Immune Related Rheumatological Adverse Events.
Data collection from patients with cancer to evaluate rheumatological adverse events in patients treated with immune-checkpoint inhibitors.

Published: 27-12-2021
Last updated: 10-01-2025

This study has been transitioned to CTIS with ID 2024-516631-27-00 check the CTIS register for the current data. The evaluation of R-IrAE's after ICI therapy, specifically incidence, treament of R-IrAE's, response to said treatment,...

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

Summary

ID

NL-OMON54205

Source
ToetsingOnline

Brief title
IRRAE-study

Condition

- Autoimmune disorders
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Rheumatological side effects to therapy

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: CCA funding a.i.o. 50%,EU COFUND 50% a.i.o.,Het onderzoek wordt heden voorgefinancierd door de Afdeling Reumatologie en Klinische Immunologie, Amsterdam Universitair Medisch Centrum. Echter, tijdens de looptijd van de studie zullen aanvullende sponsoren worden geworven via "grant proposals". Zodra deze wervingsactie succesvol is, zal dit worden aangegeven. Uitvoering van onderzoek blijft hierbij haalbaar.

Intervention

Keyword: Immune-checkpoint inhibitors, Immune-related rheumatological adverse events, IRRAE

Outcome measures

Primary outcome

Compiling a comprehensive dataset on R-irAE and immune related arthritis, including incidence (expressed as odds-ratio(OR), relative risk (RR) and progression free survival (PFS)), (time to) diagnosis, management of said R-irAE*s including treatment type, duration, intensity and outcomes of both the adverse event itself and functional repercussions. Additional data regarding disease-specific serological markers and general inflammatory serology will be included, as well as quality of life (QOL) evaluations using standardized questionnaires.

Secondary outcome

(Immunohistochemical) phenotype (determined in blood, synovial fluid and synovial tissue) of patients who develop irAE arthritis as compared to those who develop classical RA and to those who do not develop irAE while treated with immunotherapy.

Qualitative (and potentially semi-quantitative) evaluation and comparison of

whole body 18F-FDG PET-CT imaging in R-irAE arthritis and de novo RA patients

to investigate presence and biodistribution of inflammatory activity in joints

and other tissues.

Study description

Background summary

Advances in systematic anticancer treatment using the patient's own immune system through immunotherapy are the standard of care in an increasing number of indications. Through blocking immune checkpoints (PD-1, PD-L1, CTCLA-4 and Lag-3), T-cell activity can be increased, thereby enhancing immune response. A notable side-effect of these treatments is an increasing number of immune-related side-effects (irAE's), of which some (10-43%) are very similar to known rheumatological diseases. These adverse events result in pain and functional impairment at short term and can potentially lead to permanent damage to specific tissues in case of longstanding/relapsing inflammatory activity with significant reduction of quality of life (QoL). Due to the relatively recent increase in clinical use of these treatments there is a current lack of diagnostic and clinical research and resultant guidelines. This study will therefore attempt to collect a broad variety of diagnostic, clinical and treatment data.

Study objective

This study has been transitioned to CTIS with ID 2024-516631-27-00 check the CTIS register for the current data.

The evaluation of R-IrAE's after ICI therapy, specifically incidence, treament of R-IrAE's, response to said treatment, baseline and follow-up serology (general and symptom specific) to be combined with quality of life assessment and symptom specific questionnaires in a prospective cohort study in a multicenter setting.

Study design

The main study consists of 3 cohorts, in which prospective clinical data will be collected in a multicenter setting, with a substudy consisting of a further 3 cohorts (2 subgroups of main study cohorts, 1 comparator cohort) subjected to further evaluation. Specific information (clinical, serological, imaging,

oncological and treatment-related) will be collected from patients who develop a R-irAE (broad rheumatological spectrum of disease manifestations as defined below) during or after ICI therapy within a period of 1 year after start of treatment. Patients with or without a preexisting rheumatological disease will be divided between specific cohorts. A combined database will be created for the gathered information in preparation for the planned analyses. Similar data collection is applicable for all participating centers and an expanded dataset, collected only at the main study center, Amsterdam UMC (AUMC). Any additional data concerning clinical status, imaging, tissue biopsies and serology collected during clinical care will also be included where available.
Additionally, a substudy will be performed to collect specific histological and imaging data in patients with arthritis as the R-irAE. These data will be compared with data extracted from patients with de novo rheumatoid arthritis (RA), as the comparator cohort. In this substudy, the immunological phenotype characterizing arthritis irAE will be investigated via further serological sampling, as well as histological sampling of synovial tissue and whole body18F-FDG PET-CT imaging. This substudy will only include patients at the AUMC (monocenter), either locally included or through specific referrals from other participating centers.

