A Phase I/II, multi-center, open label study of DYP688 in patients with MUM and other GNAQ/11 mutant melanomas (study CDYP688A12101)

Published: 26-07-2022
Last updated: 05-10-2024

This study has been transitioned to CTIS with ID 2023-509451-14-00 check the CTIS register for the current data. Primary:Phase I: • To characterize the safety and tolerability and to identify the maximum tolerated dose (MTD) and/or recommended dose...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Ocular neoplasms
Study type	Interventional

Summary

ID

NL-OMON53721

Source
ToetsingOnline

Brief title
CDYP688A12101

Condition

- Ocular neoplasms

Synonym
other melanoma, uveal melanoma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis

Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: DYP688, GNAQ/11 mutant, Metastatic, Uveal melanoma

Outcome measures

Primary outcome

Phase I:

Safety : Incidence and severity of dose limiting toxicities during the first 28

days of treatment. Incidence and severity of (serious) adverse events,

including changes in laboratory values, ECGs, and vital signs.

Tolerability: Frequency of dose interruptions, reductions, and discontinuations.

Phase II:

Overall Response rate (RECIST 1.1).

Secondary outcome

Phase I:

PK parameters (e.g. AUG, Cmax, CL, half- life).

Prevalence and incidence of anti-DYP688 antibodies.

Best Overall Response, Overall Response Rate (RECIST v1.1).

Phase II:

Duration of response, progression free survival and Disease Control Rate

(RECIST v1.1).

Overall survival.

Safety: Incidence and severity of (serious) adverse events, including changes

in laboratory values, ECGs, and vital signs.

Tolerability: Frequency of dose interruptions, reductions, and discontinuations.

PK parameters (e.g., AUC, Cmax, CL, half- life).

Assessment of immunogenicity of DYP688

Study description

Background summary

Uveal melanoma is a malignant neoplasm of the eye and although it represents only 3-5% of all melanomas, it is the most common primary intraocular malignant tumor in adults.
Nearly 50% of patients with uveal melanoma develop metastatic disease within 15 years of their initial diagnosis. Frequent sites of metastasis are the liver, lungs, bone, and skin. The median overall survival for patients with metastatic disease ranges from 5-19 months with a one-year survival of approximately 10-15%. No standard of care exists and, due to the lack of available therapies, outcome for patients with metastatic disease remains extremely poor. Despite showing significant survival benefit in cutaneous melanoma, immunotherapies have shown modest impact on modulating the course of disease in metastatic uveal melanoma.
Most recently, clinical trial data with the bi-specific fusion protein tebentafusp demonstrate that immunotherapies that are designed to redirect T-cells to tumor cells can improve OS in patients with MUM.
Mutations in GNAQ/11 are the key drivers to the development of uveal melanoma, targeted and specific inhibition of GNAQ/11 should result in robust and durable anti-tumor activity. Melanomas that may be driven by GNAQ/11 mutations appear biologically distinct from melanomas that typically harbor BRAF or NRAS mutations and have low mutational burden.
DYP688 is an antibody-drug conjugate, a new type of biologic drug where an anticancer drug is attached to an antibody. The antibody that is part of DYP688 is designed to bind the protein PMEL17 that is present on GNAQ/11 mutant cancer cells. After binding to PMEL17 on cancer cells, DYP688 is then able to deliver the anticancer drug. Experiments in animal cancer models show that DYP688 has the potential to be a promising therapy for patients with MUM and other melanomas with GNAQ/11 mutations.
This Phase I/II, First-in-Human study has two parts: a dose escalation part (for patients >=18 years with metastatic uveal melanoma) to identify the MTD and RD and regimen for future studies as a single agent and a dose expansion part (for patients >=12 years worldwide, in Netherlands >= 18 year, with other GNAQ/11 mutant metastatic melanomas as well) to evaluate the anti-tumor activity of DYP688 as a single agent.

Study objective

This study has been transitioned to CTIS with ID 2023-509451-14-00 check the CTIS register for the current data.

Primary:
Phase I:
• To characterize the safety and tolerability and to identify the maximum tolerated dose (MTD) and/or recommended dose (RD) and regimen for future studies of DYP688 as a single agent.
Phase II:
• To evaluate the anti-tumor activity of DYP688 as a single agent.

Secondary:
Phase I:
• To characterize the pharmacokinetics (PK) of DYP688 as a single agent.
• To assess the immunogenicity of DYP688 as a single agent.
• To evaluate the preliminary anti-tumor activity of DYP688 as a single agent.
Phase II:
• To further evaluate the anti-tumor activity of DYP688 as a single agent.
• To evaluate overall survival of DYP688 as a single agent.
• To further characterize the safety and tolerability of DYP688 as a single agent.
• To further characterize the PK of DYP688 as a single agent.
• To further assess the immunogenicity (IG) of DYP688 as a single agent

Study design

This is a First in Human, phase I/II, open label, multi-center single arm study. Phase I will characterize the safety and tolerability of DYP688 in adult patients with MUM and ether GNAQ/11 mutant melanomas After the determination of the MTD/RD whichever occurs first, for DYP688, phase II will access the anti-tumor activity and further access the safety, tolerability, and PK/PO at the MTD/RD.

