Follow that CAR! - A prospective observational cohort study on CAR T-cell therapy for B-cell malignancies in the Netherlands

Published: 04-11-2021
Last updated: 24-05-2024

• To set up a national prospective observational cohort study of patients who have a hematological B-cell malignancy and are referred to the national CAR T-cell tumorboard for evaluation of eligibility for treatment with CAR T-cell therapy and to...

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

Summary

ID

NL-OMON51188

Source
ToetsingOnline

Brief title
Follow that CAR

Condition

- Other condition
- Lymphomas non-Hodgkin's unspecified histology

Synonym
B-cell malignancies and blood-, bone marrow- or lymph node cancer

Health condition

leukemie en plasmacelziekten

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: B-cell malignancies, CAR T-cell therapy

Outcome measures

Primary outcome

Prescreening cohort (All patients with haematological B-cell malignancies who

are referred to the Dutch CAR T-cell tumorboard for treatment eligibility

screening):

• Information entered on tumorboard referral form

- Referring center and physician

- Patient characteristics and demographics

- Medical history and disease characteristics

- Comorbidities

- Imaging results

- Laboratory results

- Pathology results

• Evaluation by Tumorboard

- Tumorboard outcome regarding eligibility (reason)

• Survival and subsequent therapies (if patients are considered not eligible by

the tumorboard)

• Survival

- Overall survival (OS)

- Progression-free survival (PFS)

- Time to progression

- Time to death

• Subsequent therapies

- Description therapy (name regimen, dose, number of cycles,

dates)

- Response (CR, PR, SD, PD)

- Duration of response (DOR)

- Time to response

• Cost-effectiveness

- Incremental cost-effectiveness ratio (ICER)

- Life years (LYs) accrued

- Quality adjusted life years (QALYs) accrued

Screening and treatment cohort (Patients who are considered eligible by the

tumorboard for CAR T-cell therapy screening in a CAR-T treatment center):

• Patient characteristics

- Age

- Sex

- Height

- Weight

- Place of residence

• Medical history, disease characteristics, treatment evaluation and follow-up

- General medical history

- Medication use

- Toxicities (smoking, alcohol, drugs use)

- Hematological history (diagnosis, prior treatment lines and response to treatment, risk factors such as FLIPI, MIPI, IPI score, CNS-IPI score, Ann Arbor stage, extranodal involvement, bulky disease, histological subtype)

- Clinical examination (ECOG-PS, body temperature, blood pressure, heart rate, respiratory rate, oxygen saturation, B-symptoms, clinical signs of progression)

- Laboratory results (haematology panel, chemistry panel, immunology panel, serology panel)

- Imaging results (Response according to Lugano criteria, target- and non-target lesions, tumour volume)

- Pathology results (morphology, immunohistochemistry)

- Results of cytogenetics and molecular biology

• Screen failures/apheresis only

- Failure during screening phase (reason)

- Failure during bridging phase (reason)

- Treatment after not receiving CAR T (Description of therapy (name regimen, dose, number of cycles, etc.), Response (CR, PR, SD, PD), DOR, Time to response)

- Survival status after not receiving CAR T (OS, PFS, time to progression, time to death)

• CAR-T treatment characteristics

- Pre-apheresis bridging therapy (if received type, name regimen, dosage, number of cycles/RT, response, dates)

- Apheresis (date, product characteristics)

- Bridging (if received type, name regimen, dosage, number of cycles/RT, response, dates)

- Lymphodepleting chemotherapy (type, dosage, date)

- CAR-T infusion (product characteristics)

- Prophylactic medication

• Efficacy

- ORR/ best ORR

- PMR

- CMR

- SD

- PD

- DOR

- Time to response

• PROMS

- General QoL (EORTC CLC Q30 score, EQ5D score, FACT-LYM score and

domain scores,

- Psychosocial determinants of Qol: Qualitop score and domain scores

• PREMS

- CQI Oncology score

• Cost-effectiveness

- Incremental cost-effectiveness ratio (ICER)

- Life years (LYs) accrued

- Quality adjusted life years (QALYs) accrued

- Resource use to calculate costs (direct medical costs, direct

non-medical costs, indirect medical costs and indirect non-medical costs)

Secondary outcome

Not applicable

Study description

Background summary

Chimeric Antigen Receptor T-cell (CAR T) therapy is a unique form of cellular immunotherapy using autologous genetically modified T cells that express a synthetic receptor (the **CAR**) combining the specificity of a monoclonal antibody for a specific tumor surface antigen with the cytolytic power and capacity for immune surveillance of a T cell. CAR T-cell therapy revolutionized the field of hemato-oncology and is becoming an increasingly important part of standard of care. For decades, attempts at improvement of the poor prognosis of relapsed/refractory B-cell malignancies with new treatment regimens have been

