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Alliance A031501: AMBASSADOR study of adjuvant pembrolizumab (Pembro) in muscle-invasive urothelial carcinoma (MIUC) vs observation (Obs): Extended follow-up disease-free survival (DFS) results and metastatic (met) disease recurrence distribution

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Background

The AMBASSADOR study (NCT03244384) demonstrated a significant improvement in DFS for adjuvant Pembro vs Obs in patients (pts) with high-risk MIUC after radical surgery. We report extended DFS (19 additional median (m) months (mo)) follow-up data, sites of met recurrence, and lymph node (LN) status outcomes.

Methods

This is an open label, randomized, phase 3 trial that enrolled pts with MIUC of the bladder, upper tract (UT), or urethra. Pts were randomized 1:1 to receive Pembro 200 mg every 3 weeks for 1 year or Obs. The dual primary endpoints were DFS and OS. Final OS analysis requires additional events.

Results

702 pts were randomized. mDFS follow-up was 41.3 mo. DFS benefit was seen in most subgroups analyzed including pathologic stage, +margins, NAC (yes/no), PD-L1 status (+/-), age, and ECOG PS. DFS benefit for UT ureter tumors was observed but not for renal pelvis tumors. DFS benefit with Pembro was seen in all pts with NO and N+ stage and UT tumors with N+ stage. Common sites of met included LN, pelvic mass, lung, bone, liver (Table, \*non-mutually exclusive; NE-Not Estimable).Table: 1964MO

	Pembro mDFS (95% CI), mo N events/ N total		Obs mDFS (95% CI), mo N events/ N total		HR (95% CI)
All pts	29.6 (21.8-41.9)	182/354	14.5 (11-20.2)	194/348	.72 (.59-.89)
UT Ureter	54.0 (43.8-NE)	10/28	17.7 (8.2-NE)	16/33	.58 (.26-1.32)
UT Renal Pelvis	26.6 (9.7-NE)	26/53	60.5 (60.5-NE)	11/40	1.99 (.98-4.02)
LN Status					
All pts					
NO	NE (NE-NE)	39/132	35.2 (18.1-NE)	67/148	.52 (.35-.77)
N+	14.5 (11.3-20)	121/186	8.8 (6.9-11.8)	119/174	.75 (.59-. 97)
UT pts					
NO	NE (26.6-NE)	6/22	60.5 (30.2-NE)	13/36	.7 (.27-1.85)
N+	54.0 (8.2-NE)	12/27	17.7 (12.1-NE)	7/14	.95 (0.37-2.41)
DFS events		N=147		N=165	
Met Site %					
Chest LN		17		8.5	
Abdominal LN		23.1		32.7	

	Pembro mDFS (95% CI), mo N events/ N total	Obs mDFS (95% CI), mo N events/ N total	HR (95% CI)
Pelvic LN	21.8		24.2
Pelvic Mass	11.6		15.2
Lung	10.9		13.9
Bone	19.7		18.8
Liver	10.2		14.5

Conclusions

With extended DFS follow-up, Pembro continues to show DFS benefit vs Obs. All pts, including UT pts (trend) had DFS benefit with Pembro regardless of LN status (NO or N+). Met recurrences were more common in pts on Obs vs Pembro and the sites of distribution were similar.

Clinical trial identification

NCT03244384.

Legal entity responsible for the study

Alliance.

