

47360

Results from a phase 3 trial of neoadjuvant (neoadj) chemotherapy alone vs in combination with nivolumab followed by postsurgical adjuvant nivolumab in patients (pts) with muscle-invasive bladder cancer (MIBC)

A. Necchi¹, S. Gupta², M.S. van der Heijden³, M.D. Galsky⁴, G.D. Steinberg⁵, J. Gschwend⁶, J.P. Sade⁷, D. Bimbatti⁸, U. De Giorgi⁹, S. Vazquez Estevez¹⁰, S.E. Panay Serra¹¹, G. Schinzari¹², A. Kotsakis¹³, H. Miyake¹⁴, J.J. Oh¹⁵, J. Zhang¹⁶, C. Jeyamohan¹⁷, M. Jacques¹⁶, Q. duong¹⁸, G.P. Sonpavde¹⁹

¹ Medical Oncology Department, IRCCS Ospedale San Raffaele, Milan, Italy, ² Medicine Department, Taussig Cancer Center-Cleveland Clinic, Cleveland, United States of America, ³ Medical Oncology Department, Netherlands Cancer Institute, Amsterdam, Netherlands, ⁴ Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, United States of America, ⁵ Department of Urology, Rush University Medical College, Chicago, United States of America, ⁶ Department of Urology, Technical University Munich, Germany, Klinikum Rechts der Isar - Technische Universitaet Muenchen, Munich, Germany, ⁷ Genitourinary Department, Instituto Alexander Fleming, Buenos Aires, Argentina, ⁸ Department of Medical Oncology, IOV - Istituto Oncologico Veneto IRCCS, Padua, Italy, ⁹ Department of Medical Oncology, IRST - Istituto Romagnolo per lo Studio dei Tumori Dino Amadori IRCCS S.r.l., Meldola, Italy, ¹⁰ Department of Medical Oncology, Hospital Universitario Lucus Augusti de Lugo, Lugo, Spain, ¹¹ Medical Oncology Department, FALP - Fundacion Arturo Lopez Perez - Instituto Oncologico, Providencia, Chile, ¹² Department of Medical Oncology, Università Cattolica del Sacro Cuore, Rome, Italy, ¹³ Medical Oncology Department, University of Thessaly, Larissa, Greece, ¹⁴ Department of Urology, Kobe University Graduate School of Medicine, Kobe, Japan, ¹⁵ Urology, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, ¹⁶ Department of Medical Oncology, Bristol-Myers Squibb, Princeton, United States of America, ¹⁷ Global Drug Development, Bristol-Myers Squibb, Princeton, United States of America, ¹⁸ GBDS, Bristol-Myers Squibb, Princeton, United States of America ¹⁹ Medical Oncology, Genitourinary Section, Dana-Farber Cancer Institute, Harvard Medical School, Boston, United States of America

Background

Cisplatin-based neoadj chemo followed by surgery has been a standard of care for eligible pts with MIBC. Neoadj therapy has evolved with the emergence of perioperative checkpoint inhibition. Adjuvant (adj) nivolumab (NIVO) has improved outcomes in high-risk muscle-invasive urothelial carcinoma after surgery. We report the final analysis (FA) of CA017-078, a phase 3 trial of neoadj NIVO + gemcitabine/cisplatin (GC) and adj NIVO vs neoadj GC in pts with MIBC.

Methods

Pts with previously untreated MIBC (cT2-T4aN0M0) were randomized to NIVO 360 mg + GC Q3W × 4 cycles, surgery, then adj NIVO 480 mg Q4W × 9 cycles (NIVO+GC/NIVO) or neoadj GC Q3W × 4 cycles, followed by surgery. Randomization was stratified by clinical tumor stage (T2 vs T3/T4a), GFR (50 to < 60 vs ≥ 60 mL/min), and tumor PD-L1 status (≥ 1% vs < 1%/indeterminate). Primary endpoints: event-free survival (EFS) by blinded independent review committee and pathologic complete response (pCR) rate by BICR (measured earlier at FA of pCR). Secondary endpoints: overall survival (OS) and safety.