disappointing. Based on high response rates and prolonged progression-free survival in pivotal phase 1/2 trials different CAR T-cell products are FDA and EMA approved. Three CAR T-cell products for relapsed or refractory (R/R) diffuse Large B-cell lymphoma (DLBCL) are FDA approved; axicabtagene ciloleucel (axi-cel) (Yescarta® in 2017), tisagenlecleucel (tisa-cel) (Kymriah® in 2017) and lisocabtagene maraleucel (liso-cel in 2021). Axi-cel and tisa-cel are also EMA approved since 2018. In the Netherlands, the *Zorginstituut Nederland* (ZIN) has until now only approved the product axi-cel for the treatment of R/R DLBCL (May 2020). Tisa-cel (Kymriah®) is also FDA and EMA approved for the treatment of R/R B-cell Acute Lymphoblastic Leukemia (B-ALL) in children and adults up to and including 24 years of age, since 2017 and 2018 respectively. In the Netherlands, ZIN has also approved tisa-cel for treatment of R/R B-ALL in children and adults up to and including 24 years of age (December 2018). Additionally, the FDA has granted accelerated approval of brexucabtagene autoleucel (brexu-cel, Tecartus®) in 2020 for treatment of R/R mantel cell lymphoma (MCL) and EMA has granted a conditional marketing authorization. It is expected that many more CAR T-cell products will be approved in the foreseeable future. Despite the hopeful response rates, challenges remain.

Study objective

• To set up a national prospective observational cohort study of patients who have a hematological B-cell malignancy and are referred to the national CAR T-cell tumorboard for evaluation of eligibility for treatment with CAR T-cell therapy and to follow them from time of referral until 30 years follow-up or death.
o To prospectively collect accurate data on medical history, comorbidities, medication use, disease characteristics, baseline clinical parameters, laboratory results, imaging results, pathology results, CAR T tumorboard evaluation outcomes, treatment outcomes, treatment related adverse events, (new) interventions and treatment strategies and patient reported outcome and experience measures.
o To facilitate the evaluation of quality of standard of care in this patient population in the Netherlands.
o To serve as a continuous basis for a large variety of research purposes regarding CAR T-cell therapy in the Netherlands including:
* Efficacy and safety studies
* Prognostic and predictive studies
* Biological studies
* Health technology assessment studies
* Evaluation studies of patient reported outcome measures (PROMs, to measure a.o. quality of life, psycho-social functioning and side effects) and patient reported experience measures (PREMs, to measure a.o. quality of care).
* Studies on evaluation and development of education materials for patients and their relatives and healthcare professionals.

* Studies to compare new interventions in a target population according to the Trials within Cohorts Design (TwiCs)

Study design

A prospective national multicentre observational cohort study.

Extension to the study design:
As the study initiation was delayed due to organizational and legal constraints and some participating centers were not able to include patients before May 2024, not all patients referred to the Dutch CAR T-cell tumorboard can be asked informed consent before they received CAR T-cell therapy. In order to be able to still include all referred patients from establishment of the CAR T-cell tumorboard as soon as CAR T-cell therapy became available outside clinical trials in the Netherlands, we will also allow that informed consent is asked after screening for CAR T-cell infusion for patients treated with CAR T-cell therapy up to and including December 31st 2024. Subsequently, after signing the informed consent, prospective data collection will follow. In order to have the same information for all included patients available for analyses, the data until informed consent was signed will also be collected but then retrospectively. However, due to the aggressive disease course some patients referred to the CAR T-cell tumorboard have already deceased before obtaining informed consent. To avoid selection bias we need to include these patients. For this subcohort retrospective data collection is allowed on the ground of general no-objection.

Study burden and risks

Since this is an observational study there are no additional risks associated with participation. Clinical parameters will be collected during routine care and derived from medical charts. If patients also give their consent on collecting PROMs and PREMs through validated questionnaires, patients will be informed about the extra time effort to complete these questionnaires. A possible advantage is that the answers to these questions can directly be shared with the treating healthcare professional to improve patient-centered care, if sharing this information is desired by the patient.
If a patient gives informed consent to be approached for future studies including studies on experimental treatment strategies according to the TwiCs design, they will be informed that their data may be used for comparative evaluation of safety and effectiveness of these new treatment strategies. They are also informed about the possibility that they may be randomly selected to being offered an experimental treatment strategy. If they are selected for this experimental treatment strategy they will receive separate information and will have to give separate informed consent. Patients will always have the option to choose the standard of care treatment strategy. Patients are informed about the fact that if they are not selected for a certain experimental treatment

strategy, and therefore are part of the control arm, they will not be informed about this and may be (temporarily) ineligible for some future other experimental treatment strategies within this cohort, without knowing. However, in any instance, standard, evidence-based treatments will never be withheld from patients. Also, patients within the Follow that CAR project may still participate in other research such as traditional RCTs.

Contacts

Public
Amsterdam UMC

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
Amsterdam UMC

De Boelelaan 1117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- 18 years or older
- have a haematological B-cell malignancy

- be able to read, understand and give informed consent
- be referred to the CAR T-cell tumorboard for treatment eligibility screening

Exclusion criteria

- unable to sign informed consent according to GCP guidelines

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-07-2022
Enrollment:	5250
Type:	Actual

Ethics review

Approved WMO Date:	04-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214

Postbus 22660

1100 DD Amsterdam

020 566 7389

mecamc@amsterdamumc.nl

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	NL76835.018.21