A single arm, open-label, phase II, multicentre study to assess the safety of vismodegib (GDC-0449) in patients with locally advanced or metastatic basal cell carcinoma (BCC).

Published: 23-03-2012
Last updated: 01-05-2024

The primary objective of this phase II study is to assess the safety of vismodegib in patients with (inoperable) locally advanced BCC or metastatic BCC.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39484

Source
ToetsingOnline

Brief title
STEVIE

Condition

- Skin neoplasms malignant and unspecified

Synonym
basal cell-carcinoma, cancer

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Hoffman-La Roche

Intervention

Keyword: basal cell carcinoma, safety, vismodegib

Outcome measures

Primary outcome

- To assess the safety of vismodegib in patients with (inoperable) locally advanced or metastatic BCC.

Secondary outcome

- To assess the overall response rate (ORR; according to RECIST, v1.1) in those patients with measurable disease, as permitted by local regulatory requirement.
- To assess other efficacy parameters, such as time to response, duration of response, progression-free survival (PFS), and overall survival (OS).
- To assess patient quality of life (QoL).
- To assess the impact of vismodegib treatment on disease symptoms in patient with metastatic BCC who enrolled after apporval of the Study Protocol, version 4.0, using the M.D. Anderson Symptom Inventory.
- To assess the status of the Hedgehoc pathway and/or other modifiers of vismodegib activity in tumor tissue obtained from patients with metastatic BCC who have disease progression on vismodegib therapy.

Study description

Background summary

Basal cell carcinoma (BCC) is the most common malignancy. Almost all of these cases are small BCCs that can be effectively treated by dermatologists using several surgical modalities. However, in a small subset of patients, invasion of the BCC into subcutaneous structures can occur. In some cases, this results from neglect of indolent BCCs, whereas in other cases patients may develop particularly aggressive BCCs that recur and progress despite standard surgical treatment. If further surgical resection is not possible, there is no approved therapy and no standard of care exists. Although palliative radiation therapy may be used, its use may be limited by the location of the tumor and the involved structures, as well as prior cumulative radiation dosage. Locally advanced BCC can be associated with significant morbidity as the result of chronic pain, risk of bacterial infection and sepsis, bleeding/oozing, and compromise of function, resulting from invasion of structures such as the ear, nose and eye. In some cases, invasion can progress to involve critical organs such as the meninges, brain, and spinal cord, resulting in death.
Metastatic BCC is extremely rare, with a reported metastasis rate ranging from 0.0028% to 0.55%. A total of approximately 300 cases of metastatic BCC have been reported in the literature. Once metastasis is detected, survival can be short for some patients, with a range of 8 to 14 months reported by some Investigators. No standard therapy for metastatic BCC exists, although there is anecdotal use of chemotherapeutic agents such as platinum compounds.
The Hedgehog (Hh) signaling pathway presents a novel and potentially beneficial target for cancer therapy. Two mutations commonly found in BCC result from either the inactivation of the PTCH1 receptor or the activation of SMO protein. Both have the same functional consequence, i.e., the uncontrolled activation of the Hh signaling pathway in the absence of the Hh protein. High expression levels of Hh target genes, such as GLI1 and PTCH1, are found in nearly all cases of human BCC examined, suggesting that activation of this pathway is a causal event in the initiation of tumor formation. These data suggest that blocking the Hh signaling pathway at the level or downstream of SMO may provide a therapeutic benefit in the treatment of BCC. Vismodegib (also known as GDC-0449) is a small molecule antagonist of the Hh signaling pathway. Vismodegib binds to and inhibits SMO, thereby preventing the Hh signal. Vismodegib has proven to be efficacious in nonclinical tumor models of both mutated and ligand-overexpressing tumors as well as in preious phase II-studies.

Study objective

The primary objective of this phase II study is to assess the safety of vismodegib in patients with (inoperable) locally advanced BCC or metastatic BCC.

Study design

Enrolled patients will receive continuous once-daily oral dosing of vismodegib

at a dosage of 150 mg per administration. One cycle of therapy will be defined as 28 days of treatment. All patients will receive study drug until the development of progressive disease (as determined by the Investigator), unacceptable toxicity, consent withdrawal, death, reasons deemed by the treating physician, or study termination by the Sponsor. The trial will consist of a Screening Period (Day *28 to *1), a Treatment Phase, an End of Treatment Visit when the patient received the last dose of vismodegib and thereafter discontinues vismodegib (regardless of when it occurs), and one Safety Follow-Up Visit 30 days, 3, 6, 9 and 12 months after the last dose of vismodegib.

Intervention

Enrolled patients will receive continuous once-daily oral dosing of vismodegib at a dosage of 150 mg per administration. One cycle of therapy will be defined as 28 days of treatment. All patients will receive study drug until the development of PD (as determined by the Investigator), unacceptable toxicity, consent withdrawal, death, reasons deemed by the treating physician, or study termination by the Sponsor (Roche).

Study burden and risks

For participating patients there is no guarantee that health will improve. Based on experience with vismodegib (GDC-0449) in a very small number of patients with advanced basal cell carcinoma, researchers believe that it may be of benefit to patients with basal cell carcinomas. Because people respond differently to therapy and because the study drug is experimental, no one can know in advance if there will be a benefit. It is possible that the condition may get worse. We do know that the information from this study will help doctors learn more about vismodegib (GDC-0449) as a treatment for advanced basal cell carcinoma. This information could help other people who have a similar medical condition in the future.
There may be side effects from the drugs or procedures used in this study, and they may vary from person to person. Doctors and the study sponsor do not know all the side effects that may happen, and unknown side effects could occur. During participation in this study, patients are at risk for the side effects mentioned in section E9 of this form.

Contacts

Public
Roche Nederland B.V.

Beneluxlaan 2a

Woerden 3446GR
NL
Scientific
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446GR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Adult patients, >/<=18 years of age;- Metastatic or locally advanced basal cell carcinoma considered inoperable or that surgery is contraindicated and radiotherapy is contraindicated or inappropriate;- Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2

Exclusion criteria

- Concurrent anti-tumor therapy;- Completion of the most recent anti-tumor therapy less than 21 days prior to the initiation of treatment;- Uncontrolled medical illness;- Patients with one of the following rare hereditary conditions: galactose intolerance, primary hypolactasia, or glucose-galactose malabsorption

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-07-2012
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Erivedge
Generic name:	vismodegib

Ethics review

Approved WMO Date:	23-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-05-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-01-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-02-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-07-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-11-2013

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-03-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-04-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	09-03-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-06-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-06-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-12-2016
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	EUCTR2011-000195-34-NL
ClinicalTrials.gov	NCT01367665
CCMO	NL39979.068.12