMI				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
"Pulmonar thromboembolism suspected"				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CVP Syndrome with cerebral filiae				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Acute febrile illness				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
death				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
sudden death				

subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Acute rejection grade IIA	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Acute vascular rejection IB in graft	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
abdominal wall hermatoma	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxemic lung failure			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bronchitis			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
accute cellular rejection type	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute T-cell mediated rejection type I	Additional description: other medically important conditions		

subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute tubular necrosis,	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
allograft dysfunction	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation		
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
acute on chronic renal failure due to rec. UTI			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
delayed graft function			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Perirenal haematoma			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
renal transplant dysfunction			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Ureteral stenosis			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
lymphocele			

subjects affected / exposed	2 / 167 (1.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxious	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation			
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute pyelonephritis	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation			
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteriemia due to Pseudomonas	Additional description: Requires inpatient hospitalisation or prolongation of existing hospitalisation			
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
urinary tract infection				
subjects affected / exposed	15 / 167 (8.98%)			
occurrences causally related to treatment / all	0 / 15			
deaths causally related to treatment / all	0 / 0			
urological sepsis				
subjects affected / exposed	5 / 167 (2.99%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Infection with staphilococcus species (shunt)				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CMV				

subjects affected / exposed	4 / 167 (2.40%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infections			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
spondylodiscitis			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Total cohort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 167 (59.88%)		
Surgical and medical procedures			
AVF shunt			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
General disorders and administration site conditions			
progressive pain left jaw and ear			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
A cold			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	3		
AF/GGT elevated			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Agitated			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
alopecia			

subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
aque subjects affected / exposed occurrences (all)	2 / 167 (1.20%) 2		
belly pain subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
Diarrhea subjects affected / exposed occurrences (all)	33 / 167 (19.76%) 45		
common cold subjects affected / exposed occurrences (all)	13 / 167 (7.78%) 21		
dizziness subjects affected / exposed occurrences (all)	12 / 167 (7.19%) 14		
Headache subjects affected / exposed occurrences (all)	11 / 167 (6.59%) 13		
Immune system disorders Afunctio of kidney graft subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
Reproductive system and breast disorders Afunctio of kidney graft subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
Respiratory, thoracic and mediastinal disorders Acute catarrh subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
Back pain radiating out to stomach subjects affected / exposed occurrences (all)	1 / 167 (0.60%) 1		
Psychiatric disorders			

A bit down			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
Anxiety			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences (all)	3		
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Arteria carotis externa stenosis right			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Arteria femoralis superior stenosis bilateral			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Arterial fibrillation			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
atheromatosis			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Atrium fibrillation			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
cardiac arrhythmia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
cardiac decompensation			
subjects affected / exposed	6 / 167 (3.59%)		
occurrences (all)	6		
Chest tightness and pain			

subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
congestive heart failure			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
"Decompensation of secondary hypertension"			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
dilitated aorta			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
Dyslipidemia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Dyspnoea NYHA II-III			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
Edema	Additional description: Edma foot and hand		
subjects affected / exposed	24 / 167 (14.37%)		
occurrences (all)	37		
fast heartbeat	Additional description: heartpalpitations or exercise		
subjects affected / exposed	9 / 167 (5.39%)		
occurrences (all)	9		
Hemangioma abdominal			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Hepatomegaly			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
hypertensions			
subjects affected / exposed	51 / 167 (30.54%)		
occurrences (all)	56		
Hypotension			
subjects affected / exposed	5 / 167 (2.99%)		
occurrences (all)	5		

Nervous system disorders			
aphonia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Benign paroxysmal positional vertigo			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Trembling, tremor			
subjects affected / exposed	10 / 167 (5.99%)		
occurrences (all)	11		
Blood and lymphatic system disorders			
albuminurie			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
Anemia			
subjects affected / exposed	8 / 167 (4.79%)		
occurrences (all)	12		
hypercalcemia			
subjects affected / exposed	7 / 167 (4.19%)		
occurrences (all)	7		
Leucopenia			
subjects affected / exposed	13 / 167 (7.78%)		
occurrences (all)	15		
Gastrointestinal disorders			
abdominal pain, cramps, discomfort			
subjects affected / exposed	13 / 167 (7.78%)		
occurrences (all)	15		
Air in colon			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Anal fissure			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Aerobilia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
constipation and obstipation			

subjects affected / exposed	31 / 167 (18.56%)		
occurrences (all)	31		
Nausea			
subjects affected / exposed	10 / 167 (5.99%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	7 / 167 (4.19%)		
occurrences (all)	8		
fever			
subjects affected / exposed	18 / 167 (10.78%)		
occurrences (all)	23		
Skin and subcutaneous tissue disorders			
Acne on scalp			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
acne medicemtosa/acneiforme			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Acrovesiculeus eczema,			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Actinic keratosis			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
bad scarring			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Basal cell cardinoma			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
BENIGN SKIN LESSION IN NOSE			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Renal and urinary disorders			
acute renal failure			

subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	2		
Acute tublar necrosis			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences (all)	3		
Alguria			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
acute rejection grad III			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
anuria			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Asymptomatic urinary tract infection			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences (all)	3		
AVF after biopsy in kidney graft			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
achilles tendon complaints			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences (all)	3		
Back Pain			
subjects affected / exposed	9 / 167 (5.39%)		
occurrences (all)	11		
Baker's cyst right popliteal fossa,			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Biceps rupture			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Bilateral myopathy gluteal muscles			

subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Infections and infestations			
Aspergillus nidulans (bronchial lavage)			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences (all)	1		
Bact, Infection			
subjects affected / exposed	4 / 167 (2.40%)		
occurrences (all)	11		
Unary infections			
subjects affected / exposed	9 / 167 (5.39%)		
occurrences (all)	19		
BK Virus Infections			
subjects affected / exposed	13 / 167 (7.78%)		
occurrences (all)	16		
CM Virus			
subjects affected / exposed	14 / 167 (8.38%)		
occurrences (all)	14		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences (all)	3		
Hypercalcemia			
subjects affected / exposed	23 / 167 (13.77%)		
occurrences (all)	33		
metabolic disorders			
subjects affected / exposed	13 / 167 (7.78%)		
occurrences (all)	13		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

A main limitation of the CELLIMIN trial was its premature termination due to insufficient recruitment rates, which illustrates the complexity of conducting large, prospective randomized trials using novel biomarkers.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33725408