IMMUNE CHECKPOINT BLOCKADE (ICB) IN BRAIN METASTASES (BM) FROM ADVANCED SMALL CELL UROTHELIAL CANCER (aSCUC)

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Background The risk of BMs in patients with aSCUC, having bulky tumors or non-cerebral metastasis at presentation, is high. We aimed to investigate the impact of ICB on the clinical outcomes of patients with aSCUC and BMs.

Methods Patients with aSCUC treated at MD Anderson Cancer Center between April 1992 and July 2019 were included if they had brain imaging and developed BMs during their disease course. Median overall survival (mOS) was calculated from diagnosis of BMs until death and if alive was censored at last contact. Hazard ratios (HR) and 95% confidence intervals (95% CI) were calculated using logrank test.

Results Among 216 patients with aSCUC, 111 underwent computed tomography or magnetic resonance imaging of the brain, and 34 (31%) were diagnosed with BMs. Baseline characteristics are included (table 1). At initial diagnosis of SCUC, clinical stage was cT1/x, cT2, ≥cT3/4 or N+ (15%, 44%, 41%, respectively). Twenty-three (67.6%) underwent prior cystectomy, 16 (47%) had received neoadjuvant chemotherapy (NACT). Pathologic response at cystectomy after NACT was pT0/Tis, pT1, pT2, ≥pT3b/4 or N+ (31%, 6%, 13%, 50%, respectively). Those who did not undergo cystectomy (11, 32%) were either due to progression, declining surgery, or had de novo metastatic disease (27%, 18%, 55%, respectively). Regarding localized BM management, 9 (26%) patients received whole brain radiation therapy, 7 (21%) received stereotactic radiosurgery (SRS) and 7 (21%) received both. Median follow-up from BM diagnosis was 31.7 months. Five patients elected to pursue comfort care only, with mOS 0.7 months. Twenty-three patients received systemic therapy, including 11 (48%) who received ICB during any line of therapy. Majority of patients received ICB as single agent anti-PD(L)1; one patient received a doublet of anti-PD1+anti-CTLA4. Patients who were treated with ICB had numerically longer mOS as compared to those who solely received chemotherapy (10.7 months vs. 9.0 months, HR=0.47, 95%CI=0.18–1.25, P=0.15), (figure 1). mOS decreased in patients with 1 vs 2 vs 3 vs ≥5 BMs (18.8, 8.7, 7.5 and 4.7 months, respectively, P=0.02), (figure 2). Furthermore, mOS improved with combination of ICB +SRS vs chemotherapy+SRS vs ICB without SRS vs chemotherapy without SRS (unreached, 20.9, 7.5, 8.4, respectively, P=0.03) (figure 3).

Abstract 241 Table 1 Baseline characteristics of patients

Characteristics	All patients (n=34)	Received systemic therapy not IO (n=12)	Received IO* (n=11)	P value
Age at brain mets diagnosis				
Median	65	62	63	0.804
Range	26-81	26-69	35-80	
Interquartile range	57-70	55-69	56-67	
Sex - no. (%)				
Male	26 (76)	9 (75)	10 (91)	0.590
Female	8 (24)	3 (25)	1 (9)	
Primary site - no. (%)				
Bladder	33 (97)	11 (92)	11 (100)	1
Urethra	1 (3)	1 (8)	0 (0)	
Histology - no. (%)				
Pure or Predominant small cell	27 (79)	10 (83)	8 (73)	0.640
Focal small cell	7 (21)	2 (17)	3 (27)	
Localized disease management - no. (%)				
Underwent cystectomy	23 (68)	6 (50)	10 (91)	
Received neoadjuvant chemo	19 (56)	3 (25)	10 (91)	
pCR	5 (15)	0 (0)	3 (27)	0.338
≥pT1 or N+	18 (53)	6 (50)	6 (55)	
Progressed prior to surgery	2 (6)	1 (7)	1 (9)	
Number of brain mets**				
1	8	1	4	0.383
2-4	13	7	4	
≥5	9	2	3	
Brain metastases local therapy				
Craniotomy + RT	6	2	2	
Craniotomy+SRS	3	0	1	1
Craniotomy+WBRT+SRS	2	1	1	
Craniotomy+WBRT	1	1	0	
RT alone	17	5	8	
WBRT***	8	2	3	1
SRS	4	1	3	
WBRT+SRS	5	2	2	
Sites of concomitant metastases				
Liver	10	5	2	0.710
Bone	8	5	2	
Lung	12	4	3	
Distal nodes	14	5	6	

Survival proportions: Survival of Brain mets systemic therapy

Abstract 241 Figure 1 Survival based on systemic therapy approach among all SCUC patients with brain metastases (n=34)

Survival proportions: Survival of Brain mets #mets

Abstract 241 Figure 2 Survival based on number of brain metastases among all 34 patients

Survival proportions: Survival of Brain mets systemic+local therapy

Abstract 241 Figure 3 Survival based on systemic + local therapy approach among SCUC patients with brain metastases with brain metastases who received both (n=23)

Conclusions In this first analysis to describe outcomes of patients with aSCUC and BMs with the inclusion of ICB treatment and despite the small sample size, we see a trend toward increased survival with fewer BMs, especially with combined ICB and SRS. Although challenging due to its rarity, future prospective trials evaluating the synergy between ICB and SRS in SCUC should be considered.

Ethics Approval This retrospective study received approval from the MD Anderson Cancer Center institutional review board

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