Sponsor	Società Italiana di Reumatologia SIR - Italian Society for Rheumatology Via Turati, 40 20121 Milano, Italy
Study Title	Open-label, randomized controlled trial comparing tocilizumab to anti-TNF treatment and discovery of biomarkers for treatment selection in rheumatoid arthritis patients with inadequate response to a first anti-TNF - RAFTING - Rheumatoid Arthritis treatment after First anti-TNF INvestiGation
Acronym	RAFTING
EudraCT number	2016-001987-12
Start date	17/02/2017
Completion date	11/06/2021
Reason for interruption	poor enrollment
Keywords	Rheumatoid Arthritis, tocilizumab, anti-TNF

SHORT REPORT

Rafting Study is an Italian, multicentre, randomized, open label, parallel group, active controlled, superiority, phase IV study.

Target population: patients with active rheumatoid arthritis who have not adequately responded to a previous treatment with a first anti-TNF on a background MTX treatment.

Number of patients: 208 patients will be randomized in the study

Background and rationale: New drugs for the treatment of rheumatoid arthritis (RA) with action on specific molecular target (e.g. anti-TNF) have improved the prognosis of patients with an inadequate response to conventional therapy such as methotrexate (MTX).
However, approximately 50% of patients treated with first-line anti-TNF discontinue treatment after two years due to ineffectiveness or adverse events. The second line treatment involves the use of another anti-TNF drug or switching to a different molecular target (anti-IL6, -CD20 or CTLA-4-Ig) in combination with MTX. If in the first line the choice of an inhibitor of TNF is still the most recommended and effective and cost-effective option, the choice of the biological drug for the second line is made on an empirical basis due to the lack of robust evidence from the direct comparison studies.

Systematic reviews and network meta-analysis suggest that the change of molecular target may be associated with an advantage in terms of efficacy and, in some cases, also cost-effective.

Study treatment: eligible subjects will be randomized to receive a "switching" therapy or "cycling" therapy. Randomization procedure will be centrally performed, with a 1:1 ratio, having prior TNF inhibitor and investigator's TNFi choice at randomization as stratification factors.

Patients will be randomized to receive:

- Experimental arm: "Switching" strategy (TNF→TCZ)
*Tocilizumab [originator or approved biosimilars] 8 mg/kg i.v. every 4 weeks OR 162 mg s.c every seven days
- Control arm: "Cycling" strategy (TNF→TNF)
For each patient the choice of TNFi treatment is left to the investigator's decision and have to be among one of the following TNF inhibitors:
a. Etanercept (ETA) if initial failure to monoclonal antibodies: infliximab (INF), adalimumab (ADA), golimumab (GOL) or certolizumab (CTZ)
OR
b. Infliximab, ADA, GOL or CTZ if initial failure to the receptor fusion protein, ETA.

Study aims: To compare the efficacy of switching to a different molecular target (from TNF to IL6) versus cycling to a second TNF inhibitor in patients with active RA, who have not adequately responded to a previous treatment with a first anti-TNF on a background MTX therapy.

Endpoints: The primary end-point will be the proportion of patients with good EULAR response at 24 weeks.

Conclusions: The trial has been prematurely closed on 11 July 2021, when 32 patients out of 208 were enrolled. This decision was taken due to unsatisfactory recruitment by all participating experimental centers, despite all the numerous attempts on our part to reverse this trend.

The formal communication of premature closure of the study was sent to the National Competent Authority (Italian Medicines Agency, AIFA) and to all Ethics Committees of the participating centres through a letter dated 25 June 2021.

Prof. Carlo Alberto Scirè
Sponsor Representative and
Scientific Responsible