

Isolation, immortalization and characterization of human B lymphocytes for the development of diagnostic and therapeutic antibodies against cancer.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Observational invasive

Summary

ID

NL-OMON47403

Source

ToetsingOnline

Brief title

Human antibodies against cancer.

Condition

- Leukaemias
- Malignant and unspecified neoplasms gastrointestinal NEC
- Skin neoplasms malignant and unspecified

Synonym

anti-cancer antibodies / cancer eradication

Research involving

Human

Sponsors and support

Primary sponsor: AIMM Therapeutics BV

Source(s) of monetary or material Support: VIRGO (FES) / KWF / AMC PhD Scholarship, Life Sciences Fund Amsterdam (LSFA) / Amsterdam Economic Board

Intervention

Keyword: antibody, B cells, cancer, human

Outcome measures

Primary outcome

The identification and production of tumor-specific monoclonal antibodies by the generation of tumor specific B lymphocyte clones.

Secondary outcome

not applicable

Study description

Background summary

In the defense against cancer the immune system plays an important role. In healthy individuals, the innate and the adaptive immune systems collaborate to recognize and eliminate developing tumor cells, thereby preventing the outgrowth of tumor cells (reviewed recently by Schreiber et al, Science 2011;331:1565-1570). A well known clinical example of immune mediated tumor regression is the development of vitiligo in melanoma patients, through the recognition and killing of healthy pigment bearing cells in addition to the recognition and killing of melanoma cells. Another clinical example of anti-tumor immune responses are patients with hematologic tumors who receive an allogeneic stem cell transplantation, to induce a sustained graft versus leukemia (or lymphoma) response. Similar to melanoma patients, this graft versus leukemia response is often accompanied by an immune response against healthy cells, resulting in graft versus host disease, where the donor immune system also mounts an immune response against otherwise healthy organs such as intestine, skin and liver.

Study objective

Until recently, the field of anti-tumor immunology has focussed on the role of T lymphocytes. Recently, however, the group of prof. H. Spits and dr. T. Beaumont developed an in vitro methodology to grow human, monoclonal, B cell receptor positive and immunoglobulin secreting B cells (AIMSelect). With this method it has now become possible to study the role of B lymphocytes in anti-tumor immune responses.

The objective of the current study is to identify, develop and produce tumor specific antibodies with the goal to:

- 1) further characterize the role of B cells in anti-tumor immunity; and to
- 2) develop human monoclonal tumor specific antibodies for diagnostic and therapeutic purposes.

Study design

Our research focusses on three malignancies : hematologic malignancies, melanoma and gastro-intestinal tumors.

We will recruit patients who developed an anti-tumor response against one of the above mentioned malignancies. Of these patients, B lymphocytes will be isolated from one single draw of peripheral blood that is collected through venapuncture. These cells will be immortalized in vitro, after which monoclonal B cell lines and antibodies specifically directed against the tumor cells will be selected, isolated and grown. After characterization of the specific antigen on the tumor cells, the antibody functionality will be tested (in vitro and in mouse models). In a separate study (for which we do not ask for approval here) we will study the presence of these antibodies in serum of larger series of patients and test whether these antibodies can play a role in diagnosis of anti-tumor responses. Details of the AIMSelect method are described in Kwakkenbos et al, Nature Medicine 2010;16:123-128.

Study burden and risks

Burden for participants

Single blood draw through venapuncture (55-65 ml; 6-8 tubes).

Risk associated with participation:

Neglectable (venapuncture-induced hematoma)

Benefit:

There is no direct benefit for the participants. There is a group benefit though; if we do find tumor-specific monoclonal antibodies that can be used in clinical practice, as a diagnostic tool (to assess tumor response for example after allogeneic stem cell transplantation) or as a therapeutic tool, this will be of benefit to cancer-patients in general. In any case these studies will improve our understanding of cancer-immunology, which is also beneficial to

cancer patients as a group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

- o patients with a hematologic malignancy (leukemia or lymphoma) who received a hematopoietic stem cell transplantation and subsequently developed graft-versus-host disease and/or a sustained graft-versus-leukemia response;
- o patients with melanoma who showed spontaneous or treatment induced tumor regression, preferably in the presence of signs of auto-immunity , like vitiligo;
- o patients with gastrointestinal tumors (pancreatic or oesophagus) with either tumor regression or slower then expected tumor growth.

Exclusion criteria

no

Study design

Design

Study type: Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Other

Recruitment

NL

Recruitment status: Recruiting

Start date (anticipated): 23-05-2013

Enrollment: 75

Type: Actual

Medical products/devices used

Registration: No

Ethics review

Approved WMO

Date: 11-04-2013

Application type: First submission

Review commission: METC Amsterdam UMC

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	NL42718.018.12