Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy, Speaker Bureau/Expert testimony: Ipsen; Advisory/Consultancy: Lilly; Advisory/Consultancy: Eusa Pharma; Advisory/Consultancy, Travel/Accommodation/Expenses: Roche; Advisory/Consultancy, Speaker Bureau/Expert testimony: PharmaMar; Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Bristol-Myers Squibb; Speaker Bureau/Expert testimony: Astellas Pharma; Research grant/Funding (self): AstraZeneca. P. Maroto: Advisory/Consultancy, Research grant/Funding (self): Roche; Advisory/Consultancy: Pfizer; Advisory/Consultancy: Astellas; Advisory/Consultancy: Janssen; Advisory/Consultancy: Bristol-Myers Squib; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Novartis. J. Bellmunt: Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy: MSD; Advisory/Consultancy: Merck; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Roche-Genentech; Advisory/Consultancy: Pierre-Fabre; Licensing/Royalties: UpToDate. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2256

696O_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial

T.K. Choueiri[1], T. Powles[2], M. Burotto[3], M.T. Bourlon[4], B. Zurawski[5], V.M. Oyervides Juárez[6], J.J. Hsieh[7], U. Basso[8], A.Y. Shah[9], C. Suarez[10], A. Hamzaj[11], C.H. Barrios[12], M. Richardet[13], D. Pook[14], Y. Tomita[15], B. Escudier[16], J. Zhang[17], B. Simsek[18], A.B. Apolo[19], R.J. Motzer[20]

[1]Department of Medical Oncology, Dana-Farber Cancer Institute, The Lank Center for Genitourinary Oncology, Boston, MA, USA; [2]Department of Genitourinary Oncology, Barts Cancer Institute, Cancer Research UK Experimental Cancer Medicine Centre, Queen Mary University of London, Royal Free National Health Service Trust, London, UK; [3]Department of Medical Oncology, Bradford Hill Clinical Research Center, Santiago, Chile; [4]Department of Hemato-Oncology, Urologic Oncology Clinic, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; [5]Department of Outpatient Chemotherapy, Professor Franciszek Lukaszczyk Oncology Centre, Bydgoszcz, Poland; [6]Department of Medical Oncology, Centro Universitario contra el Cáncer Hospital Universitario "Dr. José Eleuterio González" Universidad Autónoma de Nuevo León, Nuevo León, Mexico; [7]Molecular Oncology, Department of Medicine, Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [8]Department of Oncology, Istituto Oncologico Veneto IOV IRCCS, Padua, Italy; [9]Department of Genitourinary Medical Oncology, M. D. Anderson Cancer Center, Houston, TX, USA; [10]Vall d'Hebron Institute of Oncology, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona, Barcelona, Spain; [11]Department of Medical Oncology, Ospedale San Donato, Istituto Toscano Tumori, Arezzo, Italy; [12]Oncology Research Center, Hospital Sao Lucas, PUCRS, Porto Alegre, Brazil; [13]Fundacion Richardet Longo, Instituto Oncologico de Cordoba, Cordoba, Argentina; [14]Cabrini Monash University Department of Medical Oncology, Cabrini Health, Malvern, Australia; [15]Departments of Urology and Molecular Oncology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan; [16]Department of Medical Oncology, Gustave Roussy, Villejuif, France; [17]Department of Clinical Research, Bristol Myers Squibb, Princeton, NJ, USA; [18]Department of Biostatistics, Bristol Myers Squibb, Princeton, NJ, USA; [19]Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA; [20]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Background: Results from the phase 3 CheckMate 9ER trial evaluating the checkpoint inhibitor (CPI) nivolumab (N) plus the tyrosine kinase inhibitor (TKI) cabozantinib (C) v sunitinib (S) for first-line (1L) treatment of advanced clear cell renal cell carcinoma (aRCC) are reported. As monotherapies, N and C have demonstrated efficacy and a manageable safety profile in aRCC. C has immunomodulatory properties that may counteract tumor-induced immunosuppression, providing a rationale for combining N+C.

Methods: Patients (pts) were randomized 1:1 (stratified by IMDC risk score, tumor PD-L1 expression, region) to N 240 mg flat dose IV Q2W + C 40 mg PO QD v S 50 mg PO for 4 wk (6-wk cycles) until disease progression or unacceptable toxicity (max N treatment, 2 y). Primary endpoint: progression-free survival (PFS; a ¼ 0.05 final) by blinded independent central review (BICR). Secondary endpoints (hierarchical testing): overall survival (OS; a ¼ 0.011 first interim analysis), objective response rate (ORR; a ¼ 0.05 final) by BICR, and safety.

