



## Clinical trial results:

### PIK-ORL - A Phase II, multicenter trial aiming to evaluate BKM120 in monotherapy in patients with metastatic head and neck cancer recurrent or progressive under platin and cetuximab-based chemotherapy

#### Summary

EudraCT number	2012-002403-18
Trial protocol	FR
Global end of trial date	31 January 2019

#### Results information

Result version number	v1 (current)
This version publication date	18 March 2021
First version publication date	18 March 2021

#### Trial information

##### Trial identification

Sponsor protocol code	ET12-034
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01737450
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Centre Léon Bérard
Sponsor organisation address	28 rue Laennec, LYON, France, 69008
Public contact	Dr J. FAYETTE, Centre Léon Bérard, 33 4 78 78 28 28, DRCIreglementaire@lyon.unicancer.fr
Scientific contact	Dr J. FAYETTE, Centre Léon Bérard, 33 4 78 78 28 28, DRCIreglementaire@lyon.unicancer.fr

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	14 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2019
Global end of trial reached?	Yes
Global end of trial date	31 January 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the activity of BKM120 as measured by the 2-month disease control rate (Complete response + Partial Response + Stable disease according to RECIST 1.1) in adult patients with recurrent or metastatic head and neck cancer progressive under platin and cetuximab or anti-EGFR-based chemotherapy

Protection of trial subjects:

At pre-registration visit, the investigator or its designee will:

1. Inform the patient of the study, the investigator is obliged to give the patient all information about the study and the study related assessments, and the patient should be given ample time to consider his/her participation.
2. Check the eligibility criteria using medical records of the patient and ask him/her to sign the ICF 1 (ICF dedicated to PI3KCA pre-screening). Of note, the inclusion criteria I3 and I4 must be validated before treatment start i.e. before C1D1: the investigator can initiate the pre-registration procedure and the molecular pre-screening before documented progression but will need to document the progression of the disease before treatment start. The investigator is obliged to give the patient thorough information about the study and the study related assessments, and the patient should be given ample time to consider his/her participation. The investigator must not start any study related procedure before ICF is signed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2013
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	France: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	58
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Availability of a tumor sample (either an archival tumor block \* or a minimum of 20-25 unstained slides, or pre-treatment fresh biopsy) is mandatory for all patients in order to be enrolled in the study. Tumor tissues samples will be collected with the purpose of analyzing PIK3CA mutation using Sanger's sequencing method.

### 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

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	COHORT PIK3CA mutated
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Arm description:

The study will be an open-label, Phase II, multicentric study using an optimal two stage Simon design with two parallel cohorts. The use of 2 parallel but independent cohorts (PIK3CA mutated and PIK3CA non-mutated) will assist the Sponsor to fully explore the safety and activity of BKM-120 whilst collecting a wide range of tolerability and activity data.

Arm type	COHORT PIK3CA mutated
Investigational medicinal product name	BKM120 (Buparlisib)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Buccal use

Dosage and administration details:

Administration: Continuous once daily orally dosing schedule at a dose of 100 mg. Self administration at home. Patients should be instructed to take the dose of BKM120 daily in the morning, at approximately the same time each day with a large glass of water. BKM-120 can be taken with or without food. Patients should swallow the capsules as a whole and not chew them.

Treatment duration: One study cycle equals 28 days. Patients will be treated until disease progression, unacceptable toxicity, or willingness to stop. Dose adaptation guidelines are presented in the protocol in case of toxicity.

<b>Arm title</b>	COHORT – PIK3CA non mutated
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Arm description:

The study will be an open-label, Phase II, multicentric study using an optimal two stage Simon design with two parallel cohorts. The use of 2 parallel but independent cohorts (PIK3CA mutated and PIK3CA non-mutated) will assist the Sponsor to fully explore the safety and activity of BKM-120 whilst collecting a wide range of tolerability and activity data.

Arm type	COHORT – PIK3CA non mutated
Investigational medicinal product name	BKM120 (Buparlisib)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Buccal use

Dosage and administration details:

Administration: Continuous once daily orally dosing schedule at a dose of 100 mg. Self administration at home. Patients should be instructed to take the dose of BKM120 daily in the morning, at approximately the same time each day with a large glass of water. BKM-120 can be taken with or without food. Patients should swallow the capsules as a whole and not chew them.

Treatment duration: One study cycle equals 28 days. Patients will be treated until disease progression, unacceptable toxicity, or willingness to stop. Dose adaptation guidelines are presented in the protocol in case of toxicity.

<b>Number of subjects in period 1</b>	COHORT PIK3CA mutated	COHORT – PIK3CA non mutated
Started	22	36
Completed	22	36

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	COHORT PIK3CA mutated
Reporting group description: The study will be an open-label, Phase II, multicentric study using an optimal two stage Simon design with two parallel cohorts. The use of 2 parallel but independent cohorts (PIK3CA mutated and PIK3CA non-mutated) will assist the Sponsor to fully explore the safety and activity of BKM-120 whilst collecting a wide range of tolerability and activity data.	
Reporting group title	COHORT – PIK3CA non mutated
Reporting group description: The study will be an open-label, Phase II, multicentric study using an optimal two stage Simon design with two parallel cohorts. The use of 2 parallel but independent cohorts (PIK3CA mutated and PIK3CA non-mutated) will assist the Sponsor to fully explore the safety and activity of BKM-120 whilst collecting a wide range of tolerability and activity data.	

