Abstract OP0195 – Figure 1 Mortality rates and HRs in patients categorised by (A) double ACPA and RF serostatus; (B) serostatus and DMARD exposure

Conclusions: Elevated ACPA and RF titres were independently associated with increased mortality among pts with RA. The associations between ACPA/RF and mortality persisted in those treated with cDMARDs but not with bDMARDs. Further studies are warranted to evaluate the effect of bDMARDs on mortality in seropositive pts.

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OP0196 SAFETY AND EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH CANCER AND PREEXISTING AUTOIMMUNE DISEASES: A NATIONWIDE MULTICENTER RETROSPECTIVE STUDY

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Background: Immune Checkpoint Inhibitors (ICI) have revolutionised the management of several cancers, enhancing the anti-tumoral immune response. However they are responsible for many Immune Related Adverse Effects (IRAE), and therefore most patients with Preexisting Autoimmune Diseases (PAD) have been excluded from clinical trials.

Objectives: The aim of this study was to evaluate the safety and efficacy of ICI in patients with PAD.

Methods: Three national expert networks, focusing respectively on skin cancers, thoracic cancers and inflammatory diseases participated in this study. All patients who received an ICI despite a PAD in clinical practice were included in this nationwide retrospective study.

Results: 112 patients were included: 64 men (57.1%), median age 66.5. Most patients received an anti-PD1 or anti-PD-L1 drug (84.8%). Main cancer types were melanoma (n=66, 58.9%) and Non-Small Cell Lung Carcinoma (NSCLC) (n=40; 35.7%). Median follow-up was 8 months [0–52].

Most frequent PAD were psoriasis and psoriatic arthritis (27.6%), rheumatoid arthritis (17.8%), inflammatory bowel disease (12.5%), spondyloarthritis (4.5%), lupus (6.3%), polymyalgia rheumatica and/or giant-cell arteritis (6.3%). 24 patients (21.6%) were receiving an immunosuppressive therapy (IS) at ICI initiation

(including steroids in 15, sDMARD in 10 and rituximab in 1). 37 patients (33%) had an active disease.

PAD flares were frequent (n=47; 42%) and 30.4% of them were severe (grade CTCAE 3–4). 26 patients (56.5%) received an IS treatment for a flare (22 received steroids and 7 a DMARD). Other IRAEs not related to the PAD occurred in 43 patients (38.4%), 41.5% were severe. 23 patients (56.1%) required an IS (including a DMARD in 4). 36 patients (32.1%) discontinued ICI temporarily or definitively because of a flare or an IRAE. One patient died due to an IRAE.

Concerning the anti-tumoral response, the Overall Response Rate (ORR) was 48.3% for melanoma and 53.8% for NSCLC. The median Progression Free Survival (PFS) was 12.4 months for melanoma and 9.7 for NSCLC. Median overall survival (OS) was not reached in any group. PFS and OS were shorter in patients receiving an IS treatment at ICI initiation (p=0.007, figure 1A, and p=0.003, respectively). PFS and OS were longer in patients who experienced a PAD flare or other IRAE, but this gain was lost when an IS was used to treat the flare/IRAE (p=0.008, figure 1B, and p=0.01, respectively). Conversely, this gain was not impacted with ICI discontinuation.

Conclusions: PAD flares and other IRAEs are frequent during ICI therapy and may be severe. The OS, ORR and PFS seem high in patients with PAD. The occurrence of a flare/IRAE is associated to a better outcome, gain lost when IS are used, while ICI discontinuation has no impact on PFS. Further prospective studies are needed to confirm our findings.

Disclosure of Interest: None declared

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OP0197 RHEUMATIC AND MUSCULOSKELETAL ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS: DATA MINING OF THE US FOOD AND DRUG ADMINISTRATION ADVERSE EVENT REPORTING SYSTEM

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Background: Immune-modulating monoclonal antibodies directed against immune checkpoints (cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), programmed cell death-1 receptor (PD-1) and its ligand PD-L1), have demonstrated tremendous promise in the treatment of diverse solid tumour types, including melanoma, non-small cell lung cancer, among others and have improved survival rates of these cancer patients. However, these advances have created a new set of challenges in identifying and managing toxicities.

Objectives: To identify emerging trends of rheumatic and musculoskeletal adverse events by immune checkpoint inhibitor (ICI) treatment in the US Food and Drug Administration (FDA) Adverse Events Reporting System (FAERS).

Methods: We used AERSMine, an open-access web based application to mine the FAERS database from the first quarter (Q1) of 2011 to the third quarter (Q3) of 2017, approximately 7.1 million patients. Measures of disproportionality were calculated using well-established pharmacovigilance metrics, Relative Risks (RR) and safety signals (information component, (IC)), in a subset of patients with a cancer diagnosis. Terminology used for categorization of adverse events was as included in the FAERS. Fisher's exact test was used to determine significant adverse event differences by ICI treatment and age.

Results: We identified 30 939 unique patients with cancer and reports of immune checkpoint inhibitor associated toxicities. More than half of these reports were in relation with anti PD-1 inhibitors. Statistically significant adverse events associated with ICI therapy identified as toxicity signals with different agents included: NIVOLUMAB: myositis (n=102; RR, 1.35; p<0.01; IC, 0.43), rheumatoid arthritis (n=67; RR, 1.52; IC, 0.61), psoriatic arthropathy (n=20; RR, 1.93, IC, 0.95),

musculoskeletal pain (n=76; RR, 1.37; IC, 0.45) and myasthenia gravis (n=66; RR, 1.42; IC, 0.50);² PEMBROLIZUMAB: arthralgia (n=151; RR, 1.43; IC, 0.52) and pain in an extremity (n=58; RR, 1.35; IC, 0.43);³ 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);⁴ 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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THURSDAY, 14 JUNE 2018

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 no NSAID (=0) 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 low NSAID (>0 and <50) 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 high NSAID (>=50) 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, NSAID=celecoxib 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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