



Clinical trial results:

A MoLEcularly Guided Anti-Cancer Drug Off-Label Trial

– a multicenter, basket and umbrella explorative trial on the efficacy and safety of molecular profile selected commercially available targeted anti-cancer drugs in patients with advanced cancers progressive on standard therapy

Summary

EudraCT number	2018-004623-36
Trial protocol	SE
Global end of trial date	30 January 2025

Results information

Result version number	v1 (current)
This version publication date	28 January 2026
First version publication date	28 January 2026
Summary attachment (see zip file)	Publication Megalit (Publikation Megalitstudien.pdf)

Trial information

Trial identification

Sponsor protocol code	MEGALiT1901
-----------------------	-------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Uppsala university hospital
Sponsor organisation address	Sjukhusvägen, Uppsala, Sweden, 75185
Public contact	KFUE, Uppsala University Hospital, +46 0186115275, kfue@akademiska.se
Scientific contact	Peter Nygren, Uppsala University Hospital, +46 0186110000, peter.nygren@igp.uu.se

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	19 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 December 2023
Global end of trial reached?	Yes
Global end of trial date	30 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the anti-tumor activity of the genomics guided therapy.
- To describe and assess the clinical feasibility, including safety, of therapy selection based on genomic profiling of fresh tumor tissue.

Protection of trial subjects:

The study was conducted in accordance with ICH GCP and the Helsinki declaration.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	16 December 2019
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	Sweden: 153
Worldwide total number of subjects	153
EEA total number of subjects	153

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)	153
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

153 patients with cancer, where all treatment options had been exhausted, were included (i.e. treatment targets were evaluated). Actionable targets were discovered for 49 patients. 44 patients were allocated a treatment option, and of these 38 patients were treated in the trial.

Pre-assignment

Screening details:

Adult (age >18 years)

Retrievable or available tissue allowing for molecular analysis; tumor tissue procured specifically for the trial or archived tumor tissue and/or ctDNA according to triage Figure 2.

ECOG performance status 0-2 with expected stable disease for the up to 6 weeks run-in period prior to treatment decision

Period 1

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

Arms

Arm title	Treatment cohort
-----------	------------------

Arm description:

Subjects treated based on genetic markers in the trial

Arm type	Experimental
Investigational medicinal product name	niraparib
Investigational medicinal product code	L01XK02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

According to SnPC

Investigational medicinal product name	atezolizumab
Investigational medicinal product code	L01FF05
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

According to SmPC

Investigational medicinal product name	cobimetinib
Investigational medicinal product code	L01EE02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

According to SmPC

Investigational medicinal product name	Everolimus
Investigational medicinal product code	L01EG02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
According to SmPC

Number of subjects in period 1^[1]	Treatment cohort
Started	38
Completed	0
Not completed	38
Physician decision	38

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 153 patients were tested in the trial, and 38 were treated.

Baseline characteristics

Reporting groups

Reporting group title	Treatment cohort
-----------------------	------------------

Reporting group description:

Patients with actionable target for treatment based on genetic tumor analysis

Reporting group values	Treatment cohort	Total	
Number of subjects	38	38	
Age categorical			
Age 18 or more			
Units: Subjects			
18 or more	38	38	
Gender categorical			
Units: Subjects			
Female	25	25	
Male	13	13	

Subject analysis sets

Subject analysis set title	Treated patients
----------------------------	------------------

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

Patients where oncologic treatment could be administered based on actionable genetic target

Reporting group values	Treated patients		
Number of subjects	38		
Age categorical			
Age 18 or more			
Units: Subjects			
18 or more			
Gender categorical			
Units: Subjects			
Female	25		
Male	13		

End points

End points reporting groups

Reporting group title	Treatment cohort
Reporting group description:	
Subjects treated based on genetic markers in the trial	
Subject analysis set title	Treated patients
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients where oncologic treatment could be administered based on actionable genetic target	

Primary: Overall response rate

End point title	Overall response rate ^[1]
End point description:	
Objective Response Rate (ORR) and tumor control rate [Time Frame: From first dose up to 24 months]. The proportion of patients that have a best overall response of complete response (CR), partial response (PR) or stable disease ≥ 16 weeks, as assessed by RECIST 1.1 criteria (and/or, as applicable, tumor type specific criteria as defined by diagnose-specific APPENDIX VIII and efficacy evaluation criteria in APPENDIX II).	
End point type	Primary
End point timeframe:	
up to 24 months after first 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: Statistical analysis is done by descriptive analysis.

