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Durvalumab (D) in combination with Bacillus Calmette-Guérin (BCG) for BCG-naïve, high-risk non-muscle-invasive bladder cancer (NMIBC): Final analysis of the phase III, open-label, randomised POTOMAC trial

M. De Santis[1], J. Palou[2], H. Nishiyama[3], M. Krawczynski[4], A. Seyitkuliev[5], A. Novikov[6], F. Guerrero-Ramos[7], M. Kato[8], L. Goeman[9], E. Hellmis[10], T.B. Powles[11], K.M. Gust[12], P. Vasey[13], P. Bigot[14], Y. Fradet[15], J.J. Hunting[16], J. Armstrong[17], A.M. Dąbrowska[18], S. Hois[19], N.D. Shore[20]

[1] Urology Dept., Charité - Universitätsmedizin Berlin, Berlin, Germany, [2] Department of Urology, Barcelona University, Barcelona, Spain, [3] Department of Urology, University of Tsukuba, Tsukuba, Japan, [4] NA, Clinical Research Center Sp, Poznan, Poland, [5] St. Petersburg Hospital of the Russian Academy of Sciences, St. Petersburg, Russian Federation, [6] North-Western State Medical University, Saint Petersburg, Russian Federation, [7] Department of Urology, Hospital Universitario 12 de Octubre, Madrid, Spain, [8] Department of Urology, Osaka Metropolitan University Graduated School of Medicine, Osaka, Japan, [9] Department of Development and Regeneration, University Hospitals Leuven, Leuven, Belgium, Roeselare, Belgium, [10] Urologicum Duisburg, Urologicum-Duisburg - Praxis Walsum, Duisburg, Germany, [11] Department of Medical Oncology, Barts Cancer Institute, Cancer Research UK; Experimental Cancer Medicine Centre, Queen Mary University of London, Royal Free National Health Service Trust, London, United Kingdom, [12] Department of Urology and Comprehensive Cancer Centre, MedUni Wien - Medical University of Vienna, Vienna, Austria, [13] NA, Icon Cancer Centre Wesley, Auchenflower, Australia, [14] Department of Urology, Angers University Hospital, Angers, France, [15] Urology, CHU de Québec - Université Laval, Quebec City, Canada, [16] Department of Medical Oncology, St. Antonius Hospital, Nieuwegein, Netherlands, [17] Department of Oncology Biometrics, AstraZeneca, Northolt, United Kingdom, [18] Late-stage Development Oncology R&D, AstraZeneca, Cambridge, United Kingdom, [19] Oncology, AstraZeneca, Gaithersburg, United States of America[20] Department of Uro-Oncology, START Carolinas/Carolina Urologic Research Center, Myrtle Beach, SC, United States of America

Background

Standard treatment for high-risk NMIBC is transurethral resection of bladder tumour (TURBT) followed by BCG induction + maintenance therapy, but early recurrence/progression are common (⊠40% of patients [pts] within 2 years). POTOMAC (NCT03528694) evaluated whether 1 year of D (anti–PD-L1 antibody) plus BCG induction + maintenance therapy (D+BCG [I+M]) improved outcomes vs BCG (I+M) alone in pts with BCG-naïve, high-risk NMIBC.

Methods

Eligible adult pts with BCG-naïve, local histologically confirmed high-risk NMIBC who had TURBT (complete resection; including pts with residual carcinoma in situ [CIS]) were randomised 1:1:1 to receive D+BCG (I+M), D+BCG induction only (D+BCG [I]), or BCG (I+M). D was administered intravenously (1500 mg Q4W for 13 cycles). Intravesical BCG was given weekly × 6 weeks (I) and as 3 weekly doses at 3, 6, 12, 18, and 24 months (M). Pts were stratified by higher risk papillary disease and CIS. Primary endpoint was investigator-assessed disease-free survival (DFS) with D+BCG (I+M) vs BCG (I+M).

