No confirmation of increased risk of idiopathic facial nerve palsy under tocilizumab

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Conclusions

The overall incidence of idiopathic facial nerve palsies among rheumatoid arthritis patients receiving DMARDs was higher than the incidence in the general population. However, an increased risk for patients receiving tocilizumab compared to patients treated with other biologicals cannot be confirmed. The incidence of idiopathic FNP is higher for patients receiving biologicals compared to patients receiving csDMARDs. This might be due to the higher disease activity. However, the small number of cases with an idiopathic facial nerve palsy is a limiting factor in analysing and interpreting these results.

Background & Objectives

Spontaneous reports of nine facial paralyses and five facial pareses made by healthcare professionals from Europe have recently prompted EMA's Pharmacovigilance Risk Assessment Committee (PRAC) to consider a potentially increased risk of idiopathic facial nerve palsy for patients receiving tocilizumab.

Our objective was to assess whether this signal can be confirmed with data of a large data set with known denominators for various treatments, comparing the risk in patients with rheumatoid arthritis (RA) receiving tocilizumab with the risk in patients receiving other conventional synthetic (cs) or biologic (b)DMARDs.

Patients & Methods

The German register RABBIT (***R***heumatoid ***A***rthritis: O***b***servation of ***bi***ologic ***t***herapy) is a prospective longitudinally followed cohort of RA patients with a new start of a DMARD after at least one csDMARD failure. For this analysis, patients who were enrolled between 01/2007 and 04/2018 were included. All physician reported facial paresis and facial paralysis were analysed as outcomes by calculating DMARD specific, unadjusted incidence rates.

Results

Between 2007 and 2018, a total of six facial paresis and 14 facial paralyses were observed in 11,963 RABBIT patients. Of those, three were excluded due to obvious reasons for facial nerve palsies (prior stroke, prior basal cell carcinoma and buccal abscess/ dental treatment) leaving 17 idiopathic facial nerve palsies (FNP).

Age and gender were roughly equal in patients with and without idiopathic FNP (table). Patients with idiopathic FNP had longer disease duration, presented more frequently with joint erosions and with more prior bDMARD treatments. They also had lower physical function and more comorbidities. In one patient with idiopathic FNP receiving the originator rituximab, a Sjoegrens' syndrome was reported as comorbidity, which is associated with an increased risk for neuropathies.

Table: Baseline characteristics of patients with and without (w/o) facial nerve palsy (FNP).

	Patients with FNP n=17	Patients w/o FNP n=11,946
Age [years]	60.6 ± 12.6	57.5 ± 12.7
Female patients	12 (70.6%)	8,922 (74.7%)
Disease duration [years]	14.7 ± 10.7	9.4 ± 8.9
No. of prior bDMARD therapies	1.4 ± 1.3	0.5 ± 1.0
Autoantibody positivity (rheumatoid factor or anti-CCP)	14 (82.4%)	8,701 (73.4%)
Joint erosions	10 (71.4%)	5,753 (50.9%)
DAS28-ESR	4.8 ± 1.2	4.9 ± 1.3
Erythrocyte sedimentation rate	29.1 ± 17.5	28.9 ± 22.4
C-reactive protein [mg/l]	15.8 ± 15.3	14.4 ± 20.7
% of full physical function	55.3 ± 28.7	65.4 ± 23.3
Therapy with glucocorticoids	14 (82.4%)	9,280 (77.8%)
Glucocorticoid dosage [mg/d]	9.8 ± 9.7	8.9 ± 9.0
Ever smoked	8 (47.1%)	6,432 (56.9%)
No. of comorbidities	3.9 ± 3.3	2.2 ± 2.2
Sjoegrens' syndrome	1 (5.9%)	152 (1.3%)

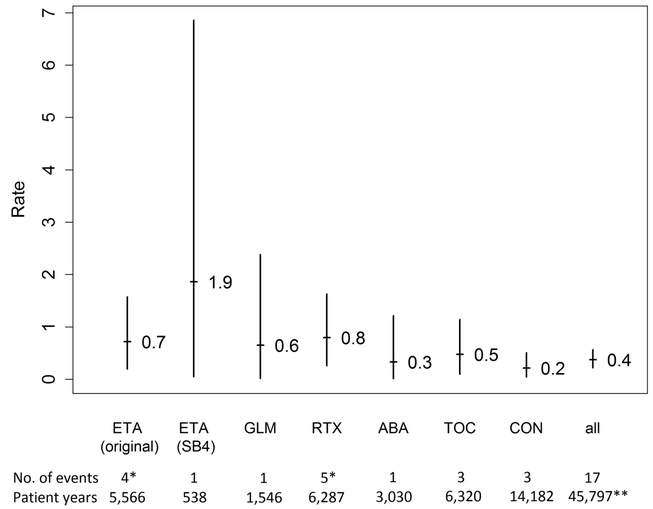
Numbers are given as mean ± standard deviation or frequency (n (%)).

Incidence of facial nerve palsies

Three of the reported FNPs were observed in tocilizumab treated patients, leading to an incidence rate of 0.47 per 1,000 patient years (PY) (95%CI: 0.10; 1.14), which is non-significantly higher than the incidence rate observed in patients receiving csDMARDs (0.21 (0.04; 0.51)) but does not stand out among the incidence rates observed for other biologicals (see figure). The overall incidence of an idiopathic FNP among patients with RA receiving csDMARDs or bDMARDs was 0.37 (0.22; 0.57), which is higher than the incidence of idiopathic FNP in the general population with 20-25 cases per 100,000 persons [1].

[1] Finsterer, J.: Management of peripheral facial nerve palsy. Eur Arch Otorhinolaryngol. 2008 265:743-752.

Figure: Unadjusted incidence rates per 1,000 PY for idiopathic facial nerve palsies stratified by treatment



** One patient was exposed to both etanercept (original) and rituximab at the time of event.*
***Encompasses all patients observed in RABBIT.*

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