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Spartalizumab plus dabrafenib and trametinib (Sparta-DabTram) in patients (pts) with previously untreated BRAF V600–mutant unresectable or metastatic melanoma: Results from the randomized part 3 of the phase III COMBI-i trial

P. Nathan[1], R. Dummer[2], G.V. Long[3], P.A. Ascierto[4], H.A. Tawbi[5], C. Robert[6], P. Rutkowski[7], O. Leonov[8], C. Dutriaux[9], M. Mandala'[10], P. Lorigan[11], P.F. Ferrucci[12], K.T. Flaherty[13], J.C. Brase[14], S. Green[15], T. Haas[15], A. Masood[16], E. Gasal[16], A. Ribas[17], D. Schadendorf[18]

[1] Department of Medical Oncology, Mount Vernon Cancer Centre, Northwood, UK, [2] Department of Dermatology, University Hospital Zürich Skin Cancer Center, Zurich, Switzerland, [3] Department of Medical Oncology, Melanoma Institute Australia, The University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, Australia, [4] Department of Melanoma, Cancer Immunotherapy and Development Therapeutics, Istituto Nazionale Tumori IRCCS "G. Pascale", Naples, Italy, [5] Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [6] Dermatology Service and Melanoma Research Unit, Gustave Roussy and Paris-Sud-Paris-Saclay University, Villejuif, France, [7] Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland, [8] Department of Medical Oncology, Clinical Oncological Dispensary, Omsk, Russian Federation, [9] Service de Dermatologie, Centre Hospitalier Universitaire de Bordeaux, Hôpital Saint-André, Bordeaux, France, [10] Department of Oncology and Haematology, Papa Giovanni XXIII Cancer Center Hospital, Bergamo, Italy, [11] Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK, [12] Cancer Biotherapy Unit, Department of Experimental Oncology, European Institute of Oncology, IRCCS, Milan, Italy, [13] Department of Medicine and Cancer Center, Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA, [14] Precision Medicine, Novartis Pharma AG, Basel, Switzerland, [15] Clinical Development and Analytics, Novartis Pharma AG, Basel, Switzerland, [16] Oncology Clinical Development, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, [17] Department of Medicine, Division of Hematology-Oncology, University of California, Los Angeles, Los Angeles, CA, USA[18] Department of Dermatology, Comprehensive Cancer Center (Westdeutsches Tumorzentrum), University Hospital Essen, Essen, and German Cancer Consortium, Heidelberg, Germany

Background

Treatment (tx) with immune checkpoint inhibitors + targeted therapy may induce durable and deeper responses in a higher proportion of pts. Results from the safety run-in (part 1) and biomarker cohort (part 2) of COMBI-i (NCT02967692) have been previously reported. Part 3 is a global, placebo (PBO)-controlled, double-blind, Phase III study evaluating the anti -PD-1 antibody Sparta + Dab and Tram in pts with previously untreated BRAF V600 -mutant unresectable or metastatic melanoma. Here we report the primary analysis for part 3 of COMBI-i.

Methods

Pts were randomized 1:1 to receive Sparta 400 mg IV Q4W + Dab 150 mg orally BID + Tram 2 mg orally QD vs PBO-DabTram. The statistical plan ensured 80% power assuming a 5-month tx delay. The primary endpoint is investigator-assessed progression-free survival (PFS) using RECIST 1.1; significance threshold was $P < .025$ [equivalent $HR < 0.801$]. Overall survival (OS) is a key secondary endpoint.

Results

532 pts were randomized to receive Sparta-DabTram (n = 267) or PBO-DabTram (n = 265). At the data cutoff (July 1, 2020), median follow-up was 27.2 mo. Baseline characteristics were balanced across tx arms. Sparta-DabTram did not significantly improve PFS vs PBO (median PFS, 16.2 mo vs 12.0 mo; HR, 0.82 [95% CI, 0.655-1.027]; P = .042). Estimated 12- and 24-mo PFS rates with Sparta-DabTram vs PBO were 58% vs 50% and 44% vs 36%, respectively. While OS was not formally tested, median OS was not reached (NR) across tx arms (HR, 0.785). The objective response rate was 69% in the Sparta-DabTram arm (complete response rate [CRR], 20%) vs 64% in the PBO arm (CRR, 18%); median duration of response was NR vs 20.7 mo, respectively. Tx-related adverse events (TRAEs) grade ≥ 3 occurred in 55% vs 33% of pts treated with Sparta-DabTram vs PBO. TRAEs leading to discontinuation of all 3 study drugs occurred in 12% vs 8% of pts, respectively.

