Synopsis

Name of sponsor/company: Abbott Laboratories

Name of finished product: Humira

Name of active ingredient: adalimumab

Title of study: Whole-body magnetic resonance imaging, conventional magnetic resonance imaging and computer tomography of wrist and metacarpophalangeal joints 2-5 and circulating biomarkers in patients with rheumatoid arthritis treated with adalimumab

Drug investigated: Adalimumab

Investigators:

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Study centres:

Copenhagen University Hospital Rigshospitalet, Glostrup, Copenhagen Center for Arthritis Research, **COPECARE**, Center for Rheumatology and Spine Diseases, Denmark; Sheba Medical Centre, Diagnostic Imaging, Tel Aviv, Israel; Herlev university Hospital, Department of Radiology, Denmark; Copenhagen University Hospital Rigshospitalet, Hillerød, Denmark; Copenhagen University Hospital Rigshospitalet, Gentofte, Denmark

Publications:

Axelsen MB, Eshed I, Østergaard M, Hetland ML, Mølle r JM, Jensen DV, Krintel SB, Hansen MS, Terslev L, Klarlund M, Poggenborg RP, Balding L, Pedersen SJ. Monitoring total-body inflammation and damage in joints and entheses – the first follow-up study of whole-body MRI in rheumatoid arthritis. Scand J Rheumatol 2017 Jul;46(3):253–262

Ng SN, Axelsen MB, Østergaard M, Pedersen SJ, Eshed I, Hetland ML, et al. Whole-Body Magnetic Resonance Imaging Assessment of Joint Inflammation in Rheumatoid Arthritis—Agreement With Ultrasonography and Clinical Evaluation. Frontiers in Medicine 2020 Jun 19;7:285

Study period: Study initiation date: First patient included the January 21, 2010

Last scanning of last patient: June 3, 2013

Phase of development: Phase IV

Objective:

The primary objective was to investigate the effect of Humira on disease manifestations in peripheral joints as examined by whole-body magnetic resonance imaging.

Methodology: Investigator initiated-multicenter longitudinal 52-weeks observational study.

Number of patients (Planned and analysed): Planned 40, followed 37

Diagnosis and main criteria for inclusion: Rheumatoid arthritis according to American College of Rhematology 1987 criteria, moderate to high disease activity disease activity score, based on 28 joint counts and CRP (DAS28) >3,2 and clinical indication to start treatment with their first biological disease modifying anti rheumatic drug.

Test product, dose, and mode of administration, batch number: Humira (adaliumab), 40 mg given subcutaneously every two weeks. Study medication was sponsored for treatment during the first 16 weeks, after which medication was given from the departments. Label identification and version numbers for study medication delivered by Abbott Laboratories: L0907122, L0907123, L0907261, L0907262

Duration of treatment: All patients were treated with Humira 40 mg subcutaneously every other week for 16 weeks, after which responders continued this treatment for a total of 52 weeks and non-responders changed treatment at the discretion of the treating physician.

Reference therapy, dose and mode of administration, batch number. No reference treatment, all patients were treated with Humira. All patients but two (due to intolerance to methotrexate) received background methotrexate.

Criteria for evaluation: All patients had clinical examination of joints and entheses at baseline and after 2, 6, 10, 16, 24, 38 and 52 weeks. Whole-body magnetic resonance imaging was performed at week 0, 6, 16 and 52.

Efficacy: Primary clinical endpoint was European Alliance of Associations for Rheumatology (EULAR) good response at week 16, primary whole-body magnetic resonance imaging endpoint was the decrease in joint count at 16 weeks.

Safety: Registration of serious adverse events and adverse events.

The study was carried out in accordance with the Helsinki declaration and the Good Clinical Practice guidelines (Good Clinical Practice (CPMP/ICH/135/95)).

Good Clinical Practice monitoring was carried out by Copenhagen University Hospital Good Clinical Practice unit.

Statistical method: The primary analysis was an intention-to-treat analyses, including all included patients with magnetic resonance imaging at baseline. Descriptive statistics, comparisons between groups (responders vs. non-responders) and time points. Descriptive statistics was presented as median (min-max), $P<0.05$ was considered statistically relevant.

Summary – conclusion

Efficacy result: 37 rheumatoid arthritis patients with a median DAS28 of 4.78 were included, 30 patients were followed to week 16. At week 16, 15 patients had achieved a good EULAR response and 14 patients had achieved a moderate response to treatment, while one patient had no response.

The reliability of whole-body magnetic resonance imaging was ≥85% for all joints except proximal interphalangeal and the distal interphalangeal joins of the feet and the elbows.

At week 16, patients with a good EULAR response had a statistically significant decrease in whole-body magnetic resonance imaging synovitis 26-joint count from median 6 (1-17) to median 4 (0-14), $p<0,04$. There was a numerical, but not statistically significant larger decrease in the whole-body magnetic resonance imaging joint count in patients with a good EULAR response compared to patients with a moderate/no EULAR response.

Safety result: No serious adverse events: None, adverse events: rash (2 patients), lower respiratory tract infection (3 patients), tooth infection (1 patient)

Conclusion

This phase IV study examining the efficacy of adalimumab we found good response to treatment as measured by EULAR response. Examination of inflammation by whole-body magnetic resonance imaging had a good reliability and found a decrease in joint inflammation and a numerical difference in inflammation load between good EULAR responders and moderate/no EULAR responders.

There were no serious adverse events during the 52 weeks follow-up.

Data of report: June 9, 2022