
2019 Genitourinary Cancers Symposium: Presentation Information

Oral Abstract Session C

Saturday, February 16, 2019: 2:00-2:10 p.m. PT
The Moscone West Building, Level 3, Ballroom

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Abstract 543: Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for locally advanced or metastatic renal cell carcinoma (mRCC): phase III KEYNOTE-426 study.

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Background: A phase 1b study of pembro (anti-PD-1) plus axi (VEGFR-TKI) showed promising antitumor activity and manageable safety in patients (pts) with previously untreated mRCC. The global, open-label, phase 3 KEYNOTE-426 study assessed the efficacy and safety of pembro + axi vs sunitinib as first-line therapy for mRCC (NCT02853331).

Methods: Eligible pts with clear-cell mRCC, no previous systemic therapy for mRCC, and KPS \geq 70% were randomized 1:1 to pembro 200 mg IV Q3W for a maximum of 35 cycles plus axi 5 mg orally BID or sunitinib 50 mg orally QD (4-wk on/2-wk off schedule). Treatment was given until PD, intolerable toxicity, or pt/investigator decision.

Randomization was stratified by IMDC risk group and geographic region. Primary endpoints were OS and PFS (RECIST v1.1 by blinded, independent central review [BICR]). ORR was the key secondary endpoint. At the protocol-specified first interim analysis, the superiority thresholds were $P = 0.0001$ for OS, 0.0013 for PFS, and 0.025 for ORR (if OS and PFS were significant).

Results: 861 pts were randomized: 432 to pembro + axi, 429 to sunitinib. After a 12.8-mo median follow-up, 59.0% of pts in the pembro + axi arm and 43.1% in the sunitinib arm remained on treatment. Pembro + axi significantly improved OS (HR 0.53 [95% CI 0.38-0.74]; $P < 0.0001$; 12-mo rate 89.9% vs 78.3%), PFS (HR 0.69 [95% CI 0.57-0.84]; $P = 0.0001$; median 15.1 vs 11.1 mo), and ORR (59.3% vs 35.7%; $P < 0.0001$). Duration of response was prolonged with pembro + axi (median not reached vs 15.2 mo). The pembro + axi benefit was observed in all subgroups tested, including all IMDC risk and PD-L1 expression subgroups. Treatment-related AEs were grade 3-5 in 62.9% of pts in the pembro + axi arm vs 58.1% in the sunitinib arm and led to regimen discontinuation in 6.3% vs 10.1%. **Conclusions:** Pembrolizumab + axitinib provided superior OS, PFS, and ORR compared with sunitinib and had manageable safety in pts with previously untreated, advanced or metastatic clear-cell RCC. These data suggest that pembrolizumab + axitinib should be a new standard of care for this population.

