BYLIEVE: A phase II, multicenter, open-label, three-cohort, non-comparative study to assess the efficacy and safety of alpelisib plus fulvestrant or letrozole in patients with PIK3CA mutant, hormone receptor (HR) positive, HER2-negative advanced breast cancer (aBC), who have progressed on or after prior treatments

Published: 25-10-2017
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To assess the proportion of patients who are alive without disease progression at 6 months based on local investigator assessment per RECIST v1.1 in cohort A and cohort B 13-03-2019: new cohort added (3 cohorts now)

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON52978

Source
ToetsingOnline

Brief title
CBYL719X2402 (BYLieve)

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
breast Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Zie G2

Intervention

Keyword: alpelisib, breast cancer, PIK3CA

Outcome measures

Primary outcome

the proportion of patients who are alive without disease progression at 6

months based on local investigator assessment using RECIST v1.1 in each cohort

Secondary outcome

PFS based on local investigator assessment using RECIST v1.1 in each cohort

PFS2, ORR, CBR based on local investigator*s assessment according to RECIST

v1.1 in each cohort

Type, frequency and severity of adverse events per CTCAE v4.03

Type, frequency and severity of laboratory toxicities per CTCAE v4.03

Study description

Background summary

promising pre-clinical data showing potential for cell death in addition to

decreased proliferation have been observed when PI3K inhibitors are given in combination with endocrine therapy

Preclinical and clinical studies of HR+ BC, alpelisib has shown synergistic antitumor effects when used with endocrine therapy (e.g. letrozole). The combination of letrozole and alpelisib was determined to be safe.

Up to 45% of HR+ BC present with a mutation in the PIK3CA gene, and thus these tumors may be particularly suited to treatment with PI3K inhibitor alpelisib. HR+ BC particularly if previously treated with endocrine agents - may display a dependency on the PI3K pathway that is independent of a PIK3CA mutation and hence confer a level of sensitivity to alpelisib in non-PIK3CA mutant BC tumors as well.

With the approval of CDK 4/6 inhibitor combinations with endocrine therapy and the clinical data adapting fulvestrant over an AI in the first line aBC, the treatment landscape for HR+, HER2-negative aBC is rapidly changing to include CDK 4/6 inhibitors in the first line and second line with an AI or fulvestrant.

Therefore, this study will assess the efficacy and safety of alpelisib combination in PIK3CA mutant HR+, HER2-negative aBC patients following progression on CDKi based regimen.

Study objective

To assess the proportion of patients who are alive without disease progression at 6 months based on local investigator assessment per RECIST v1.1 in cohort A and cohort B

13-03-2019: new cohort added (3 cohorts now)

Study design

a phase II, multicenter, open-label, three-cohort, non-comparative study of alpelisib plus either fulvestrant or letrozole

4april2022: addition of an extension phase for the patients benefitting from the treatment in the core study and for whom no PSDS is available.

Intervention

All participants will be treated with :

- alpelisib 300 mg once daily, orally
- either fulvestrant, 500 mg intra muscular, once every 28 days OR letrozol 2.5

mg once daily, orally

Study burden and risks

RISK: adverse events of treatment with PDR001 and Fulvestrant or letrozol
Burden: Cycles of 4 weeks, Cycle 1: 3 visits, cycle 2: 2 visits from cycle 3 onwards one visit
Physical examination: once per cycle.
Blooddraws : at least once per cycle
ECG: every 3 cycles
MUGA every 4 cycels
CT-/MRI-scan: during screening, cycle 4, every 8 weeks during first 6 months and every 12 weeks thereafter.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. adult male or female >= 18 years old at the time of consent
2. Patient has PIK3CA mutation confirmed by a Novartis designated laboratory, or
Patient has a pathology report confirming PIK3CA mutant status It is also mandatory to
provide a tumor sample collected after the most recent
progression or recurrence
3. Patient has a confirmed, HER2-negative aBC.
4. Patient is a men, or pre or postmenopausal woman.
Postmenopausal as defined:
• Prior bilateral oophorectomy
• Age >=60
• Age <60 and amenorrhea for 12 or more months
Special requirements are required for premenopausal women.
5. Patient has a confirmed diagnosis of ER+ and/or PgR+ breast cancer , 6. documented evidence of tumor progression
- cohort A and B : CDK 4/6 inhibitor treatment as last treatment regimen
- cohort C: AI treatment and received systemic chemotherapy or ET as last treatment regimen , 7. Patients must have either:
Measurable disease, i.e., at least one measurable lesion as per RECIST v1.1 criteria
If no measurable disease is present, then at least one predominantly lytic bone lesion must
be present
8. Patient has ECOG (Eastern Cooperative Oncology Group) Performance Status <= 2
9. Males or females with advanced breast cancer not amenable to curative therapy.

Exclusion criteria

1. Patient has received prior treatment with any PI3K inhibitors
2. Patients with central nervous system (CNS) involvement unless they meet ALL of the
following criteria:
• At least 4 weeks from prior therapy completion to starting the study treatment
• Clinically stable CNS tumor at the time of screening untreated or without evidence of
progressions for at least 4 weeks after treatment
3. Patient with clinically manifest diabetes mellitus, or documented steroid induced diabetes
mellitus

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-02-2018
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	alpelisib
Generic name:	alpelisib
Product type:	Medicine
Brand name:	Faslodex
Generic name:	Fulvestrant
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Femara
Generic name:	letrozole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lupron
Generic name:	Leuprorelin
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Zoladex
Generic name:	goserelin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-10-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	31-01-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-03-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-07-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-02-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	07-03-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-07-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-09-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-10-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-10-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-08-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-06-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-004586-67-NL
ClinicalTrials.gov	NCT03056755
CCMO	NL61664.068.17