SUPPLEMENTARY DATA

Scientific Advancements in Drug Development and Trials for Urothelial Carcinoma: Insights From the 2023 ASCO-GU Cancers Symposium

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Supplementary Table 1. Specifying novel agents and trials for UC.

Author	Country	Registration number	Patients number	Medicine	Patient feature	Main end-points	Main results
Matthew I. Milowsky et al.	International	LBA439 (NCT03288545)	152	EV vs EV+ pembrolizumab	CI patients with la/mUC.	QoL and symptoms	This study showed that EV+ pembrolizumab in cisplatin-ineligible patients with la/mUC was associated with preservation or improvement of QoL, functioning, and symptoms.
Matt D. Galsky et al.	International	LBA440 (NCT02807636)	851	Atezolizumab + plt/gem vs placebo + plt/gem	Patients with la/mUC	OS	There was no difference in OS between the two groups.
Aristotelis Bamias et al.	International	LBA441 (NCT02807636)	719	Atezolizumab monotherapy vs placebo + plt/gem	Patients with la/mUC	OS	Only in the PD-L1–high mUC subgroup, patients accepted Atezolizumab monotherapy had better OS than these received placebo + plt/gem.
Andrea Necchi et al.	International	LBA442 (NCT02625961)	132	Pembrolizumab (q3W) for <=35 cycles	Patients with BCG-unresponsive HR non-muscle-invasive bladder cancer (NMIBC) with papillary tumors only (high grade Ta or any-grade T1) at baseline and ECOG PS 0-2.	DFS in 12 months	Results suggest patients with non-CIS papillary HR NMIBC unresponsive to BCG who declined or were ineligible to undergo RC may also benefit from pembrolizumab monotherapy.
Matt D. Galsky et al.	International	LBA443 (NCT02632409)	353	Nivolumab (240 mg q2W) versus placebo	Patients with HR MIUC after radical resection.	DFS	Nivolumab continued to show DFS benefits versus placebo.
Matt D. Galsky et al.	International	LBA447 (NCT03558087)	76	Four cycles of gemcitabine, cisplatin, plus nivolumab	Patients with cisplatin-eligible with cT2-T4aN0M0 urothelial bladder cancer.	cCR	Transurethral resection of bladder tumor followed by gemcitabine, cisplatin, plus nivolumab achieves stringently defined cCR in a substantial subset of patients with MIBC. >=2-year bladder-intact survival is achieved in the majority of patients with a cCR
Jason Brown et al.	International	LBA448 (NCT02365766)	82	CE group (gemcitabine +cisplatin +pembrolizumab) vs CI group (gemcitabine+ pembrolizumab)	Patients were surgical candidates with clinical stage T2-4aN0M0 MIUC.	DFS, OS	Neoadjuvant chemoimmunotherapy demonstrated significant down staging in CE and CI MIUC pts prior to definitive surgery, meeting the primary endpoint. Survival correlated with pathologic response.
Yuki Endo et al.	Japan	Post session 452	70	PCT +pembrolizumab	Patients with mUC received PCT followed by pembrolizumab.	OS	This study reported that early introduction of pembrolizumab may be associated with longer OS in the patients with mUC who are resistant to chemotherapy.
Lorenzo Antonuzzo et al.	Italian	LBA469 (NCT02603432)	464	Avelumab 800 mg every two weeks	Patients with locally advanced or metastatic urothelial carcinoma	OS	This study supports for avelumab as a standard of care in eligible pts

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					without progression after PCT.		with locally advanced or metastatic urothelial carcinoma.
Philippe Barthelemy et al.	France	LBA471 (NCT04822350)	591	Avelumab	Patients with locally advanced urothelial carcinoma without progression after PCT.	OS	The study confirms the clinical activity and acceptable safety profile of avelumab in a heterogeneous population
Soufyan Annakib et al.	France	LBA490 (NCT03584659)	39	Pembrolizumab	Patients with la/mUC	HRQoL	HRQoL for la/mUC patients after first pembrolizumab infusion showed contradictory results with previous reports with a trend for HRQoL degradation after one treatment cycle.
AmarnathChallapalli et al.	United Kingdom	LBA493 (NCT01616875)	26	Cabazitaxel +cisplatin	Patients with MIBC were included if fit to receive NAC and to undergo RC.	PFS, OS	Neoadjuvant cabazitaxel with cisplatin chemotherapy is an effective regimen with 65.4% patients alive and progression-free at 5 years.
Karim Chamie et al.	USA	LBA495 (NCT03022825)	86	Nogapendekin alfa inbakicept+BCG	Patients with BCG-unresponsive CIS with or without Ta/T1 disease.	QoL	QOL measurement supports good tolerability of the intravesical Nogapendekin alfa inbakicept plus BCG in BCG-unresponsive, high-grade NMIBC patients with CIS.
Capucine Baldini et al.	International	LBA498 (NCT045613622)	49	BT8009	Patients with advanced malignancies.	Safety	BT8009 was well tolerated and demonstrated promising preliminary antitumor activity
Peter H. O'Donnell et al.	International	LBA499 (NCT03288545)	149	EV vs EV+ pembrolizumab	CI patients with la/mUC.	ORR	EV+ pembrolizumab showed promising ORR in CI patients with la/mUC.
Andrea Necchi et al.	International	LBA501 (NCT04045613)	282	Derazantinib 300 mg qd	Patients with advanced mUC.	ORR	Derazantinib showed signals of clinical activity in some patients with mUC and FGFR1-3 genetic aberrations but the observed ORR and PFS.
Guillermo de Velasco et al.	Spain	LBA502 (NCT04602078)	82	Atezolizumab	Patients with la/mUC considered unfit for full dose of PCT.	ORR, PFS, OS	Atezolizumab with split doses of PCT was safely administered in a population of frail patients with mUC who were unfit for PCT showing promising preliminary survival outcomes in terms of response.
James W.F.Catto et al.	International	LBA503 (NCT04172675)	10	Erdafitinib 6 mg once daily	Patients with BCG unresponsive HR NMIBC with FGFR3/2alt and CIS.	Safety	Erdafitinib is efficacy in patients with HR-NMIBC with FGFRalt.
Siamak Daneshmand et al.	International	LBA504 (NCT04172675)	10	Erdafitinib 6 mg once daily	Patients with BCG unresponsive HR NMIBC with intermediate-risk and FGFRalt, no CIS.	CR	This study demonstrates efficacy of erdafitinib in adult patients with intermediate-risk NMIBC with FGFRalt.

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F.Johannes P. van Valenberg et al.	Netherlands	LBA505 (NCT02720367)	12	TAR-200	Patients with a papillary recurrence after prior histologically proven, intermediate risk NMIBC.	Safety	TAR-200 appears to be safe and well tolerated in patients with intermediate-risk NMIBC.
Maha H. A. Hussain et al.	International	LBA506 (NCT03854474)	24	Tazemetostat 800 mg bid+ pembrolizumab 200 mg every 3 weeks	Patients with cisplatin-refractory or cisplatin/chemo-ineligible advanced urothelial cancer.	Making sure the recommended phase two dose	The recommended phase two dose for tazemetostat is 800 mg + 200 mg Pembrolizumab q 3 weeks.
Srikala S. Sridhar et al.	International	LBA508 (NCT02603432)	700	Avelumab maintenance + best supportive care vs best supportive care alone	Patients with unresectable la/mUC that did not progress after accepting PCT.	OS	Long-term follow-up confirms that avelumab maintenance provides similar OS and PFS benefits in patients with advanced UC who are progression free following standard-of-care cisplatin- or carboplatin-based chemotherapy, with an acceptable safety profile.
Fangning Wan et al.	China	LBA509 (ChiCTR2000032730)	15	Sintilimab 200 mg	Patients were cT2-T4 N0 MIBC and were considered eligible for RC.	Pathologic complete response	Neoadjuvant sintilimab was feasible and provided meaningful pathologic responses in patients with MIBC.
Zhiyong Li et al.	China	LBA510 (ChiCTR2000035275)	14	Tislelizumab 200 mg	Patients with HR NMIBC BCG-unresponsive papillary tumors.	DFS	Our preliminary results supported the use of tislelizumab combined with radiotherapy as a promising bladder-preserving therapy for patients with BCG-unresponsive HR NMIBC who were ineligible for or refused RC.
Gary D. Steinberg et al.	Canada	LBA512 (NCT04752722)	19	EG-70	Patients with BCG-unresponsive CIS NMIBC.	SD or CR	These results demonstrate the safety, tolerability and durable therapeutic potential of intravesical EG-70 in patients with BCG-unresponsive CIS.
David H Aggen et al.	International	LBA517 (NCT04044859)	43	ADP-A2M4CD8	Patients with advanced UC.	Safety	ADP-A2M4CD8 continues to show an acceptable benefit to UC.
Rohit K. Jain et al.	Orlando	LBA521 (NCT04863885)	9	Nivolumab+ Ipilimumab+ SG	Patients with CI mUC	Safety	The RP2D of SG was identified as 8mg/kg in combination with ipilimumab 3 mg/kg+ Nivolumab 1 mg/kg as first-line therapy for CI mUC.
Petros Grivas et al.	International	LBA518 (NCT03547973)	/	SG+pembrolizumab	Patients with mUC that progressed after PCT	ORR	SG plus pembrolizumab demonstrated a high ORR with a manageable safety profile in mUC in patients who progressed after PCT.

la/mUC: locally advanced or metastatic urothelial cancer; EV: Enfortumab vedotin; QoL: quality of life; OS: Overall survival; plt/gem: platinum/gemcitabine; DFS: Disease-free survival; RC: radical cystectomy; cCR: clinical complete response; CE: Cisplatin eligible; CI: cisplatin ineligible; MIUC: muscle-invasive urothelial carcinoma; PCT：platinum-based chemotherapy; HRQoL: Health-related quality of life; PFS: Progression-free survival; MIBC: muscle-invasive bladder cancer; NAC: neoadjuvant chemotherapy; ORR: objective response rate.