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Disclosure

G.P. Sonpavde: Financial Interests, Personal, Advisory Board: EMD Serono, Bristol Myers Squibb, Genentech, Merck, Seattle Genetics, Exelixis, Janssen, Bicycle Therapeutics, Gilead, Scholar Rock, G1 Therapeutics, Loxo Oncology, Lucence, Tempus, Syapse, Astellas, Pfizer, Atkis, Kura, Syncorp, Vial, PrecisCa; Financial Interests, Personal, Advisory Board, Editor of Bladder cancer virtual center of excellence for Practice Update: Elsevier; Financial Interests, Personal, Other, Member of data safety monitoring board: Mereo; Financial Interests, Personal, Other, Author of chapter: Uptodate; Financial Interests, Personal, Invited Speaker: Research to practice, Seattle Genetics, Gilead, Exelixis, Janssen, Astellas, Merck, Aveo, Pfizer, Natera, Bayer, PeerView, Ideology Health, Grand Rounds in Urology, Onviv; Financial Interests, Personal, Advisory Board, to develop a trial in bladder cancer: Servier Pharmaceuticals; Financial Interests, Personal, Advisory Board, Investigational drug development for HER2+ cancers: Daiichi Sankyo/AstraZeneca; Financial Interests, Institutional, Research Grant: Gilead, EMD Serono, Jazz Pharma; Financial Interests, Institutional, Local PI: BMS; Non-Financial Interests, Principal Investigator, Steering committee of trial: Bristol Myers Squibb; Non-Financial Interests, Other, steering committee of trial: Merck; Other, Spouse employment: Myriad Genetics; Other, Travel: BMS, Astellas. S. Berg: Financial Interests, Personal, Advisory Board: Pfizer, Exelixis. W. Kim: Financial Interests, Personal, Advisory Board: Focal Medical, OncoRev, GeneCentric; Financial Interests, Personal, Other, Founder (spouse): Focal Medical; Financial Interests, Personal, Stocks/Shares: AbbVie, Amgen, Apellis, Arvin's, BeiGene, Bristol Myers Squibb, Eli Lilly, Moderna, Novo Nordisk, Revolution Medicine, Tango, Viking Therapeutics; Financial Interests, Personal, Ownership Interest: Focal Medical; Financial Interests, Personal and Institutional, Research Grant: Merck; Other, Have held Natera stock within last 2 years. Do not currently own: Natera. M.Y. Teo: Financial Interests, Personal, Research Funding: Astellas; Financial Interests, Personal, Research Grant: BMS. R.F. Sweis: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, BMS, EMD serono, Exelixis, Eisai, Janssen, Mirati, Pfizer, Seattle Genetics; Financial Interests, Personal, Invited Speaker: Aveo; Financial Interests, Personal, Stocks/Shares: AbbVie; Financial Interests, Institutional, Local PI: AbbVie, Aduro, Ascendis, Astellas, BMS, Bayer, CytomX, Eisai, Genentech/Roche, Immunocore, Merck, Mirati, Moderna, Novartis, QED, Pyxis Oncology, ALX Oncology; Financial Interests, Institutional, Research Grant: Epivax; Financial Interests, Institutional, Steering Committee Member: Gilead. D. Geynisman: Financial Interests, Personal, Advisory Board: Pfizer, Merck, Exelixis, Astellas, Genentech, Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Genentech, Merck, Harpoon, Seattle Genetics, Arvin's. P. Grivas: Financial Interests, Personal, Advisory Board: AstraZeneca, MSD, Bristol Myers Squibb, Asieris Pharmaceuticals, Merck KGaA, Seattle Genetics, Aadi Bioscience, Pfizer, Janssen, Boston Gene, Genentech/Roche, Gilead Sciences, CG Oncology, ImmunityBio, Lucence Health, G1 Therapeutics, Fresenius Kabi, PureTech, Strata Oncology, Astellas Pharma, AbbVie; Financial Interests, Institutional, Local PI: Pfizer, Gilead Sciences, Bristol Myers Squibb, MSD, QED Therapeutics, GSK, Mirati Therapeutics, G1 Therapeutics, Merck KGaA, Acrivon Therapeutics, ALX Oncology, Genentech. Z. Reichert: Financial Interests, Personal, Advisory Board: Huff Powell Bailey, Astrazeneca; Financial Interests, Institutional, Coordinating PI: AstraZeneca, Cellgene. J.W. Kim: Financial Interests, Institutional, Local PI: Regeneron, Janux, Cosmo, Genentech/Roche, Antengene Biologics Limited, Hummingbird Bioscience, Acrivon Therapeutics, IGM Biosciences, Inc; Financial Interests, Institutional, Research Grant: Dendreon; Financial Interests, Personal, Local PI: AstraZeneca; Non-Financial Interests, Principal Investigator: AstraZeneca, Takeda. M.A. Bilen: Financial Interests, Personal, Advisory Board: Exelixis, Bayer, BMS, Eisai, Pfizer, AstraZeneca, Janssen, Calithera Biosciences, Nektar, EMD Serono, Seagen, Sanofi; Financial Interests, Institutional, Local PI: Merck, Xencor, Bayer, Bristol Myers Squibb, Genentech/Roche, Seagen, Incyte, Nektar, AstraZeneca, Tricon Pharmaceuticals, Genome & Company, AAA, Peloton Therapeutics, Pfizer. B.A. McGregor: Financial Interests, Personal, Advisory Board: Exelixis, BMS, Dendreon, Seagen, Astellas, Eisai, Pfizer, Gilead, Arcus, Loxo/Lily; Financial Interests, Personal, Invited Speaker: EMD Serono, Seagen; Financial Interests, Institutional, Trial Chair: Pfizer, Exelixis, Exelixis, BMS, Gilead;

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