Clinical trial results:
A Single Arm, Open-Label, Multi-Centre, Phase I/II Study Evaluating the Safety and Clinical Activity of AUTO2, a CAR T Cell Treatment Targeting BCMA and TACI, in Patients with Relapsed or Refractory Multiple Myeloma.

Summary

EudraCT number	2016-003893-42
Trial protocol	GB NL
Global end of trial date	05 September 2019

Results information

Result version number	v1 (current)
This version publication date	20 September 2020
First version publication date	20 September 2020

Trial information

Trial identification

Sponsor protocol code	AUTO2-MM1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03287804
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Autolus Limited
Sponsor organisation address	Forest House, 58 Wood Lane, White City, London, United Kingdom, W12 7RZ
Public contact	Clinical Project Manager, Autolus Limited, +44 1483 920748, clinicaltrials@autolus.com
Scientific contact	Clinical Project Manager, Autolus Limited, +44 1483 920748, clinicaltrials@autolus.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1: Assess the safety and tolerability of AUTO2, identify the recommended Phase II dose and maximum tolerated dose (MTD), where applicable.

Phase 2: To evaluate the anti-tumour effect of AUTO2.

Long term follow-up is conducted under the separate long term follow-up study protocol AUTO-LT1.

Protection of trial subjects:

The Investigator was responsible for conducting the study in full accordance with the clinical study protocol, the latest revision of the Declaration of Helsinki, the Good Clinical Practice: Consolidated Guideline, and all applicable national and local laws and regulations for clinical research. Information regarding any investigational sites participating in this study that cannot comply with these standards was documented and appropriate actions taken. For studies conducted in the EU/European Economic Area countries, the Investigator has ensured compliance with the EU Clinical Trial Directive [2001/20/EC]. For studies conducted in the United States or under a United States investigational new drug (IND), the Investigator has additionally ensure adherence to the basic principles of "Good Clinical Practice" as outlined in the current version of 21 Code of Federal Regulations, subchapter D, part 312, "Responsibilities of Sponsor and Investigators", part 50, "Protection of Human Subjects", and part 56, "Institutional Review Boards".

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 May 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	15 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	9
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited at two study centres in the United Kingdom and one study centre in the Netherlands.

Pre-assignment

Screening details:

Screening procedures were performed up to 12 weeks before study drug was administered.

Period 1

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

Arms

Arm title	AUTO2

Arm description:

Relapsed or refractory myeloma subjects.

Arm type	Experimental
Investigational medicinal product name	AUTO2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose as an intravenous infusion on Day 0.

Number of subjects in period 1	AUTO2
Started	12
Received Study Treatment	11
Completed	1
Not completed	11
Physician decision	2
Death before study treatment	1
Progressive disease	8

Baseline characteristics

Reporting groups	
Reporting group title	AUTO2
Reporting group description:	
Relapsed or refractory myeloma subjects.	

Reporting group values	AUTO2	Total	
Number of subjects	12	12	
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)	9	9	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	9	9	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	12	12	
Race Units: Subjects			
Black/African American	2	2	
White	10	10	

End points

End points reporting groups

Reporting group title	AUTO2
Reporting group description:	
Relapsed or refractory myeloma subjects.	

Primary: Phase 1: Number of Subjects with Grade 3 to 5 Toxicity during the Dose Limiting Toxicity (DLT) Period

End point title	Phase 1: Number of Subjects with Grade 3 to 5 Toxicity during the Dose Limiting Toxicity (DLT) Period[1]
End point description:	

End point type	Primary
End point timeframe:	
Up to 28 days post-infusion	

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: Only descriptive summary statistics were planned for this endpoint.