Results

653 pts were randomized to NIVO+GC/NIVO (n = 325) or GC (n = 328). 76.6%/17.2%/5.5% vs 77.4%/14.9%/6.7% of pts had T2/T3/T4a stage tumors, respectively. With median follow-up of 54.5 mo, EFS did not differ significantly between arms (HR 0.94 [95.74% CI 0.71–1.25]; P = 0.67; median not reached [95% CI not estimable (NE)] for NIVO+GC/NIVO vs 67.6 [63.0–NE] mo for GC). pCR rate did not differ significantly for NIVO+GC/NIVO vs GC (39.1% vs 29.6%; OR 1.54 [99.91% CI 0.88–2.69]). OS was immature at EFS FA (HR 0.88 [95% CI 0.64–1.21] for NIVO+GC/NIVO vs GC). TRAEs (grade ≥ 3) were reported in 45.9% of pts with NIVO+GC/NIVO and 49.5% with GC. Efficacy in relevant clinical and biomarker subgroups (ie, ctDNA) will be presented.

Conclusions

No statistically significant differences in the primary endpoints of EFS and pCR were observed with neoadj NIVO+GC followed by adj NIVO vs GC in pts with resectable MIBC. Safety of NIVO+GC was consistent with the individual agents. While the primary outcomes were not significantly different between arms, the results are important to optimize future management of MIBC.

Clinical trial identification

NCT03661320.

Legal entity responsible for the study

Bristol-Myers Squibb.

Funding

Bristol-Myers Squibb.

