POS0293

TRHEUMA REGISTRY PROVIDES FIRST EVIDENCE OF DIFFERENT COURSE OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS AND TUMOUR RESPONSE RATES DEPENDING ON THE TUMOUR ENTITY

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Background: Rheumatic immune-related adverse events (irAE) are associated with a better tumour response to immune checkpoint inhibitors (ICI). In contrast to other irAEs, their potentially chronic course may require long-term immunosuppressive treatment.

Objectives: Our registry-based study analyses real-world data on the characteristics and outcome of rheumatic irAEs and underlying malignancy. Herein, we present first evidence that these parameters and the optimal clinical management may differ depending on the tumour entity.

Methods: The TRheuma registry is a prospective long-term observational study of a patient cohort suffering from rheumatic side effects of cancer therapies with focus on ICI. It is part of the Malheur project initiated in July 2018 at the University Hospital Heidelberg to explore interrelations of malignancies and RMDs.

Results: 64 patients were recruited due to a rheumatic irAE under ICI treatment (nivolumab n=30, pembrolizumab n=33, ipilimumab n=12, PD-L1i n=5, ipi/nivo n=10) with a follow-up of up to 30 months. Of these, 47% had NSCLC and 41% melanoma. In local cohorts of patients receiving ICI, 4% of NSCLC (n total=888) and 13% of melanoma (n total=195) developed a rheumatic irAE. 7% of NSCLC and 23% of melanoma patients experienced a flare of a pre-existing RMD. De novo irAE mostly resembled phenotypes of spondyloarthritis both in NSCLC (43%) as well as in melanoma patients (33%). CRP levels were increased in 83% of NSCLC and 71% of melanoma patients. Almost all irAE patients showed autoantibody negativity and signs of inflammation in ultrasound examination (96%). Comparison of best responses to treatment in patients with and without rheumatic irAE in melanoma and without any irAE in NSCLC patients were as following: Complete remission (CR) in 48% vs. 4% of melanoma patients and partial remission (PR) in 68% vs. 41% of NSCLC patients. In accordance with our severity-based treatment algorithm, 25% of the melanoma patients in CR and 16% of the NSCLC patients in PR needed add-on DMARDs for sufficient irAE-treatment. ICI-treatment was discontinued in 7 cases (17% NSCLC, 8% melanoma)

Conclusion: Prospective real-world data from the TRheuma-registry provide first evidence that rheumatic irAE have distinct characteristics depending on the underlying malignancy. Oncological outcome was better with rheumatic irAE than in their absence and this effect was more pronounced in melanoma patients despite a larger use of immunosuppressants for irAE-treatment.

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POS0294

PROFILE OF SPINAL TUMORS IN RHEUMATOLOGY DEPARTMENTS

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Background: Spine tumors remain a hot topic because of their associated morbidity by affecting motor and sensory function. Contrary to metastatic spine disease (MSD), extremely prevalent, rise within or surrounding the spinal cord and/or vertebral column, primary spinal tumors are rare, 5% of all primary skeletal tumors and frequently benign (20%). The diagnostic delay of these tumors, even when benign, is associated with a poor prognosis. Establishing the correct diagnosis is heavily reliant on magnetic resonance imaging and histological confirmation.

Objectives: to provide an overview of the epidemiology, radiological and histopathological of spinal tumors diagnosed in a rheumatology department.

Methods: A retrospective study consisting of clinical characteristics analysis, laboratory and x-ray examinations, was performed on 40 patients who were hospitalised for a spinal tumor, in a rheumatology department, over 5-year period from 2015 to 2020.

Results: A total of 40 patients with a mean age of 66 ± 13.5 years [18-93] and a sex-ratio of 1.1, were included. The most common initial complaints were inflammatory back pain (67.5%) and fatigue (52.5%), with a median duration of 5 months. Physical examination abnormalities included lumbar stiffness (32.5%), radicular signs (18.7%), hepatomegaly (12.5%), and lymphadenopathy (17.5%). Neurological deficit was found in only 3 patients (7.5%). Hypercalcemia (corrected serum calcium > 105 mg/l), and anemia (hemoglobin (Hb) < 100 g/l in female, Hb < 110 g/l in male) were present initially in respectively 47.5% and 46.3% patients, while biological inflammatory syndrome was present in 89.7% patients (median C-reactive protein of 44.7). Tumor markers were performed in 12 patients and they were positive in 9 of them.

Plain radiographs findings were vertebral compression fractures (43.6%), osteolytic lesions (30.8%) and osteoblastic lesions (12.5%). Lumbar spine was the most affected (57.5%), followed by the dorsal spine (45%). Magnetic resonance imaging (MRI) was performed in 55%, and the most common lesion was low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences (68.1%).

In our study, only one patient was diagnosed for a myxopapillary ependymoma, a benign primary spinal tumor characterised by a metastatic dissemination risk. For the rest (39 patients), the diagnosis of bone metastasis, multiple myeloma (57.7%), and of solid tumor cancers (40%), were established. Primary cancers were mainly prostate cancer (37.5%), lung cancer (18.7%) and kidney cancer (18.7%). By a median follow-up time of 25 months, overall survival rate was 30%.

Conclusion: Extradural lesions are the most common, and are typically metastatic. Special attention should be paid to the patient's medical history and laboratory abnormalities. In fact, an early diagnosis requires a high index of clinical suspicion.

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POS0295

NO CAUSAL EFFECTS OF GENETICALLY DETERMINED SERUM URATE LEVELS ON THE RISK OF ALL-CAUSE AND SITE-SPECIFIC CANCER: A MENDELIAN RANDOMIZATION STUDY

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Background: Positive associations between urate levels and gout and the risk of some cancer types (urogenital, prostate, gastrointestinal and lung) have been reported in a number of observational studies; however, whether the relationship is causal remains uncertain.

Objectives: The study aim was to evaluate a causal effect of genetically determined serum urate (SU) concentrations on cancer risks (overall and major cancer types) in individuals with European ancestry using Mendelian randomization (MR) analyses design.

Methods: We used the individual-level data from two population-based Swedish cohorts including middle-aged subjects (mean follow-up = 21.2 years), Malmö Diet Cancer and Malmö Preventive Project (MDC/MPP), for one-sample MR setting. Data from a total of 17,597 individuals (n = 17,597 for SU at baseline, diagnoses during follow-up: 5659 for all-cause, 516 for bladder, 545 for lung, 791 for bowel, 1521 for prostate and 729 for breast cancer) was included. For two-sample MR, summary-statistic data for SU was obtained from Global Urate Genetic Consortium (GUGC: n = 110,347), while UK-Biobank data was employed for several major cancer outcomes (n = 36,815 for all-cause, 2,245 for

bladder, 2,590 for lung, 4,488 for bowel, 6,474 for prostate and 10,274 for breast cancer). The definitions for cancer endpoints were matched for ICD9 and 10 codes between MDC/MPP and UK-Biobank cohorts. For both MR settings, a set of 26 urate-associated single nucleotide variants was selected to build-up the SU instrument (*SU-instr*) to test for a causal effect of SU on cancer outcomes. Statistical analysis, adjusted for age and sex, was done using multiple conventional MR methodologies and MR package in R (v4.0.2). A $p < 0.05$ was designated as statistically significant.

Results: We found no causal effect of our *SU-instr* on neither all-cause nor site-specific cancer across all MR analyses (all $p > 0.05$). In MDC/MPP, *SU-instr* did not show a causal effect on the risk of all-cause [OR = 1.06, $p = 0.32$], bladder [OR = 0.96, $p = 0.84$], lung [OR = 1.26, $p = 0.17$], bowel [OR = 0.96, $p = 0.81$], prostate [OR = 1.05, $p = 0.62$], and breast [OR = 0.99, $p = 0.98$] cancer. Similar findings were made in the two-sample settings. Detailed results are provided in Table 1.

Conclusion: Our MR study, using a series of causal inference approaches, does not support a causal effect of genetically determined SU for major cancer outcomes. There is no evidence to support changing SU levels by lifestyle or pharmacological intervention to attenuate the risk of major cancer types.

Table 1. Results from a range of MR analyses for causal effect of SU on cancer risk in MDC/MPP (one-sample MR) and GUGC and UK-Biobank (two-sample MR) cohorts

One-sample MR							
Cancer type	IVW			2SLS		GRS	
	OR (95% CI)	p-causal	p-Het	OR (95% CI)	p-causal	OR (95% CI)	p-causal
Bladder	0.96 (0.68; 1.36)	0.84	0.55	0.99 (0.70; 1.42)	0.99	0.94 (0.67; 1.34)	0.76
Lung	1.26 (0.90; 1.77)	0.17	0.89	1.29 (0.91; 1.82)	0.14	1.26 (0.90; 1.77)	0.17
Bowel	0.96 (0.72; 1.28)	0.81	0.44	0.95 (0.72; 1.27)	0.77	0.97 (0.73; 1.28)	0.83
Prostate	1.05 (0.84; 1.31)	0.62	0.84	1.04 (0.83; 1.30)	0.72	1.04 (0.83; 1.30)	0.69
Breast	0.99 (0.74; 1.33)	0.98	0.11	0.98 (0.73; 1.32)	0.92	0.98 (0.73; 1.32)	0.94
All-cause	1.06 (0.93; 1.21)	0.32	0.6	1.07 (0.94; 1.21)	0.28	1.07 (0.94; 1.21)	0.29
Two-sample MR							
Cancer type	IVW			Weighted median		MR-Egger	
	OR (95% CI)	p-causal	p-Het	OR (95% CI)	p-causal	OR (95% CI)	p-causal
Bladder	1.02 (0.88; 2.16)	0.77	0.36	1.03 (0.86; 2.10)	0.7	1.03 (0.83; 2.13)	0.75
Lung	0.86 (0.73; 1.08)	0.07	0.04	0.86 (0.73; 1.09)	0.09	0.84 (0.66; 1.16)	0.15
Bowel	0.82 (0.69; 1.02)	0.03	< 0.0001	0.89 (0.78; 1.06)	0.06	0.92 (0.72; 1.67)	0.52
Prostate	1.00 (0.91; 2.64)	0.97	0.72	0.98 (0.88; 2.17)	0.77	0.94 (0.83; 1.45)	0.37
Breast	0.97 (0.88; 1.95)	0.67	0.0002	1.00 (0.91; 2.70)	0.99	0.95 (0.81; 1.59)	0.46
All-cause	0.96 (0.90; 1.20)	0.18	< 0.0001	0.97 (0.92; 1.23)	0.21	0.93 (0.86; 1.12)	0.11

OR; odds ratio, 95% CI; 95% confidence interval, IVW; Inverse variance weighted method, 2SLS; two-stage least square, GRS; genetic risk score, p-Het; p-value for heterogeneity.

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Public Health, Health Services and Health Economics

POS0296 DOSING OF BDMARDS IN AXSPA AND PSA IN A REAL WORLD SETTING

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Background: The treatment of patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) has been revolutionised by the introduction of biologic DMARDs targeting TNF, IL17, and IL23 inhibitors (i). In Germany, about 30-50% of axSpA and PsA patients receive treatment with bDMARDs. Although many patients benefit from these drugs, in some patients effectiveness of the standard dose may be insufficient and higher doses are used.

Objectives: To describe dosing of TNFi and non-TNFi bDMARDs over a 2 year period in a real world cohort of patients with axSpA and PsA managed by rheumatologists.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including axSpA and PsA patients enrolled at the start of a new conventional treatment (including NSAID) or b/tsDMARD treatment. Description of dosing of TNFi (adalimumab bio-original (bo), adalimumab bio-similar (bs), etanercept bo, etanercept bs, golimumab, certolizumab) in comparison to nonTNFi-bDMARDs (secukinumab, ustekinumab, ixekizumab, guselkumab) in axSpA and PsA. Standard dosing was defined according to the current labels for axSpA and PsA.

Results: 1628 patients (axSpA: n=903, PsA: n=725) were included in this analysis. At inclusion mean age was 44 years in axSpA and 51 years in PsA. 44% of patients with axSpA and 58% of those with PsA were female. The mean disease duration of axSpA was 7.6 years, of PsA 6.4 years.

Standard doses of TNFi were used during a 2 year period in > 90% of patients with axSpA and PsA (Figure 1). In contrast, standard doses of non-TNFi-bDMARDs were only used in 70-80% of patients. The percentage of documented higher doses in patients with axSpA ranged from 20-30% at different time points. In PsA, this percentage increased from 27% at baseline to 44% at 2 years. On the other hand, TNFi were used in lower doses than the label in up to 9% and 7 % of patients with axSpA and PsA, respectively, after 2 years.

Figure 1. Percentages of patients with axSpA or PsA who received less than, equal to, or more than the approved doses of bDMARDs at baseline and at 5 follow-up visits.

Conclusion: While TNFi are used in licensed doses in most patients, non-TNFi-bDMARDs were often used in higher doses, which corresponds to higher doses approved in other indications like psoriasis. The effectiveness of this treatment strategy in axSpA and PsA needs to be analysed further.

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POS0297 HOSPITAL ADMISSIONS FOR PATIENTS WITH RHEUMATOID ARTHRITIS IN WESTERN AUSTRALIA HOSPITALS HAVE DECLINED OVER TIME

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Background: Rheumatoid arthritis (RA) represents a substantial burden on patients and society in terms of morbidity, enduring disability, and medical expenses (1). RA prevalence is poorly described in Australia, and linked health datasets can provide a more meaningful picture for RA epidemiology in the Australian population.

Objectives: To describe the period prevalence rate of RA patients per 1000 hospital separations coded as RA primary or secondary diagnosis in Western Australia (WA) hospitals between 1995 and 2014.