HANDSCAN OPTICAL MEASUREMENTS IN RHEUMATOID ARTHRITIS: AN INVENTORY COMPARING SERUM LEVELS OF CRP, ESR, IL-6, CLINICAL ARTHRITIS AND REPRODUCIBILITY OF DAS28.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20393

Source
Nationaal Trial Register

Brief title
HANDRAIL

Health condition

Rheumatoid Arthritis

Sponsors and support

Primary sponsor: Investigator initiated via Leiden University Medical Center (LUMC) department of Rheumatology with a grant from Sanofi with no conditions set
Source(s) of monetary or material Support: Investigator initiated via LUMC with a grant from Sanofi, with no conditions set

Intervention

Outcome measures

Primary outcome

Sensitivity to change of the Handscan during consecutive visits after initiation of different treatment strategies. In this, the percentage of patients with an initial response detected by the Handscan (= at least 2 points reduction in TOS) at the different moments in time will be determined (% initial response at week 1 (early), week 3 (early), week 6 (intermediate), week 9 (late), week 12 (late), respectively).

Secondary outcome

- Sensitivity to change of the currently used parameters SJC, TJC, DAS28, CRP, BSE and IL-6 during the consecutive visits after initiation of different treatment strategies.
In this, the same endpoint parameter will be used with the applicable response definition for each of the instruments.
- Difference in response time between Handscan response detection and response detection by the currently used instruments. Differences will be categorized as within patient difference in response time (Handscan response x weeks earlier to x weeks later)
- Handscan TOS and SJC, TJC, DAS28, CRP, BSE and IL-6 at baseline and during the consecutive visits.
- Defining the Handscan optical scores in untreated early RA patients at baseline
- Establish reproducibility of Handscan measurements with interobserver variability of DAS28
- Association between Handscan total optical score and DAS28
- Describing the effects of Sarilumab therapy in MTX naïve patients compared to the monotherapy MTX group
- Establish IL-6 levels with rate of severity of arthritis activity, DAS28 categories

Study description

Background summary

A better tool for monitoring disease activity in RA is necessary for several reasons.
The Handscan is a new (Dutch) non invasive imaging device that visualizes inflammation in the joints of hands and wrists in patients with rheumatoid arthritis (RA). The technique is based on optical spectral transmission measurements. By using this technique, the Handscan is supposed to be an objective measurement tool. We will elaborate on the underlying physiological principles, practical set up and use of the Handscan in Chapter 7.
The Handscan already demonstrated its ability to visualize subclinical inflammation when compared to ultrasound imaging and DAS28 scores (1)
At this time, only a few institutes (including MCL and LUMC) have access to and experience with this new device. Until now there are no data comparing the Handscan with systemic parameters of inflammation, such as ESR, CRP, IL-6 and arthritis activity. Also, the range of the optical score in different patients is not known.

With this study proposal we will gather data, which may lead to more specific clinical Handscan studies. First we have to define its association with current objective inflammatory parameters and its quality to sense small (subclinical) changes in a short treatment period. If this quality exists, than the Handscan might be a new tool for objective and better measurement of disease activity. Preliminary data suggest that the Handscan is more sensitive to change than clinical examination. If persistence of subclinical arthritis may be an indicator of difficult to treat disease, one intriguing application could be the use of the Handscan as a classification tool for early patients, who would benefit most from rapid onset initiation of biologic treatment at the beginning of the disease.
Furthermore, use of the Handscan as an instrument for substitution of medical healthcare workers in controlling disease activity could be an important answer to the expected shortage of healthcare workers in rheumatology.
Study design: Randomized open label trial.
Study population: Early MTX naive RA patients, who will be randomized in three subgroups: I. methotrexate monotherapy, II. methotrexate plus depomedrol and III. methotrexate plus Sarilumab.
Main study parameters/endpoints:
Describing the association between Handscan optical scores and markers of inflammation (levels of CRP, serum IL-6) and clinical swollen joint score in three treatment groups with different pharmacokinetic modes of action for RA activity. Each of these groups has its own time to response due to differences in pharmacodynamic properties of the used medication. If the Handscan is really sensitive to early response then a difference in Handscan scores between treatment groups should be detected.
Secondary endpoints are:
- a comparison of differences in time to response between the three treatment groups for swollen joint count, tender joint count, DAS28, CRP, ESR and IL-6
- Defining the Handscan optical scores in untreated early RA patients at baseline
- Establish reproducibility of Handscan measurements with interobserver variability of DAS28.
- Association between Handscan total optical score and DAS28
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Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Six visits (week 0, 1, 3, 6, 9 12), with three Handscans at each visit. DAS28 scores will be performed by three independent assessors at each visit. Blood samples for ESR, CRP and IL-6 at each visit. There is no additional discomfort associated with the Handscan and no sequels or further complications are involved. Sarilumab in combination with MTX is not yet registered for prescription in MTX naïve patients, however we judge that this combination can safely be administered in this group of RA patients. As a benefit, experimental data obtained through this experiment may result in validating the Handscan as a diagnostic tool.

Study objective

First we have to define its association with current objective inflammatory parameters and its quality to sense small (subclinical) changes in a short treatment period. If this quality exists,

than the Handscan might be a new tool for objective and better measurement of disease activity. Preliminary data suggest that the Handscan is more sensitive to change than clinical examination. If persistence of subclinical arthritis may be an indicator of difficult to treat disease, one intriguing application could be the use of the Handscan as a classification tool for early patients, who would benefit most from rapid onset initiation of biologic treatment at the beginning of the disease.

Study design

week 1 (early), week 3 (early), week 6 (intermediate), week 9 (late), week 12 (late)

Intervention

Early MTX naive RA patients will be randomized in three subgroups: I. methotrexate monotherapy, II. methotrexate plus depomedrol and III. methotrexate plus Sarilumab. After randomisation the study is an open label observational study, which focusses on the characteristics of different modes for scoring RA disease activity during 12 weeks.

In this study the Handscan is used as an investigational product and is compared to current methods for quantification of disase activity in Rheumatoid Arthritis, such as physical examination (clinical judgement) of a rheumatologist and composite scores of disease activity such as DAS28, ACR response criteria and laboratory measurements as CRP en ESR.

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Eligibility criteria

Inclusion criteria

- Able and willing to give written informed consent

- Patients aged ≥18 years
- Recent (< 2 yr) diagnosis of Rheumatoid Arthritis (RA) according to the 2010 American College of Rheumatology/European League Against Rheumatism (EULAR/ACR) classification criteria (8)
- At least two swollen joints of wrists, PIP or MCP joints.
- No previous methotrexate and/or biologic treatment
- No systemic steroid within 6 weeks prior to baseline

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Deformity of the hand or an allergy to light is an exclusion criteria for valid use of the Handscan
- A recent (< 2 months) or planned carpal tunnel operation
- Female who is pregnant, breastfeeding, or is considering becoming pregnant during the study or a male planning to father a child.
- Any active or recurrent viral infection that, based on the Investigator's clinical assessment, makes the subject an unsuitable candidate for the study, including hepatitis B virus (HBV) or hepatitis C virus (HCV), recurrent or disseminated (even a single episode) herpes zoster, disseminated (even a single episode) herpes simplex, or human immunodeficiency virus (HIV).
- History of any malignancy within the last five years except for successfully treated NMSC or localized carcinoma in situ of the cervix.
- Laboratory values meeting the following criteria within the Screening period prior to the first dose of study drug:
Serum aspartate transaminase (AST) > 2 × ULN
Serum alanine transaminase (ALT) > 2 × ULN
Estimated glomerular filtration rate (GFR) by simplified 4-variable Modification of Diet in Renal Disease (MDRD) formula < 40 mL/min/1.73 m2
Total white blood cell (WBC) count < 2,500/µL
Absolute neutrophil count (ANC) < 1,500/µL
Platelet count < 100,000/µL
Absolute lymphocyte count < 850/µL
Hemoglobin < 5.8 mmol/L
- Uncooperative patients, or any condition that could make the patient potentially noncompliant to the study procedures
- Patients for whom Sarilumab is contra-indicated as described in the local label
- Patients currently participating in any interventional clinical trials
- Previous experience with Sarilumab either through a clinical trial or treatment
- Concomitant use of any biologic DMARDs or any tsDMARDs, including but not limited to etanercept, adalimumab, infliximab, anakinra, rituximab, abatacept, tociluzumab, certolizumab, golimumab, tofacitinib

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2020
Enrollment:	45
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
NA

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL8663
Other	RTPO Leeuwarden, submitted, evaluation 28 may 2020 : ABR NL72546.099.20

Study results

Summary results
Only planned publications: first manuscript