End point values	Treated patients			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Recist 1.1				
number (not applicable)	38			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Duration of trial

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	CTCAE
-----------------	-------

Dictionary version	4.03
--------------------	------

Reporting groups

Reporting group title	Treated patients
-----------------------	------------------

Reporting group description:

Patients who were treated based on actionable genetic target in the trial

Serious adverse events	Treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 38 (39.47%)		
number of deaths (all causes)	33		
number of deaths resulting from adverse events	1		
Investigations			
Hospitalisation	Additional description: Unplanned hospitalization due to syncope		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Vomiting			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pain			

subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Embolism	Additional description: Thromboembolic event		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Myositis	Additional description: Immune-related myositis		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Perforation	Additional description: Perforation of intestine due to carcinomatosis		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis	Additional description: Autoimmune Hepatitis		

subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Liver disorder	Additional description: High liver values		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Prolonged hospitalization and death		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pleural effusion	Additional description: Pleaura fluid		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Headache			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever	Additional description: Fever		
subjects affected / exposed	1 / 38 (2.63%)		
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	Treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 38 (86.84%)		
Investigations			

Laboratory test abnormal subjects affected / exposed occurrences (all)	Additional description: increased liver enzes, hypoalbumiemi, Low LPK, Creatinin koinase increase, Hopo-natremia,		
	7 / 38 (18.42%) 8		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all) Embolism subjects affected / exposed occurrences (all)			
	1 / 38 (2.63%) 1		
	Additional description: Thromboembolic event		
	1 / 38 (2.63%) 1		
Nervous system disorders Cognitive disorder subjects affected / exposed occurrences (all) Hydrocephalus subjects affected / exposed occurrences (all) Balance disorder subjects affected / exposed occurrences (all)			
	Additional description: Cognitive disturbance		
	1 / 38 (2.63%) 1		
	Additional description: Worsening hydrocephalus		
	1 / 38 (2.63%) 1		
	Additional description: balance worsening		
	1 / 38 (2.63%) 1		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)			
	7 / 38 (18.42%) 10		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all) Ascites subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Oedema			
	Additional description: Abdominal pain, joint pain, myalgia, increased cancer pain, arthralgia, intermittent headache, pain after biopsy		
	8 / 38 (21.05%) 11		
	2 / 38 (5.26%) 2		
	1 / 38 (2.63%) 1		

subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	8 / 38 (21.05%)		
occurrences (all)	8		
Syncope			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Immune system disorders			
Immune system disorder	Additional description: Bullous Pemphigoid, Immune related reaction		
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Gastrointestinal disorders			
Gastrointestinal disorder	Additional description: Abd pain, nausea, diarrhea, vomiting, stomatitis, anorexia		
subjects affected / exposed	14 / 38 (36.84%)		
occurrences (all)	23		
Respiratory, thoracic and mediastinal disorders			
Lung disorder	Additional description: Pleural effusion left lung, cough, dyspnoea		
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Skin disorder	Additional description: pruritus, rash, atoma, photosensitivity, scalp pain, genital blisters, hematoma around nails		
subjects affected / exposed	8 / 38 (21.05%)		
occurrences (all)	12		
Endocrine disorders			
Diabetes mellitus	Additional description: Diabetes, diabetes worsening		
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Infections and infestations			
Infection	Additional description: Fever, Covid-19, Flu-like symptoms, common cold, infection other		
subjects affected / exposed	9 / 38 (23.68%)		
occurrences (all)	11		
Metabolism and nutrition disorders			

Weight decreased subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
--	---------------------	--	--

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2020	Amendment 01 IB Atezolizumab v15 & v15 add 2, Cobimetinib v12 5.1-2020-67147
16 January 2021	Amendment 02 delayed opening of 4th treatment cohort 5.1-2020-86074
12 April 2022	Amendment 03 IB Niraparib v 13, IB Atezolizumab Version 18, IB Cobimetinib Version 14 5.1-2022-27257
19 August 2022	Amendment 04 protokoll v 2.0 5.1-2022-55217
04 January 2023	Amendment 05 IB Niraparib V. 14 5.1-2022-91841
03 May 2023	Amendment 06 protokoll v 3.0 5.1-2023-28319

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported