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A subgroup analysis from the IMvigor130 study in patients with upper tract vs. lower tract locally advanced or metastatic urothelial carcinoma treated with atezolizumab plus platinum-based chemotherapy

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Introduction & Objectives: IMvigor130 demonstrated statistically significant improvement in progression-free survival (PFS) and encouraging interim overall survival (OS) results in pts treated with atezo (anti–PD-L1) + plt/gemcitabine (gem; Arm A) vs placebo + plt/gem (Arm C) as 1L tx for mUC (Galsky 2020). To determine whether differences in primary tumor site biology influence treatment (tx) outcomes, we performed an exploratory subgroup analysis of efficacy and safety in pts with UT or LT mUC from IMvigor130.

Materials & Methods: Pts were randomized to Arms A, B (atezo monotherapy) or C; data from Arms A and C are reported here. Chemotherapy was gem + investigator's (inv) choice of plt (cisplatin or carboplatin). Inv-assessed RECIST 1.1 PFS and OS (co-primary endpoints), and objective response rate (ORR) and safety (secondary endpoints) for pts in Arms A and C with UT (renal pelvis, ureter) or LT (bladder, urethra) disease were descriptively evaluated.

Results: Baseline characteristics between Arm A and C were generally comparable in UT (n=223) and LT (n=620) subgroups; slight imbalances were seen within the UT subgroup, including more pts with PD-L1 IC2/3 status (27% vs 15%) and fewer pts with Bajorin risk score of 2 and/or liver metastases (21% vs 27%) in Arm A vs C, respectively. Median follow-up was 11.8 mo. Efficacy data are included in the Table; PFS and OS results were consistent in multivariable analyses adjusting for key prognostic characteristics. In Arm A, Grade 3-4 tx-related adverse events (AEs) were seen in 86% (107/124) of safety-evaluable pts with UTUC and 79% (255/323) of pts with LTUC; the respective frequencies in Arm C were 78% (75/96) and 82% (238/292). All-cause AEs leading to discontinuation of any tx occurred at comparable frequencies across subgroups (33-35%).

	UT		LT	
	Arm A	Arm C	Arm A	Arm C

n	123	100	322	298
PFS				
Events, n (%)	89 (72)	84 (84)	240 (75)	240 (81)
Median (95% CI), mo	8.2 (6.5-10.2)	6.2 (6.1-6.4)	8.1 (6.3-8.3)	6.5 (6.3-8.1)
Stratified HR (95% CI)	0.69 (0.51-0.94)		0.85 (0.70-1.02)	
Interim OS[a]				
Events, n (%)	60 (49)	57 (57)	171 (53)	169 (57)
Median (95% CI), mo	16.9 (12.5-25.5)	13.5 (10.1-17.6)	15.8 (12.9-18.9)	13.4 (11.7-15.3)
Stratified HR (95% CI)	0.78 (0.54-1.12)		0.87 (0.70-1.08)	
Objective response	n=123	n=99	n=318	n=296
ORR (95% CI), %	50 (40-59)	40 (31-51)	47 (41-53)	45 (39-51)
CR rate, %	13	8	12	6
Duration of response	n=61	n=40	n=149	n=133
Events, n (%)	35 (57)	26 (65)	96 (64)	95 (71)
Median (95% CI), mo	9.3 (6.4-18.7)	8.3 (6.2-15.2)	8.3 (7.0-10.4)	6.9 (6.2-8.5)

[a] For descriptive purposes only; not formally tested per pre-specified analysis hierarchy

Conclusions: This IMvigor130 subgroup analysis demonstrated clinical activity of atezo + plt/gem in pts with UT or LT mUC. Efficacy and safety outcomes were comparable between both subgroups. Further OS analyses will be conducted to confirm benefit.