RHEUMATIC IMMUNE- AND NONIMMUNE-RELATED ADVERSE EVENTS IN PHASE 3 CLINICAL TRIALS ASSESSING PD-(L)1 CHECKPOINT INHIBITORS FOR LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Several adverse events (AEs) occurring during immune checkpoint inhibitors (ICIs) therapy are clearly related to their mechanisms of action, and in this case they are indicated as immune-related AEs (irAEs). Every organ may be affected, including the musculoskeletal system; myositis, polymyalgia rheumatica, arthritis or arthralgia has been reported in several retrospective and prospective case series and cohorts, with an incidence between 1.5% and 22%. While arthritis, vasculitis, myositis, and polymyalgia rheumatica are usually defined as “irAE” in RCTs, other rheumatic musculoskeletal conditions such as arthralgia, myalgia, back pain and muscular pain are often reported under the umbrella of “general” AEs.

Objectives: We aimed to analyse rheumatic irAE and non-irAE due to immune-checkpoint inhibitors (ICIs) targeting programmed cell death-1 or its ligand PD-(L)1 in lung cancer patients from the available literature.

Methods: We performed a systematic review and meta-analysis of phase III randomised clinical trials (RCTs) assessing PD-(L)1 -ICIs in lung cancer patients, from inception until January 12, 2021. We extracted data of each trial to estimate odds ratio (OR) for rheumatic ir or non-irAE as classified in RCTs safety data.

Results: Eighteen RCTs met the inclusion criteria (n=12172 subjects). The OR [95%IC] for rheumatic irAE in ICIs versus controls (either placebo or chemotherapy) was 2.20 [0.85,5.72].

Among rheumatic non-irAEs, both overall (any grade, Figure 1A) and severe (grade≥3, Figure 1B) back pain were significantly more frequent in ICIs versus controls (2.01 [1.09,3.73] and 2.90 [1.18,7.08], respectively).

Figure 1. Forest plot showing pooled odds ratio (OR) for back pain (5 phase III trials) (A) and severe back pain (4 phase III trials) (B), respectively.

The overall frequency of arthralgia and severe arthralgia was similar between ICIs and controls (1.13 [0.86, 1.47] and 1.69 [0.68, 4.20], respectively). By sensitivity analysis RCTs assessing ICIs in combination with chemotherapy versus chemotherapy alone showed a significant association with arthralgia (1.55 [1.16:2.10]). Similarly, the frequency of myalgia did not differ between ICIs and controls, but was significantly lower in RCTs assessing ICIs alone versus chemotherapy (OR 0.32 [0.24:0.42]). Muscular pain was not significantly increased with ICI.

Conclusion: Rheumatic irAEs are not increased in RCTs assessing PD-(L)1 inhibitors, not reflecting the real-life incidence, therefore likely underreported or misclassified. Back pain is significantly associated with PD-(L)1-ICIs regardless its severity, suggesting a possible implication of the PD-(L)1 axis in the development of inflammatory back pain in some patients. In addition, PD-(L)1-ICIs added on conventional chemotherapy are associated with a significantly higher frequency of arthralgia than ICI alone. This trend was seen in the other rheumatic AEs, conventional chemotherapy are associated with a significantly higher frequency of arthritis, vasculitis, and myositis, and in this case they are indicated as immune-related AEs (irAEs). Every organ may be affected, including the musculoskeletal system; myositis, polymyalgia rheumatica, arthritis or arthralgia has been reported in several retrospective and prospective case series and cohorts, with an incidence between 1.5% and 22%. While arthritis, vasculitis, myositis, and polymyalgia rheumatica are usually defined as “irAE” in RCTs, other rheumatic musculoskeletal conditions such as arthralgia, myalgia, back pain and muscular pain are often reported under the umbrella of “general” AEs.

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Results: The average age of all patients was 61.4±11.77 years (p=0.007) with predominant female gender in all groups, 81.3% (p=0.139). Anti-ENA1 IgM antibodies were present in 95%, 92%, and 98% (p=0.474), anti-EBV-CA IgM antibodies in 95%, 60%, and 100% (p=0.001), anti-EBV-CA IgG antibodies in 25%, 40%, and 4% (p=0.008), anti-EBV-EA IgM antibodies in 14.1%, 20%, and 4% (p=0.084), and anti-EBV-EA IgG antibodies in 20%, 16%, and 6% (p=0.094) in RAa, RAb, and OA, respectively. There was statistically significant difference in the titers of anti-EBV-CA IgM and IgG antibodies between all three groups (p=0.001 and p=0.007, respectively). According to serology findings active EBV infection was present in 47.5%, 40%, and 12% in RAa, RAb, and OA, respectively (p=0.001). On the other hand, corresponding to PCR results only, active EBV infection was detected in 6.3%, 0%, and 20% in RAa, RAb, and OA, respectively (p=0.010). There was statistically significant difference in way of detecting active EBV infection based on serology or PCR only (p=0.001). Further analysis showed that over 80% of all RA patients (81% in RAa and 96% in RAb), whilst 48% of OA had elevated values of sedimentation (SE) (p=0.001). C-reactive protein (CRP) was raised in 43% in RA (79% in RAa and 100% in RAb) and in 26.5% of OA patients (p=0.001). The majority of all RA patients had elevated rheumatoid factor (RF) and ACPA (84% and 92%) with no difference between RAa and RAb patients (p=0.361 and p=0.203, respectively). Among patients with active EBV infection (based on both serology and PCR results), there was a significantly higher level of antiendothelial cell IgG (p=0.012) and antiendothelial cell IgM (p=0.009) autoantibodies in RAa patients, while the level of SSA autoantibodies (p=0.024) was higher in RAb patients. On the other side, there was no significant difference in the level of any autoantibody or factors of acute inflammation (SE and CRP) in patients with past EBV infection.

Conclusion: This study demonstrated linkage between an active EBV infection and elevation of some autoantibodies in RA pathogenesis. As EBV DNA was not found only in a group of RA patients under immunosuppressive therapy, it is suggested that EBV clearing from blood could be direct consequence of methotrexate use. Collectively, these findings indicate that determining of EBV activity must be based on both serology and molecular methods in order not to oversee EBV reactivation during follow-up of these patients.

References:

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AB1465
BLACK PATIENTS ARE LESS SATISFIED WITH THE PROCESS OF CARE FOLLOWING PRIMARY HIP AND KNEE ARTHROPLASTY: A RETROSPECTIVE STUDY

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Background: Patients’ post-operative satisfaction with their hospital experience is important to patient care, hospital reimbursement, and comparison between hospitals. The Press Ganey (PG) inpatient survey is commonly administered to assess patient satisfaction with the process of care. However, whether patient PG survey scores following primary unilateral hip and knee arthroplasty are associated with a patient’s race and socioeconomic status (SES) is unknown.

Objectives: We aimed to determine whether patient PG survey overall assessment scores differ by race and SES.

Methods: We linked data for patients in large institutional hip and knee arthroplasty registries consisting of surgeries from July 2010–February 2012 to their PG survey responses. Patients undergoing primary unilateral surgery of Black or White race who resided in New York, New Jersey, or Connecticut at the time of surgery were included in the analysis. The primary outcome variable was the PG overall assessment score, calculated as the mean of a patient’s ratings for the three questions in the “Overall Assessment” section of the PG survey and dichotomized as either completely satisfied (score of 100) or not completely satisfied (score <100). Primary payor was used as a proxy for patient SES. Multivariable logistic regression was performed for the hip and knee cohorts separately to determine if patient race and primary payor were associated with not being completely satisfied, adjusting for age, sex, and American Society of Anesthesiology (ASA) score.

Results: There were 2,256 hip patients and 2,113 knee patients with PG overall assessment scores included in the analyses (Table 1). Black patients were more likely to be not completely satisfied compared to White patients in both cohorts [hip (odds ratio (OR)=1.64; 95% confidence interval (CI): 1.03, 2.61; p=0.041); knee (OR=1.83; 95% CI: 1.16, 2.88; p=0.01)]. In the hip cohort, patients between 70-79 years old (OR=1.71; 95% CI: 1.09, 2.67; p=0.02) and older than 80 years (OR=2.00; 95% CI: 1.20, 3.32; p<0.01) were more likely to be not completely satisfied. In the knee cohort, patients 50-59 years old (OR=0.56; 95% CI: 0.33, 0.97; p=0.04) and 60-69 years old (OR=0.57; 95% CI: 0.33, 0.96; p=0.03) were less likely to be not completely satisfied compared to patients <50 years old.

Table 1. Likelihood of not being completely satisfied with the process of care (PG score <100)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hip Cohort (n=2,256)</th>
<th>Knee Cohort (n=2,113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>1.02 (0.69, 1.50)</td>
<td>0.93 (0.56, 0.97)</td>
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<tr>
<td>50-69</td>
<td>1.01 (0.70, 1.54)</td>
<td>0.85 (0.57, 1.30)</td>
</tr>
<tr>
<td>70-79</td>
<td>1.71 (1.09, 2.67)</td>
<td>0.09 (0.03, 0.27)</td>
</tr>
<tr>
<td>&gt;79</td>
<td>&lt;0.01 (0.00, **)</td>
<td>&lt;0.01 (0.00, **)</td>
</tr>
<tr>
<td>Sex Male</td>
<td>1.03 (0.69, 1.50)</td>
<td>0.85 (0.57, 1.30)</td>
</tr>
<tr>
<td>Female</td>
<td>1.04 (0.70, 1.54)</td>
<td>0.87 (0.57, 1.30)</td>
</tr>
<tr>
<td>Race Black</td>
<td>1.64 (1.03, 2.61)</td>
<td>0.83 (1.16, 2.88)</td>
</tr>
<tr>
<td>White had</td>
<td>0.63 (0.41, 0.98)</td>
<td>0.70 (0.44, 1.13)</td>
</tr>
<tr>
<td>Medicare</td>
<td>1.35 (0.86, 2.15)</td>
<td>0.71 (0.44, 1.12)</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>1.24 (0.94, 1.64)</td>
<td>0.87 (0.66, 1.17)</td>
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</table>

AB1466
CORRELATION BETWEEN SALES OF CERTAIN BEVERAGES AND GOUT ATTACKS DURING THE COVID-19 CURFEW IN CAMEROON: A HOSPITAL-BASED STUDY

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Background: An unusual increase in the number of gout cases was observed in Cameroon in 2020. Was there a link with lifestyle changes during confinement, especially the consumption of certain types of beverages (beer, liquor, water, sweetened drinks)?

Objectives: To determine if there was a correlation with the consumption of different beverages (water, beer, liquor, sweetened drinks).

Methods: Cross-sectional study in the rheumatology consultation of the Douala General Hospital, from January 1 to December 31, 2020, including all patients with a diagnosis of gout (ACR/EULAR criteria of 2015). Pearson’s correlation (r) was used to determine the effect of the consumption of the different beverages on the increase in the number of gout cases. A p<0.05 was significant.

Results: We included 1952 patients, including 111 gout cases (107 men; median age: 51 years [36-81]). Compared with the same period in 2018 and 2019, a peak in gout cases was observed between May and November 2020 (Figure 1). In the same period, a positive correlation existed between the number of gout cases and the increase in sales of liquor (r=0.8434, p=0.034) and sweetened beverages (r=0.8436, p=0.034). This correlation was not significant for beer sales (r=0.7980, p=0.057) [Table 1].