The Drug Rediscovery Protocol (DRUP trial)
A Dutch National Study on behalf of the Center for Personalized Cancer Treatment (CPCT) to Facilitate Patient Access to Commercially Available, Targeted Anti-cancer Drugs to determine the Potential Efficacy in Treatment of Advanced Cancers with a Known Molecular Profile

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This study has been transitioned to CTIS with ID 2023-509152-33-00 check the CTIS register for the current data. Primary Objectives• To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs used for...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54670

Source
ToetsingOnline

Brief title
DRUP

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, tumors

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Amgen,Astra Zeneca,Farmaceutische industrie;stichting Barcode for Life;Hartwig Medical Foundation en KWF,Novartis,Pfizer,Roche

Intervention

Keyword: Biomarker-driven, Off-label, Oncology, Targeted-therapy

Outcome measures

Primary outcome

• Percentage of patients that are treated based on their molecular tumor profile

• Objective tumor response

• Stable disease at 16 weeks after treatment initiation

• Treatment-related grade>=3 and serious adverse events

Secondary outcome

• Progression-free and overall survival

• Duration of treatment on study (time on drug)

Study description

Background summary

Evidence is building that patient outcomes can be improved when a specific

targeted agent can be matched to a tumor genomic variant. Such reports have fueled interest among patients and physicians to use genomic testing as a guide to treatment planning in patients with advanced cancer when standard treatment options have been exhausted, and commercial laboratories have begun to market such genomic tests to oncologists.
A significant challenge facing oncologists who aim to provide personalized medicine services to their patients is obtaining the drug or drugs predicted to be beneficial based on the genomic testing of the tumor. Few oncologists or pathologists have expertise or access to experts to interpret genomic test reports and guide scientifically informed decisions about the optimal use of targeted agents. Off-label prescribing, while legal, is frequently not reimbursed by insurance companies. In addition, where clinicians and patients use targeted agents in routine clinical practice, efficacy and safety is generally not systematically recorded and analyzed. As a result, the research and clinical communities have a limited understanding of the clinical outcomes of patients who receive these treatments outside of formal clinical trials.
A solution to the lack of access to drugs prescribed outside of the labelled indication and lack of data collection on safety and efficacy of such treatments is creation of a drug access program in which key clinical outcomes are systematically recorded, analyzed and published. This study will focus initially on facilitating access to approved targeted therapies that are prescribed to patients with advanced cancer who have exhausted standard treatment options and for whom treatment is selected based on results of a genomic test of their tumor. The study will provide a molecular tumor board to help physicians understand the genomic profiling test results and possible treatment options and will capture patient outcomes in a prospective database that will enable insights to be gained about the utility of this approach. Furthermore, next generation sequencing will be performed on a fresh tumor biopsy specimen, to enable additional biomarker discovery.

Study objective

This study has been transitioned to CTIS with ID 2023-509152-33-00 check the CTIS register for the current data.

Primary Objectives
• To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs used for treatment of patients with an advanced solid tumor, multiple myeloma or non-Hodgkin lymphoma that harbours a genomic- or protein expression variant known to be a drug target or to predict sensitivity to a drug.
• To facilitate patient access to commercially available, targeted anti-cancer drugs of potential efficacy for treatment of an advanced solid tumor, multiple myeloma or non-Hodgkin lymphoma that harbours a genomic- or protein expression variant known to be a drug target or to predict sensitivity to a drug.

Secondary Objective

• To perform biomarkers by (for example, but not limited to) next generation sequencing on a fresh tumor biopsy specimen.

Study design

This is a prospective, non-randomized clinical trial that aims to describe the efficacy and toxicity of commercially available, targeted anticancer drugs prescribed for treatment of patients with advanced cancer with a potentially actionable variant as revealed by a genomic or protein expression test. The study also aims to simplify patient access to approved targeted therapies that are contributed to the program by collaborating pharmaceutical companies and to perform next generation sequencing on tumor biopsies for biomarker analyses. Eligible patients have an advanced solid tumor, multiple myeloma or non-Hodgkin lymphoma for which standard treatment options are no longer available and acceptable performance status and organ function. A genomic or protein expression test must have been performed on the tumor and the results must identify at least one potentially actionable molecular variant as defined in the protocol. Results from the molecular profiling test will be used to determine an appropriate drug(s) from among those available in the protocol. The choice of drug will be supported by a list of potential profiles, a molecular tumor board, a knowledge library and by study coordinators for review and approval of the match. The protocol-specified treatment will be administered to the patient once any drug-specific eligibility criteria are confirmed and a fresh pretreatment biopsy is performed for future genetic studies. All patients who receive treatment with a drug available in the protocol will be followed for standard efficacy outcomes including tumor response, progression-free and overall survival as well as duration of treatment. In addition, treatment related toxicity will be evaluated.

Intervention

A new, fresh-frozen, pre-treatment tumor biopsy specimen will be obtained from all patients for biomarker analysis. Treatment with a commercially available, targeted anticancer drug matched to the patients molecular tumor profile.

Study burden and risks

Burden and risk of tumor biopsy are considered to be minimal. Burden and risk of treatment with a commercially available drug are conform treatment in daily practice. There's a risk of side effects and a risk of no benefit from treatment. The same holds true for any other treatment options that study participants might have.

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

INCLUSION CRITERIA:
1. Adult (age >18 years) patient with a histologically-proven locally advanced or metastatic solid tumor, multiple myeloma or non-Hodgkin lymphoma with symptomatic disease progression or progression according to RECIST-criteria after standard anti-cancer treatment or for whom no such treatment is available or indicated.
For patients with a primary brain tumor:
Histologically confirmed recurrent or de novo primary brain tumor, with unequivocal progression after prior therapy, at least 3 months after radiotherapy (either first line chemo-radiotherapy or re-irradiation), and with stable or decreasing dosage of steroids for at least 7 days prior to the baseline MRI scan.

2. ECOG performance status 0-2
3. Patients must have acceptable organ function as defined below. However, specific inclusion/exclusion criteria specified in the drug-specific study manual will take precedence:
a. Absolute neutrophil count >= 1.5 x 109/l
b. Hemoglobin > 5.6 mmol/l
c. Platelets > 75 x 109/l
d. Total bilirubin < 2 x ULN
e. AST (SGOT) and ALT (SGPT) < 2.5 x institutional ULN (or < 5 x ULN in patients with known hepatic metastases)
f. Serum creatinine <= 1.5 × ULN or calculated or measured creatinine clearance >= 50 mL/min/1.73 m2
4. Patients must have objectively evaluable or measurable disease (by physical or radiographic examination, according to RECIST v1.1 for patients with solid tumors, or according to IMWG, Lugano, RANO or GCIG criteria, resp., for patients with multiple myeloma, non-Hodgkin lymphoma, glioblastoma or ovarian cancer in case of CA125-based evaluation (please refer to appendices for further details) [15, 16].
5. Results must be available from a tumor genomic or protein expression test. Eligible tests may include any of the following technologies: fluorescence in situ hybridization (FISH), polymerase chain reaction (PCR), comparative genomic hybridization (CGH), next generation sequencing (NGS) or immunohistochemistry (IHC). The test may have been performed on the primary tumor or a metastatic deposit, in a diagnostic laboratory or within the context of another CPCT study, and must reveal a potentially actionable variant as defined in Section 5. The test results (full pathology or molecular diagnostics report) must be uploaded in the eCRF.
6. Patients must have a tumor profile for which treatment with one of the FDA and / or EMA approved (or under revision for approval) targeted anti-cancer drugs included in this study has potential clinical benefit based on preclinical data or clinical information (see section 5).
7. A new (obtained <=2 months before inclusion, and without any type of anti-cancer therapy within those <=2 months) fresh frozen tumor biopsy specimen for extensive biomarker testing is mandatory before the start of treatment with a targeted agent included in the protocol. Alternatively, fresh frozen tumor tissue acquired in the context of a standard care procedure may be used, provided that no systemic anti-cancer treatment was given between the procedure and start of study treatment within DRUP.
The following exceptions are made:
a. An exception is made for patients with a primary brain tumor, only if the mandatory DRUP pre-treatment biopsy for biomarker analysis cannot safely be obtained:
i) The fresh frozen tumor biopsy sample may be replaced by fresh frozen tumor tissue, obtained earlier from recurrent disease, as part of standard of care surgical procedure (i.e., performed at progression)
ii) If no fresh frozen tumor tissue is available for NGS, and the risk of obtaining a new tumor biopsy is considered too high, no biopsy will be

required. In this case, the study coordinators must be informed in advance, and there will be no reimbursement for the biopsy procedure.
b. In case WGS is performed on tumor tissue outside the context of a clinical trial before inclusion, and without any type of anti-cancer therapy between the collection of tissue and inclusion in DRUP, this can replace the DRUP pre-treatment biopsy, provided that the patient gives consent to use his/her WGS data for biomarker analysis in DRUP.
c. An exception is made for patients that underwent an allogeneic hematopoietic stem cell transplantation prior to study enrollment, since this will prevent a correct WGS analysis due to a mismatch between the biopsy specimen and the required blood sample.
8. Ability to understand and the willingness to sign a written informed consent document.
9. For orally administered drugs, the patient must be able to swallow and tolerate oral medication and must have no known malabsorption syndrome.10. Because of the risks of drug treatment to the developing foetus, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) for the duration of study participation, and for four months following completion of study therapy. Male patients should avoid impregnating a female partner. Male patients, even if surgically sterilized, (i.e. post-vasectomy) must agree to one of the following: practice effective barrier contraception during the entire study treatment period and through 4 months after the last dose of study drug, or completely abstain from sexual intercourse.

For each drug included in this protocol, specific inclusion and exclusion criteria (based on the Package Insert or manufacturers recommendations) may also apply. These can be found in the supplemental information about each agent included in the drug-specific study manuals. Drug-specific inclusion and exclusion criteria will take precedence over the inclusion/exclusion criteria listed above.

Exclusion criteria

EXCLUSION CRITERIA:
1. Ongoing toxicity > grade 2, other than alopecia.
2. Patient is receiving any other anti-cancer therapy (cytotoxic, biologic, radiation, or hormonal other than for replacement). Required wash out period prior to starting study treatment is at least two weeks. An exception is made for:
• Patients suffering from CRPC are allowed to continue androgen deprivation therapy.
• Medications that are prescribed for supportive care but may potentially have an anti-cancer effect (e.g., megestrol acetate, bisphosphonates). These medications must have been started >= 1 week prior to enrollment on this study.

3. Patient is pregnant or nursing.
4. Patients with known active progressive brain metastases. Patients with previously treated brain metastases are eligible, provided that the patient has not experienced a seizure or had a clinically significant change in neurological status within the 3 months prior to registration. All patients with previously treated brain metastases must be stable for at least 1 month after completion of treatment and off steroid treatment prior to study enrollment.
Additional exclusion criteria specific for GBM patients:
a. Patients who require anti-convulsant therapy must be taking non-enzyme inducing antiepileptic drugs (non-EIAED). EIAED are prohibited. Patients previously on EIAED must be switched to non-EIAED at least 2 weeks prior to randomization.
b. No radiotherapy within the three months prior to the diagnosis of progression.
c. No radiotherapy with a dose over 65 Gy, stereotactic radiosurgery or brachytherapy unless the recurrence is histologically proven.
5. Patients with clinically significant preexisting cardiac conditions, including uncontrolled or symptomatic angina, uncontrolled atrial or ventricular arrhythmias, or symptomatic congestive heart failure are not eligible.
6. Patients with known left ventricular ejection fraction (LVEF) < 40% are not eligible
7. Patients with stroke (including TIA) or acute myocardial infarction within 3 months before the first dose of study treatment are not eligible
8. Patients with any other clinically significant medical condition which, in the opinion of the treating physician, makes it undesirable for the patient to participate in the study or which could jeopardize compliance with study requirements including, but not limited to: ongoing or active infection, significant uncontrolled hypertension, or severe psychiatric illness/social situations.

For each drug included in this protocol, specific inclusion and exclusion criteria (based on the Package Insert or manufacturers recommendations) may also apply. These can be found in the supplemental information about each agent included in the drug-specific study manuals. Drug-specific inclusion and exclusion criteria will take precedence over the inclusion/exclusion criteria listed above.

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):	19-08-2016
Enrollment:	1550
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cotellic
Generic name:	Cobimetinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lynparza
Generic name:	Olaparib
Product type:	Medicine
Brand name:	Mekinist
Generic name:	Trametinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tasigna
Generic name:	nilotinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Vectibix
Generic name:	Panitumumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-12-2015
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-04-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	20-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-09-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-04-2017

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-01-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2020

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-12-2022

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-10-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	CTIS2023-509152-33-00
EudraCT	EUCTR2015-004398-33-NL
ClinicalTrials.gov	NCT02925234
CCMO	NL54757.031.16