

musculoskeletal pain (n=76; RR, 1.37; IC, 0.45) and myasthenia gravis (n=66; RR, 1.42; IC, 0.50);<sup>2</sup> PEMBROLIZUMAB: arthralgia (n=151; RR, 1.43; IC, 0.52) and pain in an extremity (n=58; RR, 1.35; IC, 0.43);<sup>3</sup> DURVALUMAB: polymyositis (n=2; RR, 4.41; IC, 2.15), rhabdomyolysis (n=4; RR, 2.68; IC, 1.42), and autoimmune arthritis (n=2; RR, 8.83; IC, 3.14);<sup>4</sup> IPILIMUMAB: muscular weakness (n=157; RR, 1.70; IC, 0.76) and back pain (n=105; RR, 1.27; IC, 0.34). In general, rates of rheumatic and musculoskeletal adverse events were higher in men and in the elderly population (>65 years).

**Conclusions:** A wide spectrum of rheumatic and musculoskeletal toxicity signals were detected with ICI's. Clinicians need to be vigilant about these rare but debilitating complications. Future studies to explore mechanisms and optimal management strategies of these toxicities are warranted.

**REFERENCE:**

[1] Sarangdhar M, Tabar S, Schmidt C, et al. Data mining differential clinical outcomes associated with drug regimens using adverse event reporting data. *Nat Biotechnol* 2016;34:697–700.

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**Can we halt progression of structural damage in axial SpA?**

OP0198

**COMBINED EFFECTS OF TUMOUR NECROSIS FACTOR INHIBITORS AND NSAIDS ON RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS**

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**Background:** The potential of TNFi or NSAIDs to reduce radiographic progression in AS is uncertain and causal effects of both exposures on radiographic progression have not been convincingly demonstrated. In addition, no study has evaluated whether effects are comparable among different NSAIDs in this setting. **Objectives:** The objective of this study was to explore causal effects of NSAIDs and TNFi on radiographic progression in Ankylosing Spondylitis (AS) and to compare effects of celecoxib to other NSAIDs.

**Methods:** We included all patients meeting the modified New York criteria in a prospective cohort with at least 4 years of clinical and radiographic follow up. Clinical and medication data were collected every 6 months and radiographs were performed at baseline and every 2 years. We used longitudinal targeted maximum likelihood estimation to estimate the causal effect of TNFi and NSAIDs (using the NSAID index) on radiographic progression as measured by the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at 2 and 4 years, accounting for time-varying covariates. We controlled for sex, race/ethnicity, education, symptom duration, enrollment year, number of years on TNFi, symptom duration at time of TNFi start, baseline mSASSS, ASDAS-CRP, current smoking, and missed visit status.

**Abstract OP0198 – Table 1**

	TNF use	No TNF use	Mean Difference	P-value
Comparing TNF use vs no TNF use, given <b>no NSAID (=0)</b> at time t:				
mSASSS @ 2 years	13.94	14.92	-0.98 (-2.77, 0.81)	0.28
mSASSS @ 4 years	16.12	15.62	0.50 (-0.63, 1.64)	0.38
Comparing TNF use vs no TNF use, given <b>low NSAID (&gt;0 and &lt;50)</b> at time t:				
mSASSS @ 2 years	15.43	15.49	-0.06 (-1.63, 1.51)	0.94
mSASSS @ 4 years	15.52	16.76	-1.24 (-1.80, -0.68)	<0.001
Comparing TNF use vs no TNF use, given <b>high NSAID (&gt;=50)</b> at time t:				
mSASSS @ 2 years	14.79	15.13	-0.34 (-1.46, 0.78)	0.56
mSASSS @ 4 years	14.17	17.47	-3.31 (-4.02, -2.59)	<0.001
Comparing TNF use vs no TNF use, <b>NSAID=celecoxib</b> at time t:				
mSASSS @ 2 years	11.63	15.62	-3.98 (-4.51, -3.45)	<0.001
mSASSS @ 4 years	14.37	19.06	-4.69 (-5.08, -4.30)	<0.001

