T and NK cell mediated immunotherapy in Ewing's sarcoma (P03.040 amended version of December 2006)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON31114

Source
ToetsingOnline

Brief title
T and NK cell mediated immunotherapy in Ewing's sarcoma

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
bone tumors

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NKB/KWF,Europese Unie

Intervention

Keyword: Ewing's sarcoma, immunotherapy, NK cells, T cells

Outcome measures

Primary outcome

This preclinical study will provide insight in the molecular mechanisms

involved in directional migration, recognition and elimination by T/NK cells of

ES. In addition, we will identify potential immune evasion strategies in ES.

Potential differences between autologous and allogeneic effector cells will be

identified.

Together, this study will provide evidence for the implementation of NK and/or

T cell-mediated immunotherapy strategies in future clinical studies.

Secondary outcome

not applicable

Study description

Background summary

ES is the second most common primary malignant bone tumor in childhood and adolescence. In the last decades, the introduction of (neo-)adjuvant chemotherapy combined with radical resection of the tumor and optional radiotherapy has resulted in an improved overall survival from less than 30% to 60-70%. However, further intensification of chemotherapeutic interventions has not resulted in an additional improvement in survival, indicating that a significant subgroup of ES patients is resistant to currently used cytostatic agents. Therefore, novel therapeutic modalities are required to improve outcome in high risk and relapsed patients. The therapeutic potential of T and/or NK cell-mediated immunotherapy in the treatment of various types of malignancies has been demonstrated in preclinical and clinical studies. However, at present experimental evidence on the susceptibility of ES to autologous and/or allogeneic T/NK cell-mediated effector mechanisms is limited. In addition, the occurrence and functional relevance of immune evasion mechanisms in the various

clinical stages of ES is undefined.

Study objective

We hypothesize that NK and/or T cell-mediated immunotherapy may represent a novel therapeutic option for patients with refractory and/or metastatic ES. Therefore, we will study molecular mechanisms that determine the susceptibility of ES to T and NK cell mediated immunotherapy in both an autologous and allogeneic setting. The final aim is to provide evidence for the implementation of NK and/or T cell-mediated immunotherapy strategies in future clinical studies.

Study design

On a large cohort of both historical and prospectively obtained primary ES and ES cell lines representing various stages of disease the following studies will be performed we will:
1. Characterize in primary ES and ES cell lines the expression of gene products/proteins that are known to be involved in T/NK cell-mediated recognition, directional migration and immune-mediated cytolysis, study the expression of candidate T cell target antigens, and identify potential immune evasion strategies in ES.
2. Evaluate the correlation between immunological phenotype and clinical behavior/outcome.
3. Characterize the NK and T cell effector potential towards ES cell lines and the correlation with (immunological) phenotype, and provide evidence whether allogeneic effector cells act favorably in comparison with autologous effectors.

Study burden and risks

The burden for the participants is very limited. The extra tumor biopsy is performed during the regular session The marrow aspirate is performed under routine anesthesia when the central venous access is being implanted. The extra blood samples will be obtained via the central venous access together with a routine blood examination. Based on our experience with these procedures, the additional risk associated with participation in this study is negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

All newly diagnosed Ewing's sarcoma patients in the LUMC.

Exclusion criteria

Lack of written informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2007
Enrollment:	25
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL16912.058.07