Leflunomide is an acceptable combination partner for TNF inhibitors if methotrexate is not tolerated – results from the German biologics register

342

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RABBIT
www.biologika-register.de

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

Patients

2,862 patients with rheumatoid arthritis (RA) and a new prescription of ETA, ADA or INF were enrolled into the German Biologics Register RABBIT between May 2001 and December 2006.

Methods

Treatment details were assessed at baseline and after 3,6,12,18,24, 30 and 36 months by the treating rheumatologist.

Investigation of

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

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

Results

	n	12 months	24 months	36 months
Etanercept	1,103	65.5	53.7	47.9
Adalimumab	1,252	62.0	54.2	46.4
Infliximab	507	55.9	41.8	35.4

Tab. 1: Treatment continuation in percent of patients

Continuation rates were lower in patients receiving INF than in those receiving ETA (p<0.001) or ADA (p<0.001). The difference mostly resulted from adverse events. It remained significant when combination therapies with methotrexate (MTX) were compared. Treatment continuation in INF was possibly influenced by the way of administration and the availability of other treatment options (ADA).

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.

Concerning treatment continuation of ETA, there was no difference between MTX and LEF as combination partners whereas for ADA and INF continuation rates of the biologic were higher with MTX 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: 43%), lack of efficacy (MTX: 13%, LEF: 34%), remission (MTX: 16% , LEF: 16%).

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.

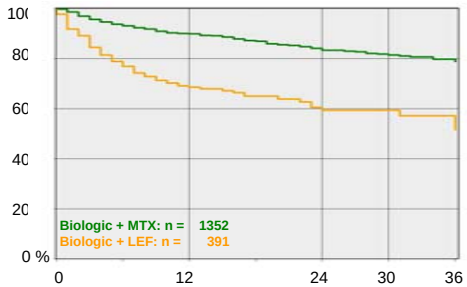

Fig. 2: Treatment continuation of LEF or MTX as combination partners of anti-TNF agents.

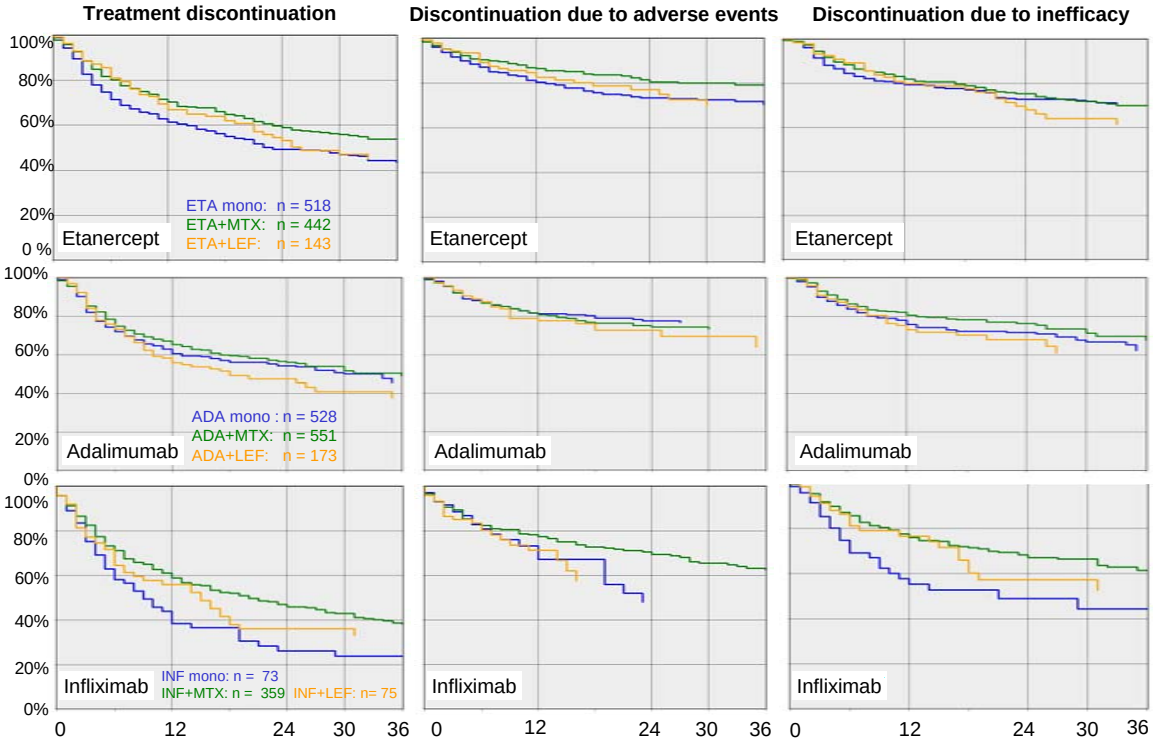

Fig.1: Treatment continuation in patients treated with ET A, ADA, INF

		% of patients who restarted at month	
1st. drug	Stopped because of	3	12
ETA	Adverse events	40.8	65.1
	Lack of efficacy	69.4	79.8
ADA	Adverse events	38.5	53.9
	Lack of efficacy	56.6	70.7
INF	Adverse events	49.0	76.1
	Lack of efficacy	67.2	81.7

Tab.1: Time to restart with another biologic

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