Results: A total of 651 pts (22.6% favorable risk, 57.6% intermediate risk, 19.7% poor risk; 24.9% PD-L1 _1%) were randomized to N+C (n ¼ 323) v S (n ¼ 328). With 18.1 mo median (10.6 mo minimum) study follow-up, all 3 efficacy endpoints were met. N+C significantly improved PFS (HR 0.51 [95% CI 0.41e0.64], $P < 0.0001$; median, 16.6 v 8.3 mo) and OS (HR 0.60 [98.89% CI 0.40e0.89]; P ¼ 0.0010; medians not reached) v S, and results were consistent across prespecified IMDC risk and PD-L1 subgroups. ORR (95% CI) was significantly higher with N+C v S (55.7% [50.1e61.2] v 27.1% [22.4e32.3]; $P < 0.0001$), and 8.0% v 4.6% of pts achieved complete response. Median duration of response was 20.2 v 11.5 mo for N+C v S. Any-grade TRAEs occurred in 96.6% v 93.1% of pts treated with N+C v S (60.6% v 50.9% grade _3). One treatment-related death occurred with N+C v 2 with S. TRAEs led to discontinuation of S in 8.8%, N or C in 15.3%, N+C in 3.1%, N only in 5.6%, and C only in 6.6% of pts.

Conclusions: N+C demonstrated superior PFS, OS, and ORR v S in 1L aRCC. The safety profile of this combination was manageable and consistent with the known single-agent AE profiles of N and C. These results support N+C as a new CPI+TKI option for aRCC pts.

Clinical trial identification: NCT03141177.

Editorial acknowledgement: Professional medical writing assistance was provided by Jen Tyson, PhD, of Parexel, funded by Bristol-Myers Squibb Company.

Legal entity responsible for the study: Bristol-Myers Squibb Company.

Funding: Bristol-Myers Squibb Company (Princeton, NJ), Ono Pharmaceutical Company Ltd. (Osaka, Japan), and Exelixis Inc. (Alameda, CA).

Disclosure: T.K. Choueiri: Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: BMS; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Exelixis; Advisory/Consultancy, Research grant/Funding (self), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Pfizer; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Merck; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: AstraZeneca; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Lilly; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Eisai; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: Novartis; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: GSK; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses, Manuscript preparation, Clinical trials grants: EMD Serono; Shareholder/Stockholder/Stock options: Pionyr; Shareholder/Stockholder/Stock options: Tempest. T. Powles: Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self), Advisory/Consultancy: BMS; Honoraria (self), Advisory/Consultancy: Exelixis; Honoraria (self), Advisory/Consultancy: Incyte; Honoraria (self), Advisory/Consultancy: Ipsen; Honoraria (self), Advisory/Consultancy: Merck/MSD; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self), Advisory/Consultancy: Pfizer; Honoraria (self), Advisory/Consultancy: Seattle Genetics; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Roche. M.T. Bourlon: Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses, Slide reviews: BMS; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Ipsen; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: MSD; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Bayer; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Janssen. J.J. Hsieh: Research grant/Funding (self), Sponsered Clinical trial: BMS; Advisory/Consultancy, Research grant/Funding (self), Sponsored Clinical trial: Eisai; Research grant/Funding (self), Sponsored Clinical trial: Calithera; Research grant/Funding (self), Investigator initiated trial and correlate studies: AstraZeneca. U. Basso: Speaker Bureau/Expert testimony, Research grant/Funding (self), Carry out activities of the study: BMS. C. Suarez: Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: BMS; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Pfizer; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Roche/Genentech; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Astellas; Honoraria (self), Advisory/Consultancy: AtraZeneca; Honoraria (self), Advisory/Consultancy: Bayer; Honoraria (self), Advisory/Consultancy: Eusa; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): Ipsen; Honoraria (institution), Advisory/Consultancy: Novartis; Honoraria (self), Advisory/Consultancy: Sanofi-Aventis; Honoraria (self), Advisory/Consultancy: Merck Sharp & Dohme Corp. C.H. Barrios: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Boehringer-Ingelheim; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: GSK; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Novartis; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Lilly; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Roche/Genentech; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Eisai; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: MSD; Honoraria (self), Advisory/Consultancy: AstraZeneca; Advisory/Consultancy, Travel/Accommodation/Expenses: Bayer; Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): AstellasPharma; Research grant/Funding (institution): Celgene; Research grant/Funding (institution): Covance; Research grant/Funding (institution): Medivation; Research grant/Funding (institution): Merck Serono; Research grant/Funding (institution): PharmMar. D. Pook: Advisory/Consultancy, Commercial Study Finding: BMS; Advisory/Consultancy, Research grant/Funding (self): Pfizer; Research grant/Funding (self): Ipsen. Y. Tomita: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Ono pharmacetical; Honoraria (self): BMS; Honoraria (self), Research grant/Funding (self): Pfizer; Research grant/Funding (institution): Takeda. B. Escudier: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Novartis; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy: Ipsen; Honoraria (self), Advisory/Consultancy: Eusa Pharma; Honoraria (self): Roche/Genentech. J. Zhang: Shareholder/Stockholder/Stock options, Full/Part-time employment: BMS. B. Simsek: Shareholder/Stockholder/Stock options, Full/Part-time employment: BMS. R.J. Motzer: Advisory/Consultancy, Research grant/Funding (institution): Bristol-Myers Squibb; Advisory/Consultancy, Research grant/Funding (institution): Pfizer; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy, Research grant/Funding (institution): Eisai; Advisory/Consultancy, Research grant/Funding (institution): Exelixis; Advisory/Consultancy, Research grant/Funding (institution): Genentech/Roche; Advisory/Consultancy: Merck; Advisory/Consultancy: Incyte; Advisory/Consultancy: Lilly. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2257