Study burden and risks

Patients will be asked to fill in questionnaires or answer questions by the researchers, in addition to a physical exam and serological evaluations. As these blood draws will be planned to coincide with regular, planned venous blood draws before and during treatment, this will not increase their burden beyond removing up to a maximum 280ml of blood over the course of the study. In the subgroups S2.1 and S3.1(part of the substudy focused on arthritis), N=15 (N=10 from S2.1, N=5 from S3.1) patients are additionally subjected to a 18F-FDG PET-CT scan and an synovial biopsy of an affected joints. This will be combined where possible with the first study visit or planned within 1 week of the baseline assessment. The total radiation burden per patient will be around 5.4mSv, which is within the range of risk category IIb of the IRCP 62 guidelines: acquisition of knowledge aimed at prevention or cure of disease.
Attendant to undergoing the synovial biopsy is a small risk of bleeding, longstanding pain, haemarthros, swelling of the joint (all less than 1,5%) after synovial biopsy.
The benefits of collecting biological and immunological information about the nature of irAE-arthritis outweigh the described very low risks of PET-CT scanning and synovial biopsie.

Contacts

Public

Vrije Universiteit Medisch Centrum

Boelelaan 1117
Amsterdam 1081HV
NL
Scientific
Vrije Universiteit Medisch Centrum

Boelelaan 1117
Amsterdam 1081HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

8 Cohorts in study: M1-3, S1-3, S2.1 and S3.1: Main cohort M1/Subgroup S1: - >=18 yr. - Diagnosed with any oncological disease - Starting with ICI therapy (ICI therapy defined as treatment with anti-PD1, anti-PDL1, anti-CTLA-4 or anti-Lag3, either in mono- or combination therapy) Main cohort M2: - >=18 yr. - Diagnosed with any oncological disease - Current or recently (<3 months) completed treatment with ICI therapy (see M1) - Development of any R-irAE diagnosed by a physician using established criteria(CTCAE) Main cohort M3: - >=18 yr. - Pre-existing rheumatological disease as diagnosed by rheumatologist - Diagnosed with any oncological disease - Initiation with ICI therapy (see M1) Subgroup S2: - Participant in M1 cohort - Specific R-irAE of arthritis in at least one joint - Subgroup S2.1: - Synovial biopsy technically possible in affected joint Subgroup S3: - >=18 yr. - De novo RA according to ACR/EULAR criteria 2010. - PET-subgroup S3.1: - Synovial biopsy technically possible in affected joint

Exclusion criteria

8 Cohorts in study: M1-3, S1-3, S2.1 and S3.1:

Main study cohort M1:
- Pre-existing rheumatological disease as diagnosed by a rheumatologist
- Previous treatment with ICI therapy

Main/substudy cohorts M2/S2/S3:
- Any other identified cause of the R-irAE or RA, not being ICI therapy
- Previous treatment with ICI therapy

Main study cohort M3:
- No cohort-specific exclusion criteria
- Previous treatment with ICI therapy

Subgroup S1:
- Pre-existing rheumatological disease
- Development of a R-irAE(in these cases switch to M2/S2 cohort possible depending on specific irAE)

Subgroup S2:
- No cohort specific exclusion criteria beyond M1 criteria
- PET group: Research related radiation exposure (cumulative >= 5 mSv) in the year before inclusion
- PET group: Pregnancy and/or breastfeeding (in female participants of reproductive potential)

- Subgroup S2.1
- Previous local injection, arthroscopy, surgery or other medical intervention on selected arthritic joint for synovial biopsy in the past 1 year
- History of joint-replacement surgery of the joint chosen for synovial biopsy.

Subgroup S3:
- Pre-existing rheumatological disease
- Previous or current use of prednisone, disease modifying anti-rheumatic drugs (DMARD*s) or biological treatment (NSAID*s/Paracetamol allowed)

Subgroup S3.1:
- Research related radiation exposure (cumulative >= 5 mSv) in the year before inclusion
- Pregnancy and/or breastfeeding (in female participants of reproductive potential)
- Previous local injection, arthroscopy, surgery or other medical intervention on selected arthritic joint for synovial biopsy in the past 1 year

- History of joint-replacement surgery of the joint chosen for synovial biopsy.

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-04-2023
Enrollment:	495
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bavencio
Generic name:	Avelumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Libtayo
Generic name:	Cemiplimab
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Opdivo
Generic name:	Nivolumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-12-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2024
Application type:	Amendment
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
EU-CTR	CTIS2024-516631-27-00
EudraCT	EUCTR2021-005613-14-NL
CCMO	NL79290.029.21