**Results:** Of the 519 patients, 75% were male with a baseline mean (SD) age and symptom duration of 41.4 (13.2) and 16.8 (12.5) years respectively. The baseline mean (SD) mSASSS was 14.2 (19.6). At baseline, NSAIDs were used in 66% of

patients, of which ½ used an index <50 and ½ an index ≥50). TNFi were used in 46% of patients at baseline. In the setting of TNFi use, the addition of NSAID therapy was associated with less radiographic progression in a dose-related manner at 4 years. When NSAID specific effects were examined, celecoxib in combination with TNFi use was associated with the greatest reduction in radiographic progression and this was significant at both 2 and 4 years (table 1).

**Conclusions:** Dose related use of NSAIDs together with TNFi in AS patients has a synergistic effect in slowing radiographic progression with the greatest effect in those using both high-dose NSAIDs and TNFi. Celecoxib appears to confer the greatest benefit in decreasing progression with effect at both 2 and 4 years.

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OP0199

**SUSTAINED REMISSION OF INFLAMMATION IS ASSOCIATED WITH REDUCED STRUCTURAL DAMAGE ON SACROILIAC JOINT MAGNETIC RESONANCE IMAGING IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: EVIDENCE TO SUPPORT THE CONCEPT OF TREAT-TO-TARGET**

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**Background:** Treat-to-target is acceptable in RA; however, it is unknown whether it will reduce/prevent disability, impairment of mobility, and structural damage in early axial spondyloarthritis (axSpA) without radiographic sacroiliitis.

**Objectives:** To evaluate the impact of sustained clinical remission on MRI structural parameters. We hypothesised that patients with sustained inactive disease according to the ankylosing spondylitis disease activity score (ASDAS <1.3) are more likely to achieve reduction in erosion (structural damage) and increase in backfill (a reparative process) on MRI of the SI joints (SIJ).

**Methods:** EMBARK (NCT01258738) and DESIR (NCT01648907) enrolled patients with early axSpA. EMBARK included 12 weeks of double-blind placebo-control, then open-label etanercept for 92 weeks. Patients in the DESIR observational cohort had no history of biologics and received no biologics for 2 years. T1 weighted MRI images of SIJ at baseline and 104 weeks were combined and anonymized; readers were unaware of film chronology and original patient cohort. Three experienced readers evaluated MRI images using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score. Lesion change was considered present if ≥2 of 3 readers measured change in same direction. ASDAS endpoints were assessed sequentially: sustained (≥2 visits 6 months apart) inactive disease (ASDAS <1.3) or moderate disease activity (≥1.3 to <2.1); or no sustained response (≥2.1). Net proportions of patients with decrease in erosion and increase in backfill were determined, unadjusted and adjusted for covariates that may affect development of lesions on MRI.

**Results:** From EMBARK and DESIR, 161 and 76 patients, respectively, were included. For patients in EMBARK with sustained ASDAS <1.3, a greater percentage had decrease in erosion (34/104, 32.7%) than increase (5/104, 4.8%); p<0.0001; without sustained response, 5/24 (20.8%) had decrease in erosion and 1/24 (4.2%) had increase. This trend was also present in DESIR. Patients with sustained ASDAS <1.3 in EMBARK: 22.1% had increase in backfill, 0% had decrease; p<0.0001; in DESIR, 21.7% had increase, 0% had decrease; p<0.05. For those without sustained response, difference between increase and decrease was smaller. Net percent of patients (adjusted) with sustained ASDAS <1.3 and erosion decrease: 22.6% and 9.3% for EMBARK and DESIR, respectively; without sustained response: 13.3% and -10.1%. Net percent of patients with sustained ASDAS <1.3 and backfill increase: 19.6% and 25.7% for EMBARK and DESIR, respectively; without sustained response: 8.7% and 6.0%.

**Conclusions:** These data demonstrate a link between sustained ASDAS inactive disease and MRI structural endpoints. Clinical relevance of change in MRI SIJ erosion and backfill and their relationship to ankylosis development requires study.

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