Conclusions

The primary endpoint was not met. Sparta-DabTram did not significantly improve PFS vs PBO-DabTram; analyses interrogating OS benefit are ongoing. AE management was challenging and resulted in frequent dose adaptations.

Clinical trial identification

NCT02967692; conducted in accordance with Study Protocol CPDR001F2301.

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Dummer: Advisory/Consultancy: Novartis; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Roche; Advisory/Consultancy: Amgen; Advisory/Consultancy: Takeda; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy: Sun Pharma; Advisory/Consultancy: Sanofi; Advisory/Consultancy: Catalym; Advisory/Consultancy: Second Genome; Advisory/Consultancy: Regeneron; Advisory/Consultancy: Alligator. G.V. Long: Advisory/Consultancy: Aduro; Advisory/Consultancy: Amgen; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Mass-Array; Advisory/Consultancy: Merck; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Novartis; Advisory/Consultancy: OncoSec Medical; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy: Roche; Advisory/Consultancy: Sandoz. P.A. Ascierto: Advisory/Consultancy, Research grant/Funding (institution): Bristol-Myers Squibb; Advisory/Consultancy, Research grant/Funding (institution): Roche-Genentech; Advisory/Consultancy, Travel/Accommodation/Expenses: Merck Sharp & Dohme; Advisory/Consultancy: Novartis; Advisory/Consultancy, Research grant/Funding (institution): Array; Advisory/Consultancy: Merck Serono; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy: Incyte; Advisory/Consultancy: NewLink Genetics; Advisory/Consultancy: Genmad; Advisory/Consultancy: Medimmune; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Syndax; Advisory/Consultancy: Sun Pharma; Advisory/Consultancy: Sanofi; Advisory/Consultancy: Idera; Advisory/Consultancy: Ultimovacs; Advisory/Consultancy: Sandoz; Advisory/Consultancy: Immunocore; Advisory/Consultancy: 4SC; Shareholder/Stockholder/Stock options: PrimeVax; Advisory/Consultancy: Alkermes; Advisory/Consultancy: Italfarmaco; Advisory/Consultancy: Nektar; Advisory/Consultancy: Boehringer-Ingelheim; Leadership role: Fondazione Melanoma; Leadership role: Campania Society of ImmunoTherapy of Cancer; Leadership role: Society of Melanoma Research; Leadership role: Cancer Development Drug Forum; Leadership role: Society of Immuno Therapy of Cancer. H.A. Tawbi: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Novartis; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Merck; Honoraria (self), Advisory/Consultancy: Array; Research grant/Funding (institution): Celgene; Research grant/Funding (institution): GlaxoSmithKline. C. Robert: Honoraria (self), Advisory/Consultancy: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy: Pierre Fabre; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self), Advisory/Consultancy: Amgen; Honoraria (self), Advisory/Consultancy: Merck; Honoraria (self), Advisory/Consultancy: Merck Sharp & Dohme; Honoraria (self), Advisory/Consultancy: Roche; Honoraria (self), Advisory/Consultancy: Sanofi; Honoraria (self), Advisory/Consultancy: Biothera. P. Rutkowski: Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: Merck Sharp & Dohme; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self): Roche; Honoraria (self), Speaker Bureau/Expert testimony: Pierre Fabre; Honoraria (self): Amgen; Honoraria (self): Blueprint Medicines; Honoraria (self): Eli Lilly; Speaker Bureau/Expert testimony: Pfizer. C. Dutriaux: Advisory/Consultancy, Travel/Accommodation/Expenses: Bristol-Myers Squibb; Advisory/Consultancy, Travel/Accommodation/Expenses: Merck Sharp & Dohme; Advisory/Consultancy, Travel/Accommodation/Expenses: Novartis; Advisory/Consultancy, Travel/Accommodation/Expenses: Pierre Fabre; Advisory/Consultancy, Travel/Accommodation/Expenses: Merck. M. Mandala': Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Sanofi. P. Lorigan: Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: Novartis; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution), Travel/Accommodation/Expenses: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Merck Sharp & Dohme; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: Pierre Fabre; Advisory/Consultancy: Amgen; Non-remunerated activity/ies: Roche; Advisory/Consultancy: NeraCare GmbH. P.F. Ferrucci: Advisory/Consultancy: Roche; Advisory/Consultancy: Novartis; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Pierre Fabre. K.T. Flaherty: Officer/Board of Directors: Clovis Oncology; Officer/Board of Directors: Strata Oncology; Officer/Board of