Disclosure

A. Necchi: Financial Interests, Institutional, Research Grant: Merck, AstraZeneca, Ipsen, BMS, Gilead; Financial Interests, Personal, Steering Committee Member: Janssen, Astellas, AstraZeneca, Merck, Gilead, BMS, Bicycle Therapeutics, Daiichi Sankyo; Financial Interests, Coordinating PI: Incyte, Genenta Sciences; Financial Interests, Personal, Coordinating PI: Catalym; Financial Interests, Personal, Funding: Samsung Bioepis; Non-Financial Interests, Leadership Role: Global society of Rare Genitourinary Tumors (GSRGT). S. Gupta: Financial Interests, Personal, Advisory Board: BMS, Pfizer, Merck, Guardant, Foundation one, Johnson & Johnson, Novartis; Financial Interests, Institutional, Local PI: Pfizer, Merck, BMS, Novartis, Convergent Therapeutics, Flare Therapeutics; Financial Interests, Institutional, Research Grant: Gilead Sciences. M.S. van der Heijden: Financial Interests, Institutional, Advisory Board: AstraZeneca, BMS, Janssen, MSD, Pfizer, Astellas, Daiichi Sankyo; Financial Interests, Institutional, Funding, Investigator-initiated trial: Roche, MSD, BMS, AstraZeneca, 4SC; Financial Interests, Institutional, Steering Committee Member, Local PI + SSC member: Pfizer, MSD, BMS, AstraZeneca; Financial Interests, Institutional, Steering Committee Member, Local PI + study co-PI: Janssen. M.D. Galsky: Financial Interests, Personal, Advisory Board: Janssen, Merck, Pfizer, EMD Serono, AstraZeneca, Seagen, AbbVie, Gilead; Financial Interests, Institutional, Steering Committee Member: Merck, Bristol-Myers Squibb, Seagen; Financial Interests, Institutional, Coordinating PI: AstraZeneca. G.D. Steinberg: Financial Interests, Personal, Advisory Board, scientific advisor: CG Oncology, Engene, Pfizer, Aura Biosciences, Merck, AZ, Vesica; Financial Interests, Personal, Other, protocol committee member: BMS; Financial Interests, Personal, Advisory Board, I am a scientific advisor: Tyra Biosciences, Protara; Financial Interests, Personal, Advisory Board, protocol committee member: Fidia; Financial Interests, Personal, Stocks/Shares, Stock options: CGON; Financial Interests, Personal, Stocks/Shares, stock options: Engene; Financial Interests, Personal, Stocks/Shares, I am a scientific advisor and have stock options: Protara. J. Gschwend: Financial Interests, Personal, Advisory Board: BMS, Roche, Janssen, Merck, Pfizer, Astellas, Novartis, MSD. D. Bimbatti: Financial Interests, Personal, Invited Speaker: Ipsen, Astellas, Janssen, Bayer; Financial Interests, Personal, Advisory Board: MSD, Eisai. U. De Giorgi: Financial Interests, Personal, Advisory Board: Pfizer, BMS, MSD, PharmaMar, Astellas, Bayer, Ipsen, Novartis, Eisai, Janssen; Financial Interests, Personal, Invited Speaker: Roche, BMS, AstraZeneca, Merck; Financial Interests, Institutional, Research Grant: AstraZeneca, Sanofi, Roche. S. Vazquez Estevez: Financial Interests, Personal, Advisory Board: MSD, Ipsen, Recordati; Financial Interests, Personal, Invited Speaker: Astellas, Bayer, Merck, Novartis, BMS. G. Schinzari: Financial Interests, Personal, Advisory Board: Bristol-Myers Squibb; Financial Interests, Institutional, Local PI: Bristol-Myers Squibb, Novartis. H. Miyake: Financial Interests, Personal, Invited Speaker: MSD, Takeda, Astellas, Novartis, Eisai; Financial Interests, Institutional, Local PI: MSD. J. Zhang: Financial Interests, Personal, Full or part-time Employment: Bristol-Myers Squibb; Financial Interests, Personal, Stocks/Shares: Bristol-Myers Squibb. C. Jeyamohan: Financial Interests, Personal, Full or part-time Employment: Bristol-Myers Squibb; Financial Interests, Personal, Stocks/Shares: Bristol-Myers Squibb. M. Jacques: Financial Interests, Institutional, Full or part-time Employment: Bristol-Myers Squibb International; Financial Interests, Personal, Stocks/Shares: Bristol-Myers Squibb International. G.P. Sonpavde: Financial Interests, Personal, Advisory Board: EMD Serono, Bristol-Myers Squibb, Merck, Seattle Genetics, Exelixis, Janssen, Bicycle Therapeutics, Gilead, Scholar Rock, G1 Therapeutics, Loxo Oncology, Tempus, Syapse, Astellas, Pfizer, Aktis, Vial, PrecisCa, Ellipses, GSK, Biosite Research; Financial Interests, Personal, Invited Speaker: Seattle Genetics, Gilead, Exelixis, Janssen, Astellas, Merck, Aveo, Pfizer, Natera, Bayer, PeerView, Ideology Health, Onvivo, Pfizer, Bayer, AstraZeneca, Total Health, Targeted Oncology; 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, Personal, Advisory Board, consultant for cancer diagnostics: Lucence; Financial Interests, Personal, Invited Speaker, speaker: HMP Education; Financial Interests, Research Grant, Research support fund to institution for investigator initiated trial: Bayer; Financial Interests, Research Grant, Free drug supply support to trial: Sumitomo Pharma; Financial Interests, Institutional, Coordinating PI: Blue Earth Diagnostics; Financial Interests, Institutional, Coordinating PI, Trial funding: Exelixis; Non-Financial Interests, Principal Investigator, Steering committee of trial: Bristol-Myers Squibb; Non-Financial Interests, Other, steering committee of trial: Merck; Other, Other, Spouse employment: Myriad Genetics, Exact Sciences; Other, Other, Travel: BMS, Astellas; Other, Other, spouse employment: Abbott Labs. All other authors have declared no conflicts of interest.