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Subjects with a Dose Limiting Toxicity (DLT)

End point title	Phase 1: Number of Subjects with a Dose Limiting Toxicity (DLT)[2]
End point description:	

Dose limiting toxicity was defined as:
Any new non-hematological AE of Grade 3 or higher toxicity using the NCI CTCAE (Version 4.03), which is probably or
definitely related to AUTO2 therapy, which occurs within the DLT evaluation period, and which fails to resolve to Grade
2 or better within 14 days, despite appropriate supportive measures; A Grade 4 CRS; Any other reason for activation of
the safety switch after receiving AUTO2; Any other fatal event (Grade 5) or life-threatening event (Grade 4) that cannot
be managed with conventional supportive measures or which in the opinion of the SEC necessitates dose reduction
or other modification to trial treatment to avoid a similar hazard in future patients. Effort should be made to perform an
autopsy in case of fatal event where the aetiology is unclear; Any event that in the opinion of treating investigators and/
or Medical Monitor puts the patient at undue risk may also be considered a DLT.

End point type	Primary

End point timeframe:

Up to 28 days post-infusion

Notes:

[2] - 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: Only descriptive summary statistics were planned for this endpoint.

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Best Overall Response

End point title	Phase 2: Best Overall Response[3]

End point description:

The analysis population consisted of all subjects who received at least 1 dose (complete or partial) of AUTO2 therapy in Phase I of the study. No patients were enrolled in Phase II as the study was early terminated in Phase I.

Best overall response was defined as stringent complete response + complete response + very good partial response +
partial response following treatment with AUTO2. Response Criteria Per IMWG Consensus Recommendations

End point type	Primary

End point timeframe:

Up to 2 years

Notes:

[3] - 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 not performed on this endpoint as the study was early terminated and Phase 2 was never started.

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Subjects				
Progressive disease	0			
Partial response	3			
Stable disease	7			
Very good partial response	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects for Whom an AUTO2 Product Can be Generated

End point title	Proportion of Subjects for Whom an AUTO2 Product Can be Generated

End point description:

Feasibility of product generation will be examined by assessing the number of AUTO2 successfully manufactured as a fraction of the number of subjects undergoing leukapheresis.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate

End point description:

Number of subjects exhibiting stringent complete response, complete response, very good partial response, partial response or minor response following treatment with AUTO2.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11[4]			
Units: Subjects	4			

Notes:

[4] - 2 subjects were retreated; their best overall response is presented for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Calculated from the date of first observation of sCR, CR, VGPR or PR to the date of disease progression,

relapse or death, for subjects who were considered responders (achieved at least PR). Subjects who had not progressed, relapsed or died will be censored at the last adequate disease assessment.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[5] - Analysis was not performed due to the study being terminated early and Phase 2 not being started.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Disease Progression

End point title	Time to Disease Progression

End point description:

Calculated from the date of AUTO2 treatment to the date of progression. Subjects who had not progressed, relapsed or died without progression/relapse will be censored at the last adequate disease assessment.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[6] - Analysis was not performed due to the study being terminated early and Phase 2 not being started.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Calculated from the date of AUTO2 treatment to the date of progression or death. Subjects who have not progressed or relapsed was censored at the last adequate disease assessment

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[7] - Analysis was not performed due to the study being terminated early and Phase 2 not being started.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Descriptive analysis based on number of subjects alive at database lock (1-May-2020).

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Expansion Followed by Persistence of RQR8/APRIL CAR Positive T Cells in the Peripheral Blood

End point title	Number of Subjects with Expansion Followed by Persistence of RQR8/APRIL CAR Positive T Cells in the Peripheral Blood

End point description:

Expansion and persistence of RQR8/APRIL CAR positive T cells as determined by quantitative polymerase chain reaction and/or flow cytometry.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	AUTO2			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Subjects	9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 0 until Day 60 post last AUTO2 infusion.	
Adverse event reporting additional description:	
Adverse events are reported for the 11 subjects who received study treatment (safety analysis set).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	AUTO2
Reporting group description:	
Relapsed or refractory myeloma subjects. Results for adverse events are shown for the safety analysis set.	

