IgA-based immunotherapy development and evaluation using the blood of healthy volunteers

Published: 20-04-2021
Last updated: 08-04-2024

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

Summary

ID

NL-OMON54864

Source
ToetsingOnline

Brief title
INVOLVE

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cancer immunotherapy, IgA, Neutrophils

Outcome measures

Primary outcome

The main study parameter is the percent change in the tumor cell viability after addition of IgA antibody and immune effector cells. In antibody-dependent, cell-mediated cytotoxicity assays (ADCC), the tumor cell viability is the endpoint measurement. In antibody-dependent, cell-mediated phagocytosis (ADCP) assays, the endpoint measurement is the number (percent) of cancer cells phagocytosed by macrophages as immune effector cells.

Secondary outcome

Secondary study parameters: percent change in tumor cell viability in ADCC/ADCP assays when innate checkpoint inhibition is combined with IgA treatment.

Study description

Background summary

Cancer immunotherapy has established itself as one of the pillars of cancer treatment. While all clinical-stage antibodies are of IgG isotype, IgA antibodies hold great promise as therapeutic agents, and several IgA-based therapeutic approaches are currently being developed. Unlike IgGs, IgAs effectively recruit neutrophils, the most abundant cytotoxic cells in humans, mediating efficient killing of antibody-opsonized tumor cells through a unique process - trogoptosis. IgA are also much better at attracting monocytes/macrophages for effective cell killing, as has been shown by previous studies by Matlung (PMID: 31690649), Dechant (PMID: 17709508), Boross (PMID: 23918228) and others.
In this research, we will investigate the functional potential of engineered IgA antibodies against tumor markers EGFR and EpCAM to induce tumor cell killing. As immune effector cell population, cells of the myeloid lineage have to be used, namely: polymorphonuclear cells (PMNs), among which neutrophils

being the most abundant cell population with high tumor killing potential, as well as peripheral blood mononuclear cells (PBMCs) which were previously shown to be potent in tumor cell killing via IgA. To achieve required activity in tumor killing assays, PMNs and PBMCs should be used fresh. Therefore, the freshly donated blood of healthy volunteers should be used.

Study objective

The main objective of the study is to assess efficacy of engineered IgA antibodies (anti-EGFR, anti-EpCAM) in inducing specific tumor cell killing by myeloid immune effector cells.
The secondary objectives of the study will be:
-To evaluate relative efficiency in tumor cell killing via different formats of IgA antibodies;
-To investigate if innate immune checkpoint inhibition enhances the activity of myeloid cells in tumor cell killing via IgA;
-To establish relevant cell culture models of tumor microenvironment with immune effector cells, for development and investigation of IgA-based therapies.

Study design

In vitro experimental study; collection of blood from healthy donors for use in in vitro research.

Study burden and risks

The research procedure is a venapunction and implies only a minor inconvenience for the subjects. Since this is a basic procedure, the risks for the participants are negligible. The subjects would be asked to come for a short (5 min) procedure. Subjects can be asked to donate on multiple occasions, but not more frequently than once per month. The results of the study are expected to contribute to the development of a novel cancer immunotherapy modality, which in the future might benefit patients with severe health conditions (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

Healthy individual, 18-55 years of age, bodyweight: above 50 kg. Being able and willing to complete the informed consent process.

Exclusion criteria

Known to be infected with HIV, syphilis, tuberculosis, hepatitis B or hepatitis C.
A condition in which blood draw poses more than minimal risk for the subject such as hemophilia, other severe coagulation disorders or significantly impaired venous access.
A condition that requires active medical intervention or monitoring to avert serious danger to the participant's health or well-being.
IgA deficiency, as well as rheumatoid arthritis and other chronic inflammatory conditions.

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):	30-03-2022
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO

Date:	20-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL71702.091.20