Medical or Research Professionals / Clinicans

Topic area: Clinical topics by disease
Topic: 11. Rheumatoid arthritis - prognosis, predictors and outcome

EULAR12-3955
SUCCESSFUL CONTROL OF DISEASE ACTIVITY AND TREATMENT WITH BIOLOGICS INCREASE THE LIFE EXPECTANCY IN RHEUMATOID ARTHRITIS PATIENTS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2012: No
Is the First Author of this abstract an Undergraduate or a Student?: No

Objectives: To investigate the impact of disease activity, functional capacity and treatment with biologic and non-biologic disease modifying anti-rheumatic drugs (bDMARDs, nbDMARDs) on mortality risk in patients with rheumatoid arthrits (RA) enrolled in the German biologics register RABBIT.
Methods: Disease activity (measured by the DAS28 score), functional capacity and treatment details with bDMARDs, nbDMARDs and glucocorticoids were assessed at fixed time points at follow-up. Cox proportional hazard regression was applied to investigate the influence of the time varying DAS28 scores, functional capacity and treatments on the mortality risk after adjustment for age, sex, 8 co-morbid conditions and smoking. The primary analysis was based on a risk window approach assuming the patient was exposed to bDMARD treatment up to 6 months (rituximab: 12 months) after the last dose.
Results: The mean disease duration of the 8,613 RA patients was 10.3 years. The mean observation time was 3.4 years. At baseline the mean DAS28 of the bDMARD patients was 5.9, of the nbDMARD patients 4.9. Five percent (426) patients died within a period of two years after the last visit.
Compared to the general population the age and sex standardized mortality ratio was 1.6 [95%CI: 1.4 – 1.8] which corresponds to a shortening of the life expectancy in women and men of 3.5 years. Patients with a mean DAS28 over time below 4.0 had a normal life expectancy. In contrast, female and male patients with a mean DAS28 score at follow-up > 4.0 died 6.4 and 7.3 years earlier than age and sex matched subjects from the general population.
This significant association between disease activity and the mortality risk was also observed by multivariate Cox regression within the patient sample. Adjusted for age, sex, co-morbid conditions and treatment each increase in the mean DAS28 score by one unit increased the mortality risk by 15% (adjusted hazard ratio [adjHR]: 1.15 p=0.002). Treatment with glucocorticoids also increased the mortality risk (adjHR per 5mg/d: 1.2 p=0.003). Patients exposed to TNFa inhibitors had a significantly lower mortality risk (adjHR: 0.65, Tab. 1). A similar result was found for rituximab and other biologics. With a conservative ever exposed approach, we again found no increased mortality risk for patients exposed to bDMARDs (adjHR=1.0).

	Pyrs	Deaths	Rate/1,000 pyrs	Cox Regr. adjHR	p
nbDMARDS	9,785	197	20.1	Ref.	
TNF-inhibitors	15,818	179	11.3	0.65	0.0004
Rituximab	2,246	31	13.8	0.81	0.34
Other biologics	1,347	24	0.84	0.84	0.42

Table: Mortality rates per 1,000 patient years (pyrs) and adjHR based on a six (rituximab 12) months risk window

Conclusions: In patients with long standing RA an effective treatment which leads to persisting control of disease activity increases the life expectancy. Controlled for demographic and clinical parameters and for clinical effectiveness (DAS28, GC dose), biologics are associated with a lower mortality than nbDMARDs.
Supported by a joint, unconditional grant from Abbott, Amgen/Biovitrum, Bristol Myers Squibb, Essex, Pfizer, Roche, and UCB.

Disclosure of Interest: None Declared