Disclosures: Thomas Powles, MD, PhD, FCRP, Consulting or Advisory Role with Genentech/Roche, Bristol-Myers Squibb, Merck, Novartis, AstraZeneca, Other Relationship with Ipsen, Bristol-Myers Squibb, Honoraria from Roche/Genentech, Bristol-Myers Squibb, MERCK, Research Funding from AstraZeneca/MedImmune, Roche/Genentech; Brian I. Rini, MD, FACP, Consulting or Advisory Role with Pfizer, Merck, Roche/Genentech, Novartis, synthorx, Bristol-Myers Squibb, Travel, Accommodations, Expenses from Pfizer, Bristol-Myers Squibb, Merck, Merck, Research Funding (Institutional) from Pfizer, Roche/Genentech, Bristol-Myers Squibb, Merck, AstraZeneca/MedImmune, Peloton Therapeutics; Elizabeth R. Plimack, MD, MS, Consulting or Advisory Role with AstraZeneca/MedImmune, Bristol-Myers Squibb, Clovis Oncology, Exelixis, Genentech/Roche, Horizon Pharma, Incyte, Inovio Pharmaceuticals, Janssen, Merck, Novartis, Patents, Royalties, Other Intellectual Property (Institutional) with U.S. Patent No.: 14/588,503, US Patent No: 15/226,474, Research Funding (Institutional) from Bristol-Myers Squibb, AstraZeneca, Pfizer, Merck Sharp & Dohme, Peloton Therapeutics, Astellas Pharma, Genentech/Roche; Viktor Stus, Research Funding from MSD and MSD (Institutional), Travel, Accommodations, Expenses from MSD; Robert E. Hawkins, MD, PhD, Employment with Cellular Therapeutics, Immetacyte, Leadership with Cellular Therapeutics, Immetacyte, Patents, Royalties, Other Intellectual Property with Medical Research Council – Phage Antibody Patents, Stock and Other Ownership Interests with Cellular Therapeutics, Immetacyte, Honoraria from Pfizer, GlaxoSmithKline, Bristol-Myers Squibb, Ipsen, Novartis, EUSA Pharma; Dmitry Nosov, Honoraria from Bristol-Myers Squibb, MSD, Pfizer, Consulting or Advisory Role with Roche; Frederic Pouliot, Honoraria from Amgen, Pfizer, Astellas Pharma, Janssen, Bayer, Genzyme, Sanofi, Abbvie, Consulting or Advisory Role with Amgen, Pfizer, Sanofi, Astellas Pharma, Progenics, Bayer, Janssen, Genzyme, Speakers' Bureau for Astellas Pharma, Bayer, Progenics, Amgen, Sanofi, Research Funding from Sanofi, Astellas Pharma, AstraZeneca, Janssen, Travel, Accommodations, Expenses from Bayer, Sanofi; Boris Y. Alekseev, MD, Consulting or Advisory Role with Astellas Pharma, AstraZeneca, Bayer, Bristol-Myers Squibb, MSD, Roche, Sanofi, Speakers' Bureau for Astellas Pharma, AstraZeneca, Bayer, Bristol-Myers Squibb, MSD, Roche, Sanofi, Research Funding from Astellas Pharma, AstraZeneca, Bayer, Bristol-Myers Squibb, MSD, Roche, Sanofi; Denis Soulieres, Consulting or Advisory Role with Merck, Research Funding from Merck; Bohuslav Melichar, MD, PhD, Honoraria from MSD, Roche, Pfizer, Novartis, Bristol-Myers Squibb, Merck Serono, Astellas Pharma, AstraZeneca, Bayer, Pierre Fabre, Eisai, Janssen, Sanofi, Consulting or Advisory Role with MSD, Roche, Pfizer, Novartis, Bristol-Myers Squibb, Merck Serono, Astellas Pharma, Bayer, Pierre Fabre, Eisai, Janssen, Sanofi; Sergio Jobim Azevedo, MD, FACP, Consulting or Advisory Role with Bristol-Myers Squibb, MSD, Roche; Delphine Borchiellini, MD, Consulting or Advisory Role with Bristol-Myers Squibb, Roche, Novartis, Travel, Accommodations, Expenses from Bristol-Myers Squibb, Roche, Novartis; Michael B. Atkins, MD, Consulting or Advisory Role with Genentech, Pfizer, Novartis, X4 Pharma, Bristol-Myers Squibb, Merck, Exelixis, Acceleron Pharma, Eisai, Glactone Pharma, Agenus, Array BioPharma, Boehringer Ingelheim, Aduro Biotech, Newlink Genetics/Pharmatech, Arrowhead Pharmaceuticals, Werewolf Pharma, Oncolys BioPharma, Surface, Iovance Biotherapeutics, Honoraria from Bristol-Myers Squibb; Rodolfo F. Perini, MD, Employment with Merck, Stock and Other Ownership Interests with Merck, Patents, Royalties, Other Intellectual Property (Institutional) with Application 15/101/409; Qiong Shou, Employment with Merck Sharp & Dohme; Mei Chen, MD, PhD, Employment with Merck, Stock and Other Ownership Interests with Merck.

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