Results

1018 pts were randomised: 339 to D+BCG (I+M), 339 to D+BCG (I), and 340 to BCG (I+M). Median follow-up was 60.7 months. Primary endpoint of DFS was met with a 32% reduction in risk of recurrence of high-risk disease or death by any cause for D+BCG (I+M) vs BCG (I+M) (HR 0.68; 95% CI 0.50–0.93; log-rank P=0.0154); 24-month DFS rates (95% CI) were 86.5% (82.2–89.8) for D+BCG (I+M) and 81.6% (76.9–85.3) for BCG (I+M). Secondary endpoint of DFS with D+BCG (I) vs BCG (I+M) was not statistically significant (HR 1.14; 95% CI 0.86–1.50). No evidence of overall survival detriment was seen with D+BCG (I+M) vs BCG (I+M) (descriptive analysis: HR 0.80; 95% CI 0.53–1.20). Grade 3/4 treatment-related adverse events (TRAEs) occurred in 21% of pts with D+BCG (I+M), in 15% with D+BCG (I), and in 4% with BCG (I+M). No TRAEs led to death.

Conclusions

D plus BCG (I+M) demonstrated a statistically significant and clinically meaningful improvement in DFS vs BCG (I+M), with a safety profile consistent with that of each therapy. POTOMAC supports 1 year of D in combination with BCG (I+M) as a new treatment option for pts with BCG-naïve, high-risk NMIBC.

Clinical trial identification

NCT03528694; EudraCT: 2017-002979-26.

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J. Palou: Financial Interests, Personal, Speaker, Consultant, Advisor, Consulting fees: AstraZeneca , Fidia, Jemedis , Olympus , Pfizer ; Financial Interests, Personal, Advisory Board: Pfizer, AstraZeneca, Fidia . H. Nishiyama: Financial Interests, Institutional, Research Grant: Chugai Pharma , Astellas ; Financial Interests, Personal, Speaker, Consultant, Advisor, Consulting fees: Ono Pharmaceutical, Janssen, AstraZeneca, Merck Sharpe & Dohme; Financial Interests, Personal, Speaker's Bureau: Astellas, Pfizer , Bristol Myers Squibb, Ono Pharmaceutical, Merck Sharpe & Dohme, AstraZeneca, Merck Biopharma , Nippon Kayaku Co. A. Novikov: Financial Interests, Personal, Speaker, Consultant, Advisor: Eisai; Financial Interests, Personal, Other, Travel, accommodation and expenses: Biocad. F. Guerrero-Ramos: Financial Interests, Personal, Speaker, Consultant, Advisor, Consulting fees: Johnson & Johnson , Pfizer, Merck, Roche, Taris Combat Medical , AstraZeneca, MSD, BMS, enGene, Nanobots Therapeutics ; Financial Interests, Personal, Speaker's Bureau: Janssen, Nucleix, MSD, Pfizer, Merck, BMS, AstraZeneca, Palex, Combat Medical , Johnson & Johnson , Recordati ; Financial Interests, Personal, Other, Support for attending meetings/travel: Pfizer, Recordati , Ipsen, Combat Medical, Alter, Salvat, Nucleix, AstraZeneca, Fidia, Johnson & Johnson ; Financial Interests, Personal, Other, Patents planned, issued or pending: Danae Urogenomics; Financial Interests, Personal, Advisory Board: MSD, EnGene; Financial Interests, Personal, Stocks/Shares: CG Oncology , Johnson & Johnson , Pfizer. M. 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Armstrong: Financial Interests, Personal, Stocks/Shares: AstraZeneca; Financial Interests, Personal, Full or part-time Employment: AstraZeneca. A.M. Dąbrowska: Financial Interests, Personal, Full or part-time Employment: AstraZeneca. S. Hois: Financial Interests, Personal, Full or part-time Employment, Information from the time of study conducted: AstraZeneca. N.D. Shore: Financial Interests, Personal, Advisory Board: Amgen, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Dendreon, Invitae, Janssen, MDxhealth, Merck, Pfizer, Sanofi Genzyme, Speciality Networks, Tolmar, Urogen, Clarity, Lantheus, Lilly, Photocure, Telix, Asieris, Alessa Therapeutics, Fize medical, GConcology, Ferring, Immunitybio,

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