### Primary: Primary end point

End point title	Primary end point <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: To determine the activity of BKM120 as measured by the 2-month disease control rate (CR+PR+SD - RECIST 1.1) in adult patients with recurrent or metastatic head and neck cancer progressive under platin and cetuximab or anti-EGFR-based chemotherapy	

#### 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: The non-progression rate will be analyzed using central read tumor assessments and summarized by a proportion together with its 95% confidence interval. Duration of response, PFS, TTP and TTF and will be estimated as a function of time by the Kaplan-Meier method. Descriptive statistics will be provided for characterizing and assessing patient tolerance to treatment using CTC-AE-V4.0 scale.

End point values	COHORT PIK3CA mutated	COHORT – PIK3CA non mutated		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	36		
Units: percentage of patient	22	36		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

The investigator collects (spontaneous patient report or questioning) and immediately notifies the sponsor of all SAEs, in a written report, whether or not they are deemed to be attributable to research and which occur during the study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Frequency threshold for reporting non-serious adverse events: 5 %

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#### 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: 31 patients (53.4%) who presented at least one treatment-related AE of  $\geq 3$  grade: 12 patients (54.5%) in the PIK3CA mutation cohort and 19 patients (52.8%) in the absence of PIK3CA mutation cohort.

SAEs concerned 35/58 patients (60.3%), and SAEs linked to the treatment of the study 18/58 patients (31.0%): 7 patients (31.8%) in the PIK3CA mutation cohort and 11 patients (30.6%) in the cohort without PIK3CA mutation.

2 SUSARs were reported in the PIK3CA absence cohort.



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2012	Addition of a non-inclusion criterion(E6) to insure a wash-out period before BKM120 start Precisions on tumor evaluation methods Details about the period between the confirmation of inclusion and study drug start (7 days) Modification of the completion date of blood samples for translational study (14 days) Precision on the need to document the first disease progression for patients who have permanently discontinued study drug
22 February 2013	Precisions on the inclusion criterion I2 about authorized subtypes (metastatic or relapsed squamous cell head and neck carcinoma (oropharynx, oral cavity, hypopharynx and larynx) except cancer of nasopharynx (i.e. cavum cancer)) Addition of an inclusion criterion (I8 : Patients able to swallow capsules) Update of the protocol and associated documents following the new investigator brochure release (v5.0 dated 15 November 2012)
10 September 2013	To Complete a non-inclusion criterion (E4) to exclude patients with active severe personality disorders Modification of the management of grade 2 hyperglycemia (Recommended dose modifications for BKM120) Modification of the maximum period for study treatment interruption (28 instead of 21 days) in order to allow adverse events resolution To authorize the molecular pre-screening of patients without documented PD (modification of inclusion criteria I3 et I4, description of the pre-screening visit and precision on the assessment of benefit/risk) Addition of 3 glucose test at C1J8, C1J22 and C3J1 to strengthen patient monitoring Modification of informations about potential risks (on FDA request)
10 March 2014	Modification of an inclusion criterion (I3) to expand the target population to patients previously treated with anti-EGFR* based chemotherapy other than cetuximab (+ modification of the title)
27 May 2014	Update of the protocol and associated documents following the new investigator brochure release (v6.0 dated 13 November 2013) Clarification and precision on the management of some expected adverse events (blood rates alteration, hepatic AST/ALT, rash) 18-month extension of the study recruitment period (until January 2016)
10 July 2014	Clarification of the separation of the study into 2 phases (amendment 8): 1. Precision on the inclusion criterion I3 (allow inclusion of patient without documented PD but start of study drug not allowed before disease progression) 2. Separation of patient recruitment into 2 stages with 2 ICF : one for pre-screening phase (all patients) and one another for treatment phase (only after documented disease progression) 3. After ICF1 (pre-screening) but prior to ICF2 and initiation of study drug, only SAEs caused by a protocol-mandated intervention will be collected
06 February 2015	Update of the protocol and associated documents following the new investigator brochure release (v7.0 dated 3 November 2014) - Clarification and precision of the management and dose modification of some adverse events (rash, stomatitis and oral mucositis) - Modification of concomitant therapies allowed and consequently precision on exclusion criterion E17 (moderate inhibitors or inducers of isoenzyme CYP3A allowed)

08 September 2015	Update of clinical data related to the hepatic toxicities on BKM120 by Novartis: - Addition of a non-inclusion criterion (E23) to exclude patients having acute viral hepatitis or a history of chronic or active HBV or HCV infection - Update of dose modification guidelines and management of hepatotoxicity
17 November 2015	Change of the reference study for IMPD by Novartis (new study Eudract n° 2013-000744-26)
27 October 2016	Update of the protocol and associated documents following the new IB release: - Change in conditions of administration of study drug : taken with or without food - Update of number of patients treated with study drug and some AE frequency - BKM INN : buparlisib 24-month extension of the study recruitment period (until January 2018). To be noted: inclusions are closed in cohort PIK3CA non mutated Pharmacovigilance: inform Sponsor's PV and coordination center

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 July 2018	Inclusions in the PIK3CA mutation cohort were prematurely stopped due to recruitment difficulties linked to the rarity of the anomaly	-

Notes:

## Limitations and caveats

None reported