Intervention

Treatment with DYP688.

Study burden and risks

Risk: Adverse events of the study medication.
Burden:
• Visits: screening, week 1-8 (cycle 1 and 2) and week 1 and 3 of cycle 3 and onwards.
• Physical examination: week 1 and 3 of every cycle.
• Tanner staging: twice.
• Blood draws: cycle 1, 3 visits, kuur 3 and onwards 2 visits, 10 to 73 mL

blood per occasion.
• Pregnancy tests: monthly in blood (during a study visit) or in urine (at home if no study visit planned).
• ECG: 4 visits during treatment phase.
• Eye examination: 5 times in total.
• Scan chest, abdomen, pelvis: every 12 weeks.
• Bone marrow biopsy: <=once (only if not performed in the 2 months prior to screening).
• Questionnaire: if pediatric formulation is used (e.g. taste).

Optional:
• Tumor biopsy: once
• Use of data and remaining body material for other research.

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patients in the dose escalation part must be >=18 years of age at the time of informed consent (ICF) signature. In the phase II part, patients >=12 years of age at the time of informed consent may be eligible for enrollment (for Netherlands only >=18 years of age are eligible). Patients must have a minimum weight of 40 kg.
• ECOG performance status <=1 for patients >=18 years of age; Karnofsky performance status >=70
• Patients must be suitable and willing to undergo study required biopsies according to the treating institution's own guidelines and requirements.
For all patients in Dose Escalation:
• MUM: uveal melanoma with histologically or cytologically confirmed metastatic disease. Patient must be either treatment naive or have received any number of prior lines and progressed on most recent therapy.
• Non-MUM: advanced cutaneous or mucosal melanoma with histologically or cytologically confirmed metastatic disease that has progressed following all therapies or that has no satisfactory alternative therapies and has evidence of GNAQ/11 mutation based on local data.
For patients in Phase II:
• Tebentafusp naïve group: Diagnosis of uveal melanoma with histologically or cytologically confirmed metastatic disease that has progressed following standard therapies or that has no satisfactory alternative therapies.
• Tebentafusp pre-treated group: Diagnosis of uveal melanoma with histologically or cytologically confirmed metastatic disease. Patients must be previously treated with tebentafusp and have progressed.
• Non-MUM: patients with diagnosis of cutaneous or mucosal melanomas harboring GNAQ/11 mutations based on local data, with histologically or cytologically confirmed metastatic disease that has progressed following all standard therapies or that has no satisfactory alternative therapies.

Exclusion criteria

• Malignant disease, other than that being treated in this study.
• Active brain metastases, i.e. symptomatic brain metastases or known leptomeningeal disease.
• Evidence of active bleeding or bleeding diathesis or significant coagulopathy (including familial) or a medical condition requiring long term systemic anticoagulation that would interfere with biopsies.
• History of anaphylactic or other severe hypersensitivity / infusion reactions to antibody-drug conjugate or monoclonal antibodies, which in the opinion of the investigator may pose an increased risk of serious infusion reaction.
• Treatment with any of the following anti-cancer therapies prior to the first dose of study treatment within the stated timeframes:

• <=2 weeks tor fluoropyrimidine therapy
• <=4 weeks for radiation therapy or limited field radiation for palliation within <=2 weeks prior to the first dose of study treatment.
* <=4 weeks or <=5 half-lives (whichever is shorter) for chemotherapy or biological therapy (including monoclonal antibodies) or continuous or intermittent small molecule therapeutics or any other investigational agent.
• <=6 weeks for cytotoxic agents with major delayed toxicities, such as nitrosourea compounds and mitomycin C.
• <=4 weeks for immuno-oncologic therapy, such as CTLA-4, PD-1, or PD-L1 antagonists.
• Clinically significant and / or uncontrolled heart disease such as congestive heart failure requiring treatment (NYHA grade >=2) or clinically significant arrhythmia despite medical treatment.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-11-2022
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DYP688
Generic name:	DYP688

Ethics review

Approved WMO Date:	26-07-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-08-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-09-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-10-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	30-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	07-12-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	09-01-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	04-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	26-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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
EU-CTR	CTIS2023-509451-14-00
EudraCT	EUCTR2021-003380-95-NL
ClinicalTrials.gov	NCT05415072
CCMO	NL81906.058.22