Long-term continuation of anti-TNF in combination with either methotrexate or leflunomide compared to monotherapy – results from the German biologics register

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Angela Zink[1,5], Anja Strangfeld[1], Peter Herzer[2], Christina Bungartz[1], Ulrich von Hinueber[3], Siegfried Wassenberg[4], Joachim Listing[1]

[1] German Rheumatism Research Centre Berlin, [2] rheumatologist München, [3] rheumatologist Hildesheim, [4] Ev. Fachkrankenhaus Ratingen, [5] Charité Univ. Hospital, all Germany

www.biologika-register.de

DRFZ German Rheumatism Research Center, Berlin

Epidemiology Unit

Conclusion

Combination of ETA or INF with either MTX or LEF increases the treatment duration, mainly because of higher efficacy. There is no increase in termination due to adverse events with combination therapy. If MTX is not tolerated, combination with LEF seems to be an acceptable alternative. However, MTX is continued significantly longer than LEF.

Objective

To investigate therapy continuation over 3 years in a large prospective cohort study of patients treated with etanercept (ETA), adalimumab (ADA) or infliximab (INF).

Patients

Patients with rheumatoid arthritis (RA) enrolled into RABBIT (German biologics registry)

New prescription of ETA, ADA or INF at enrollment

Methods

Follow-up at 3,6,12,18,24, 30 and 36 months

Assessment of treatment details at each follow-up visit by treating rheumatologist

Investigation of

- treatment continuation of initial anti-TNF therapy
- time to restart of a new anti-TNF treatment

by means of Kaplan-Meier method and log-rank test.

Results

	12 months	24 months	36 months
Etanercept	66.5	55.1	49.5
Adalimumab	62.6	41.9	46.4
Infliximab	55.9	54.6	35.9

Tab. 1: Treatment continuation in percent of patients

Discontinuation rates were higher in patients receiving INF than in those receiving ETA (p<0.001) or ADA (p<0.001). This was especially due to adverse events. The difference remained significant when combination therapies with methotrexate (MTX) were compared. It was possibly influenced by the availability of other treatment options (ADA) and the kind of the application.

For patients treated with ETA or INF continuation was generally higher when the TNF inhibitor was combined with methotrexate (MTX) or Leflunomide (LEF) compared to monotherapy. This was not the case for ADA.

In the treatment continuation of ETA, there was no difference between MTX and LEF as combination partners whereas for ADA and INF continuation rates (of ADA, INF) with MTX were higher than with LEF.

Treatment with LEF was significantly more frequently terminated than a combination with MTX (Fig.2). Reasons were adverse events (MTX: 55%, LEF: 48%), lack of efficacy (MTX: 13%, LEF: 31%), remission (MTX: 13% , LEF: 14%).

After treatment termination with one biologic, more than half of all patients received another biologic agent within three months (Tab 2). Change was more frequent after termination because of inefficacy.

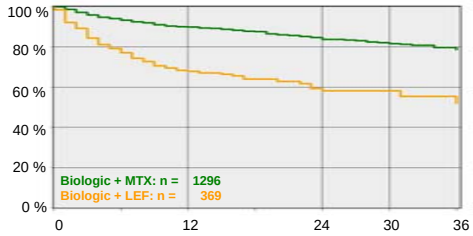

Fig. 2: Treatment continuation of LEF or MTX as combination partner of anti-TNF agents.

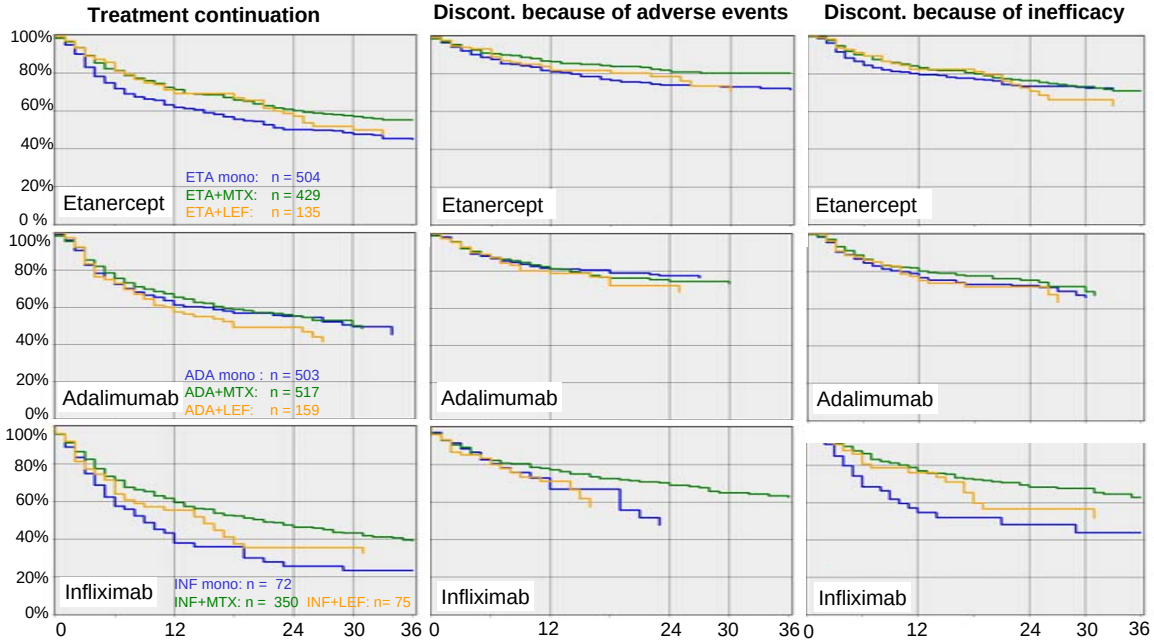

Fig.1: Treatment continuation in patients treated with ETA, ADA, INF.

		% of patients who restarted at month	
1st. drug	Stopped because of	3	12
ETA	Adverse events	41.0	65.0
	Lack of efficacy	70.1	79.6
ADA	Adverse events	38.1	56.4
	Lack of efficacy	57.4	72.3
INF	Adverse events	47.4	73.5
	Lack of efficacy	66.9	80.9

Tab.1 Time to restart with another biologic

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Zink@drfz.de