Serious adverse events	AUTO2		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 11 (54.55%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	1		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metaplastic breast carcinoma			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 11 (9.09%)		
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	AUTO2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter site bruise			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	6 / 11 (54.55%)		
occurrences (all)	10		
Oedema peripheral			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	6 / 11 (54.55%)		
occurrences (all)	8		
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Dyspnoea			

subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	5		
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Tachypnoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Psychiatric disorders			
Hallucination			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Neutrophil count decreased			
subjects affected / exposed	7 / 11 (63.64%)		
occurrences (all)	71		
Platelet count decreased			

subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	12		
Respiratory syncytial virus test positive			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Serum ferritin increased			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	6		
Paraesthesia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Tension headache			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 11 (81.82%)		
occurrences (all)	31		
Febrile neutropenia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	29		
Thrombocytopenia			

subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 7		
Ear and labyrinth disorders Ear disorder subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Haematochezia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all)	 2 / 11 (18.18%) 3 5 / 11 (45.45%) 6 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 2 / 11 (18.18%) 3 3 / 11 (27.27%) 3		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 2 / 11 (18.18%) 2		
Renal and urinary disorders			

Micturition urgency subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Musculoskeletal chest pain subjects affected / exposed occurrences (all) Musculoskeletal discomfort subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 6 1 / 11 (9.09%) 1 4 / 11 (36.36%) 6 1 / 11 (9.09%) 1 2 / 11 (18.18%) 2 1 / 11 (9.09%) 1 3 / 11 (27.27%) 3 1 / 11 (9.09%) 1		
Infections and infestations Enterovirus infection subjects affected / exposed occurrences (all) External ear cellulitis subjects affected / exposed occurrences (all) Metapneumovirus infection	1 / 11 (9.09%) 1 1 / 11 (9.09%) 1		

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Parvovirus B19 infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pseudomonal bacteraemia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rhinovirus infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Fluid overload			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2017	Protocol Version 2 - Summary of changes: - Administrative changes - Clarification of study design and eligibility criteria - Clarification for subjects who receive rituximab - Reduced biomarker sampling frequency - Safety Evaluation Committee monitoring introduced - Independent Data Monitoring Committee introduced
07 November 2017	Protocol Version 3 - Summary of changes: - Administrative changes - Updated study design - Updated patient numbers - Increased study duration - Modification of Schedule of Assessments - Update on Safety Management Guidelines - Clarifications in Eligibility section - Uniform descriptions added for product descriptions and pre-clinical information - Modifications to AE reporting period and conmeds
19 December 2017	Protocol Version 4 - Summary of changes: - Typographical and administrative changes - Updates to study design - Updates to overall patient number - Duration of study participation updated - DLT criteria updated - Update on general supportive care guidelines - Clarifications added for AE reporting - Updates to eligibility section - IMWG update 2016 for disease response evaluation - Statistical analysis modification
30 January 2018	Protocol Version 5 - Summary of changes: - Typographical changes - Updated summary of clinical studies - Dose-escalation details added - Schedule of assessments and sampling schedule updated - Updates to Inclusion/exclusion criteria - Re-treatment criteria clarification added - Discontinuation and re-enrolment into the study clarification added - Additional study visit and procedures added - Lifestyle restrictions added - Monitoring access clarified

15 May 2018	Protocol Version 6 - Summary of changes: - Typographical changes - DLT criteria modified - Re-treatment criteria modified - Inclusion/exclusion criteria amended - Guidelines for prevention, monitoring and management of adverse events amended - Pharmacologic Management of CRS aligned with packaging - Additional language added to Allowed Concomitant Medications/Therapies - Additional samples will be taken for Rituximab Rescue Therapy
27 June 2018	Protocol Version 7 - Summary of changes: - Typographical changes - Update on clinical experience so far - Decrease of Cohort 4 - Increase in DMSO quantity - Updated dosing information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported