Assessing Frequency of HLA-Genotype and Tumor Antigen Expression in Subjects with Relapsed/Refractory, Advanced-Stage Solid Tumors that may Qualify for Novel T Cell Receptor Based Therapies

Published: 06-07-2023
Last updated: 07-04-2024

The primary objective of this study is to assess the frequency of human leukocyte antigen (HLA)-A*02:01genotype and tumoral expression of melanoma-associated antigen 1 (MAGE-A1) in subjects with relapsed/refractory, advanced-stage solid tumors that...

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

Summary

ID

NL-OMON53305

Source
ToetsingOnline

Brief title
Assessing Frequency of HLA-Genotype for TCR Based Therapies

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Solid Tumor; Malignant Solid Tumor

Research involving
Human

Sponsors and support

Primary sponsor: T-knife GmbH
Source(s) of monetary or material Support: T-knife GmbH

Intervention

Keyword: Advanced stage solid tumors, MAGE-A1, TCR-transgenic T-cells

Outcome measures

Primary outcome

The primary objective of this study is to assess the frequency of HLA-A*02:01 genotype and tumoral expression of MAGE-A1 in subjects with relapsed/refractory, advanced-stage solid tumors that may express MAGE-A1, are in advanced, non-curable state, and have received at least one line of systemic therapy for their disease.

The primary endpoints of this study are:

• Frequency of HLA-A*02:01 genotype

• Frequency of immunohistochemically MAGE-A1 positive tumors in subjects with HLAA*02:01 genotype

Secondary outcome

The secondary objective of this study is to further explore the percentage of positive tumor cells within the tumor and the overall intensity of target expression.

The secondary endpoint of this study is:

• Percentage of positive tumor cells within the tumor, staining intensity (+, ++, +++) of the tumor cells, and derived histoscore for MAGE-A1 staining in the tumor.

Study description

Background summary

Following the concept that the human immune system in principle is capable of eliminating tumor cells, new T cell-based therapies have emerged that use modification of the subject*s own immune cells to achieve an anti-tumor response. One such promising approach is to make the subject*s own T cells express a T cell receptor that recognizes a target antigen present via major histocompatibility complex (MHC) on the subject*s tumor cells: a T cell receptor (TCR) based therapy.

Such therapies, using autologous T cells, require that the target is expressed by the tumor cells that are to be removed and that it is presented via MHC. However, for many target antigens, the tumoral expression pattern has not been well investigated across different indications and available research data may only be partly reliable due to use of suboptimal techniques or reagents (e.g., use of non-specific antibodies) in many studies conducted so far.

One target antigen of interest is the melanoma-associated antigen 1 (MAGE-A1). The presence of this antigen in a patient*s tumor may qualify them for participation in currently ongoing clinical trials exploring TCR therapies targeting this antigen. Yet, so far, no established standard screening methods exist in clinical routine, assessing the presence of this antigen in tumors. At of the date of initiation of this study, screening for this antigen is not routinely done at clinical sites treating advanced-stage cancer patients who may qualify for such treatments

Study objective

The primary objective of this study is to assess the frequency of human leukocyte antigen (HLA)-A*02:01genotype and tumoral expression of melanoma-associated antigen 1 (MAGE-A1) in subjects with relapsed/refractory, advanced-stage solid tumors that may express MAGE-A1, are in advanced,

non-curable state, and have received at least one line of systemic therapy for their disease.

The secondary objective of this study is to further explore the percentage of positive tumor cells within the tumor and the overall intensity of target expression.

Study design

This observational, non-interventional research study intends to assess the overall frequency for positivity of HLA-A*02:01 genotype and the tumoral expression of MAGE-A1 in subjects with relapsed/refractory, advanced-stage solid tumors that may express MAGE-A1 (such as melanoma, squamous non-small cell lung cancer [NSCLC], squamous cell carcinoma of the head and neck [SCCHN], esophageal, gastric, breast [ductal, tubular, medullary], ovarian, mesothelioma, bladder, anal, sarcomas, primitive neuroectodermal [PNET], and other solid tumors), who are in advanced, non-curable state, and have received at least one line of systemic therapy for their disease.

A blood sample will be collected for HLA-A*02:01 genotyping (if not already known from medical history) during a scheduled, routine blood draw and to have a stored and accessible tumor sample available that can be stained for MAGE-A1 expression by immunohistochemistry (IHC).

Study burden and risks

This is a no treatment study, but the study has pure research purposes. The single blood sample taken in this study will ideally be taken during a routine blood draw. The usual possible risks associated with blood drawing are: pain, bleeding, fainting, bruising, infection and/or hematoma (blood clot under the skin) at the injection site.

The results from this research study may allow investigator to see if patient can be qualified or not for clinical trials with novel immunotherapies. If patient are not qualified, there is no other benefit in taking part in this study. Either way, the collection of the test results and patient data may provide valuable information to researchers on the number of certain genetic constellations or tumor protein expression. This will help them to better understand who may qualify for such treatments in the future and may help future subjects suffering from cancer.

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. Signed written informed consent.
2. Histologically or cytologically confirmed diagnosis of relapsed/refractory, advanced stage solid tumor that may express MAGE-A1.
3. Subject received at least one line of approved systemic therapy and is declared to be in a non-curable disease state as per treating physician*s current assessment.
4. Availability of a stored, accessible tumor sample for IHC.
5. Ability to provide a blood sample.
6. Age >= 18 years.
7. Life expectancy > 6 months as per treating physician*s assessment.

Exclusion criteria

1. Any bleeding or coagulation disorder or other condition that would present

the subject with an undue risk when undergoing a venous blood draw.
2. Any other condition that could interfere with subject's safety, obtaining informed consent, or compliance to the screening study procedures.
3. Presence of any organ toxicities or other conditions that would preclude intense future anticancer treatments such as required for T cell receptor therapy.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-09-2023
Enrollment:	400
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	06-07-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
CCMO	NL83819.041.23