



Clinical trial results:

A “window of opportunity” trial with Brentuximab Vedotin and Imatinib in patients with relapsed or refractory ALK+ anaplastic large cell lymphoma or patients ineligible for chemotherapy

Summary

EudraCT number	2013-003505-26
Trial protocol	AT
Global end of trial date	03 November 2021

Results information

Result version number	v1 (current)
This version publication date	16 July 2022
First version publication date	16 July 2022

Trial information

Trial identification

Sponsor protocol code	AGMT_ALCL1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02462538
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AGMT
Sponsor organisation address	Gentzgasse 60/21, Vienna, Austria, 1180
Public contact	Daniela Wolkersdorfer, AGMT, 0043 6626404412, d.wolkersdorfer@agmt.at
Scientific contact	Richard Greil, AGMT, 0043 5725525801, r.greil@salk.at

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 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of simultaneous administration of brentuximab vedotin and imatinib mesylate in substitution of conventional chemotherapeutic treatment.

Protection of trial subjects:

Safety measurements were assessed at screening, every 3 weeks during and at the end of treatment, and at final visit. All (serious) adverse events occurring during study treatment were collected from signing the informed consent form until 12 weeks after the end of study treatment.

In general, concomitant medications and therapies necessary for supportive care and safety of the patient are allowed: Because of the inherent risk of either reduced activity or enhanced toxicity of the concomitant medication and/or imatinib, drugs known to interact with the same CYP450 isoenzymes (2D and 3A4) as imatinib or MMAE should have been used with caution.

Background therapy:

None.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	16 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	Austria: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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

Subject disposition

Recruitment

Recruitment details:

Between 03-Nov-2015 and 26-September-2017 three patients were enrolled at one site in Austria.

Pre-assignment

Screening details:

Due to low recruitment study was withdrawn prematurely after inclusion of three patients on 22-Mar-2018. At time of this decision, no patients were on study treatment. Planned follow up phase was conducted and ended on 03-Nov-2021.

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	Overall trial
Arm description:	
Combination therapy	
Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Starting dose of brentuximab vedotin 1.8 mg/kg; cycles were repeated every 3 weeks up to 48 weeks (last administration: d1 week 45)

Investigational medicinal product name	Imatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

100mg daily starting from day 1 of the first cycle; increased to 200mg daily starting from day 1 of the second cycle; continued at 200mg for 48 weeks

Number of subjects in period 1	Overall trial
Started	3
Completed	1
Not completed	2
Adverse event, non-fatal	1
Progressive disease	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	3	3	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Age at enrollment			
Units: years			
median	26		
full range (min-max)	24 to 47	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	3	3	
Prior ALCL therapies			
Units: Subjects			
1 prior therapy	2	2	
3 prior therapies	1	1	

End points

End points reporting groups

Reporting group title	Overall trial
Reporting group description:	
Combination therapy	

Primary: Safety and tolerability

End point title	Safety and tolerability ^[1]
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End point description:

Due to small sample size, no evaluation of tolerability can be given, results are tabulated only.

End point type	Primary
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End point timeframe:

60 weeks - from enrollment to final visit 12 weeks after discontinuing or completion of study treatment

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: Main aim of this phase I/II pilot study is feasibility and safety. No formal hypothesis testing was planned.

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Withdrawal due to AE	1			
No withdrawal due to AE	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response rate

End point title	Clinical response rate
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End point description:

End point type	Secondary
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End point timeframe:

Response at final visit (12 weeks after discontinuing or completion of study treatment)

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Complete remission	2			
Partial remission	0			
Stable disease	0			
Progressive disease	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion of patient until final visit (12 weeks after completion or discontinuation of study treatment)

Adverse event reporting additional description:

According to protocol, an abnormal laboratory value was not assessed as an AE unless that value led to discontinuation or delay in treatment, dose modification, therapeutic intervention. Progression of disease was not to be regarded as SAE.

Relation to IMP brentuximab vedotin is given.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Overall trial
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Reporting group description:

All enrolled patients

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Oesophagitis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)		
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	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	7		
Neutrophil count decreased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Polyneuropathy			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Stenosis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Generalised oedema			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Diarrhoea			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 3 (66.67%)</p> <p>2</p>			
<p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p>			
<p>Ascites</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p>			
<p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p>			
<p>Hepatobiliary disorders</p> <p>Cholestasis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>2</p>			
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p>			
<p>Musculoskeletal and connective tissue disorders</p> <p>Joint swelling</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>Arthritis reactive</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p>			
<p>Infections and infestations</p> <p>Dermatophytosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>2</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>Influenza</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 3 (66.67%)</p> <p>2</p>			

Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		

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.

Recruitment was withdrawn prematurely due to very slow recruitment. Three patients were enrolled, planned sample size of 10 patients was not reached.

Notes: