Clinical trial results:
Inhibition of Co-Stimulation in Rheumatoid Arthritis

Summary

EudraCT number	2014-004419-35
Trial protocol	GB
Global end of trial date	02 May 2019

Results information

Result version number	v1 (current)
This version publication date	25 November 2023
First version publication date	25 November 2023

Trial information

Trial identification

Sponsor protocol code	GN13RH410

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02652273
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	Dykebar Hospital, Paisley, United Kingdom, PA2 7DE
Public contact	Dr Maureen Travers, NHS Greater Glasgow and Clyde, 0044 141 314 4012, Maureen.Travers@ggc.scot.nhs.uk
Scientific contact	Dr Maureen Travers, NHS Greater Glasgow and Clyde, 0044 141 314 4012, Maureen.Travers@ggc.scot.nhs.uk
Sponsor organisation name	University of Glasgow
Sponsor organisation address	University Avenue, Glasgow, United Kingdom, G12 8QQ
Public contact	Dr Debra Stuart, University of Glasgow, 0044 141 232 1798, debra.stuart@glasgow.ac.uk
Scientific contact	Dr Debra Stuart, University of Glasgow, 0044 141 232 1798, debra.stuart@glasgow.ac.uk

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	07 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2019
Global end of trial reached?	Yes
Global end of trial date	02 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of this study is the characterisation of the immune response to citrullinated peptides by T cells following costimulatory modulation in RA patients at 12 weeks.

Protection of trial subjects:

1) Like all the other biologics and treatments used for RA, abatacept has the potential to increase the risk of infections. As participants will receive abatacept as part of their clinical practice, regardless of participation in the study, there is therefore no additional treatment risk associated with participation in the study above that associated with routine care. Participants will still be counselled about potential adverse effects and infections as per standard clinical practice. Similarly, study participants, or a relative, will be trained in subcutaneous injection techniques. Training will be provided by experienced practitioners in line with standard clinical practice for abatacept and the other subcutaneous biologic agents used in RA. Any adverse effects will be treated as per routine clinical care, including discontinuation or interruption of abatacept according to standard protocols and clinical judgement.
2) Failure to respond: Decisions regarding response are generally only made at 6 months. As this study is only for 6 months, non responders will not be disadvantaged and will still have the option to switch therapy upon completion of the study, in line with routine care. There is no placebo arm in this study.
3) Blood volume: Study participants were invited to consent to blood sampling greater in volume than routine care. Sample volumes and timing have been carefully selected to minimise the burden on participants while still allowing investigation of the important inflammatory processes. We do not believe the proposed volumes pose any risk to participants' health.
4) Venesection: Study participants will be asked to have blood taken more regularly than routine care (7 instead of 3 times). Venesection can lead to some shortlived pain/discomfort and potentially bruising at the site of venesection. Blood samples will be taken by staff experienced and, where possible, study samples will be taken at the same time as bloods for routine care.

Background therapy:

Methotrexate at dose of 10-25mg/week, either orally or SC Methotrexate. Should be taken for at least 3 months with a stable dose for 1 month prior to enrolment.

Evidence for comparator:

N/A

Actual start date of recruitment	01 June 2015
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	United Kingdom: 25
Worldwide total number of subjects	25
EEA total number of subjects	0

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)	20
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects where identified via clinicians who recommend treatment with a biologic agent.
Participants were recruited via:

- Rheumatology out-patient clinic visits
- Referrals from other Rheumatology out-patient clinics
- If required, in response to advertising in the secondary care sector, via posters or leaflets.

Pre-assignment

Screening details:

Subjects where identified via clinicians who recommend treatment with a biologic agent. Subjects had active RA and met the relevant local or national guidelines for treatment with a biologic agent, consistent with the license and SmPC. Subjects were invited to a screening visit to assess eligibility. Only subjects HLA-DRB1*0401/0404 positive were i

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	All Participants - Abatacept

Arm description:

All study subjects should receive a 125 mg subcutaneous injection of abatacept, followed by weekly subcutaneous injections of abatacept (125mg).

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects will receive the standard dosage of 125 mg/ml and will then receive this weekly for 24 weeks. The total contents (1 ml) of the pre-filled syringe will be administered. No dose adjustments are permitted. Patients will receive study medication for 24 weeks. Patients may be trained to self-administer SC abatacept using the single-dose prefilled glass syringe according to local practices for the administration of biological therapy. Patients self-administering at home will be provided with detailed information and advised to contact the investigator or site staff in case they have experienced an AE/SAE or have any concerns. An injection diary will be provided and completed by all patients. Patients unable to self-administer will be asked if a relative can serve this purpose and if so appropriate training will be offered. Suitable injection sites are the front of the thigh and abdomen, except for the 5 cm area around the navel. Injection sites will be rotated.

Number of subjects in period 1	All Participants - Abatacept
Started	25
Completed	22
Not completed	3
Adverse event, serious fatal	1
No more Detail available	2

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	5	5	
Gender categorical Units: Subjects			
Female	20	20	
Male	5	5	

End points

End points reporting groups

Reporting group title	All Participants - Abatacept

Reporting group description:

All study subjects should receive a 125 mg subcutaneous injection of abatacept, followed by weekly subcutaneous injections of abatacept (125mg).

Subject analysis set title	Primary analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Numbers in Primary analysis

Primary: Antigen-specific T cell responses pre- and post-treatment with abatacept

End point title	Antigen-specific T cell responses pre- and post-treatment with abatacept[1]

End point description:

Ex-vivo tetramer staining using a multi-colour flow-cytometry panel to investigate T cells specific for either of the 12 different citrullinated peptide epitopes and the expression of different markers on these cells.

End point type	Primary

End point timeframe:

From Day 1 (first dose) to 12 weeks

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: Statistical analysis was performed between subjects defined as responders (+) and non-responders (-) based on whether they had a reduction of >1.2 in DAS28-ESR score at week 12 compared to baseline. (Rather than separate treatment arms)

End point values	All Participants - Abatacept			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Mean Fluorescence Intensity (MFI)	0			

Attachments (see zip file)	ICOSRA - Primary endpoint/File for Result Chart upload.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
2015 to May 2019	
Adverse event reporting additional description:	
Serious Adverse Events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	All Participants
Reporting group description: -	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Don't have access to this data to report

Serious adverse events	All Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 25 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Interstitial lung disease			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All Participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2016	Clarifications / minor amendments to the protocol, change in wording to the Patient Information Sheet, and inclusion of injection diary into the Patient Alert Card.
30 January 2017	Minor clarifications / amendents to the protocol, Update protocol version control number. Outdated addresses and email details, now amended to accurately reflect contact details. Changes to wording in WOCBP - S1 exclusion criteria; S5.2.3 eligibility criteria; S4 withdrawal of subjects, new text inserted to make instructions more detailed and S5.2.3 . Insertion of blood tests or study tests in S3.2 Trial Flowchart and throught relevant scheduled visits throughout the protocol (S6.1.1 -S6.1.2S6.1.3, S6.1.4, S6.1.5, S6.2, S6.4. Tests not mentioned in error in current protocol that were aveilable on the flowchart or scheduled vists. IMP risks new text included in this section to fully explain IMP risks Good Clinical Practice new text to be included to confirm that the study will be conducted according to Declaration of Helsinki Procedures Addition of NHS Lanarkshire as Patient Identification Centre
18 December 2017	Addition of a site. Protocol has been updated to reflect this change.
05 June 2018	Change of Laboratory exclusion criteria; Glomerular Filtration rate from <60ml/min to <30ml/min.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported