1260 COMPARATIVE SAFETY AND EFFECTIVENESS OF IL6R INHIBITORS, TNF INHIBITORS AND METHOTREXATE FOR THE TREATMENT OF IMMUNE CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS

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Background Immune checkpoint inhibitor associated arthritis (ICI-A) affects 4% of ICI-treated cancer patients and often persists, even after ICI cessation. Given its long duration, it is important to identify effective treatments that do not interfere with cancer responses. No studies have compared the safety or effectiveness of disease-modifying antirheumatic drugs (DMARDs) for ICI-A.

Methods We performed a retrospective multicenter observational study. Inclusion criteria were 1) diagnosis of ICI-A and 2) treatment with a DMARD, specifically an interleukin 6 receptor inhibitor (IL6Ri), tumor necrosis factor inhibitor (TNFi), or methotrexate (MTX). Patients with preexisting autoimmune diseases, and patients who received an IL6Ri or TNFi in combination with MTX were excluded. The primary outcome was cancer progression. The secondary outcome was arthritis control, defined as grade 1 arthritis (mild pain, not interfering with function) and prednisone 10 mg daily, within the first 90 days of DMARD treatment. Demographic and clinical features were compared between DMARD groups with Fisher's exact test, Chi-square tests, T-Tests, Wilcoxon rank sum tests and ANOVA as appropriate. Cox proportional hazard models were performed to determine hazard ratios for cancer progression and arthritis control by DMARD treatment, adjusted for confounders (age, sex, cancer type and stage, ICI type, and steroid duration).

Results One hundred sixteen patients from 6 institutions were included, mean(SD) age 62(12) years, 63(54%) male. DMARD treatment was IL6Ri in 43(37%), TNFi in 25(22%), and MTX in 48(41%) (table 1). Kaplan-Meier curves showing time from ICI initiation to cancer progression by DMARD treatment and time to arthritis control are shown in figures 1&2. Compared to patients treated with MTX, patients treated with an IL6Ri had a shorter time to cancer progression (HR 3.67, 95%CI 1.13-11.9, p=0.03) but also a shorter time to arthritis control (HR 3.98, 95%CI 1.21-13.1, p=0.02) in adjusted Cox models. Patients treated with TNFi similarly had a shorter time to cancer progression and arthritis control compared to patients treated with MTX, but these differences were not statistically significant: cancer progression (HR 3.17, 95%CI 0.95-10.5, p=0.06); arthritis control (HR 3.33, 95% CI 0.99-11.1, p=0.051).

Conclusions In this retrospective cohort study, ICI-A treatment with an IL-6i was associated with a shorter time to cancer progression but more rapid arthritis control compared to MTX. Results for TNFi were similar to those for IL6Ri but were not statistically significant likely due to sample size. A prospective randomized controlled trial is needed to confirm these findings and to optimize management of patients with high-grade ICI-A.

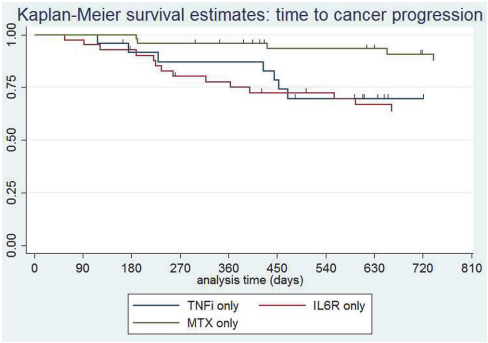
Ethics Approval This study was approved by the Hospital for Special Surgery IRB # 2017-1898 as well as the IRBs of all participating sites.

Abstract 1260 Table 1 Patient characteristicsCharacteristics of cancer patients with checkpoint inhibitor-associated arthritis who were treated with methotrexate, an IL6R inhibitor or a TNF inhibitor

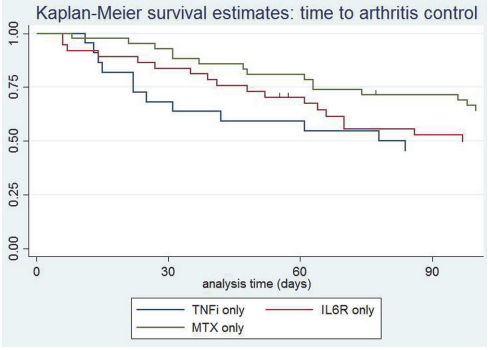
Table 1: Patient characteristics

N (%) or Median (IQR)	Total 116 (100)	TNFi 25 (22)	IL6Ri 43 (37)	MTX 48 (41)	p-value
Age, mean (SD)	62 (12)	57 (15)	62 (13)	63 (9)	0.40
Sex (male)	63 (54)	16 (64)	29 (67)	19 (40)	**0.023**
Race (white)	106 (91)	23 (92)	40 (93)	42 (88)	0.56
Smoker (ever)	60 (62)	13 (52)	22 (51)	25 (52)	0.84
Cancer type					**<0.001**
Melanoma	42 (36)	12 (48)	19 (44)	10 (21)	
RCC	18 (15)	3 (12)	11 (26)	4 (8)	
NSCLC	12 (10)	1 (4)	0 (0)	11 (23)	
Bladder	7 (6.0)	0 (0)	6 (14)	1 (2)	
Other	37 (32)	9 (36)	7 (16)	22 (46)	
Cancer Stage					0.31
II	3 (3)	2 (8)	0 (0)	1 (2)	
III	18 (15)	4 (16)	6 (14)	7 (14)	
IV	95 (82)	19 (76)	37 (86)	40 (83)	
Brain metastases present	14 (12)	1 (4)	6 (14)	7 (15)	0.37
Immunotherapy type					0.17
CTLA4 monotherapy	1 (1)	0 (0)	1 (2)	0 (0)	
PD(L)1 monotherapy	82 (71)	17 (68)	31 (72)	34 (71)	
Combination	30 (26)	6 (24)	11 (26)	13 (27)	
Concomitant chemotherapy	14 (12)	6 (24)	2 (5)	6 (13)	0.063
Concomitant targeted therapy	15 (13)	2 (8)	9 (21)	5 (10)	0.12
Total ICI duration, days	328 (175, 672)	309 (172, 596)	336 (196, 720)	351.5 (175, 594)	0.62
Maximum arthritis grade					0.81
1	2 (2)	0 (0)	1 (2)	1 (2)	
2	57 (49)	12 (48)	20 (47)	25 (52)	
3	52 (45)	13 (52)	21 (49)	18 (38)	
ICI held for arthritis	23 (20)	6 (24)	9 (21)	8 (17)	0.79
ICI discontinued for arthritis	45 (39)	10 (40)	15 (35)	20 (42)	0.75
Maximum steroid dose, mg*	40 (20, 60)	45 (40, 75)	40 (20, 60)	20 (15, 50)	**0.004**
Steroid duration, days	293 (129, 483)	257 (112, 464)	293 (122, 483)	343 (139, 606)	0.66
Concomitant irAE	45 (39)	15 (60)	10 (23)	20 (42)	**0.010**

ICI = Immune checkpoint inhibitor; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; TNFi = TNF inhibitor; IL6Ri = IL6R inhibitor; MTX = methotrexate; ICI = immune checkpoint inhibitor; irAE = immune related adverse event.
*Prednisone dose equivalent



Abstract 1260 Figure 1 Time to cancer progressionKaplan Meier curve showing time to cancer progression in patients treated with methotrexate, IL6R or TNF inhibitors for checkpoint inhibitor-associated arthritis



Abstract 1260 Figure 2 Time to arthritis controlKaplan Meier curve showing time to checkpoint inhibitor-associated arthritis control during the first 90 days of treatment with methotrexate, an IL6R inhibitor or a TNF inhibitor

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