Directors: Vivid Biosciences; Officer/Board of Directors: Checkmate Pharmaceuticals; Advisory/Consultancy: X4 Pharmaceuticials; Advisory/Consultancy: PIC Therapeautics; Advisory/Consultancy, Research grant/Funding (institution): Sanofi; Advisory/Consultancy: Amgen; Advisory/Consultancy: Asana BioSciences; Advisory/Consultancy: Adaptimmune; Advisory/Consultancy: Fount Therapeutics; Advisory/Consultancy: Aeglea BioTherapeutics; Advisory/Consultancy: Shattuck Labs; Advisory/Consultancy: Tolero Pharmaceuticals; Advisory/Consultancy: Apricity Therapeutics; Advisory/Consultancy: Oncoceutics; Advisory/Consultancy: FogPharma; Advisory/Consultancy: Neon Therapeutics; Advisory/Consultancy: Tvardi Therapeutics; Advisory/Consultancy: xCures; Advisory/Consultancy: Monopteros Therapeutics; Advisory/Consultancy: Vibliome Therapeutics; Advisory/Consultancy: Eli Lilly; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy: Genentech; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Merck; Advisory/Consultancy: Takeda; Advisory/Consultancy: Verastem Oncology; Advisory/Consultancy: Boston Biomedical; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy: Debiopharm. J.C. Brase: Shareholder/Stockholder/Stock options, Full/Part-time employment: Novartis. S. Green: Full/Part-time employment: Novartis. T. Haas: Shareholder/Stockholder/Stock options, Full/Part-time employment: Novartis. A. Masood: Full/Part-time employment: Novartis. E. Gasal: Shareholder/Stockholder/Stock options, Full/Part-time employment: Novartis. A. Ribas: Honoraria (self), Advisory/Consultancy: Amgen; Honoraria (self), Advisory/Consultancy: Chugai; Honoraria (self), Advisory/Consultancy: Merck; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self), Advisory/Consultancy: Sanofi; Honoraria (self), Advisory/Consultancy: Compugen; Honoraria (self), Advisory/Consultancy: CytomX Therapeutics; Honoraria (self), Advisory/Consultancy: Highlight Therapeutics; Honoraria (self), Advisory/Consultancy: ImaginAb; Honoraria (self), Advisory/Consultancy: Isoplexis; Honoraria (self), Advisory/Consultancy: Merus; Honoraria (self), Advisory/Consultancy: RAPT Therapeutics; Honoraria (self), Advisory/Consultancy: Rgenix; Honoraria (self), Advisory/Consultancy: Tango Therapeutics; Honoraria (self), Advisory/Consultancy, Officer/Board of Directors: Arcus Biosciences; Honoraria (self), Advisory/Consultancy, Officer/Board of Directors: Lutris Pharma; Honoraria (self), Advisory/Consultancy, Officer/Board of Directors: PACT Pharma. D. Schadendorf: Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution), Travel/Accommodation/Expenses: Novartis; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Merck Sharp & Dohme ; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution), Travel/Accommodation/Expenses: Sanofi; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution), Travel/Accommodation/Expenses: Regeneron; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution): Pierre Fabre; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution): Array; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (institution): Pfizer; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Roche; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Genentech; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: Merck EMR; Advisory/Consultancy: Immunocore; Honoraria (institution), Advisory/Consultancy: Nektar; Honoraria (self), Advisory/Consultancy: 4SC. All other authors have declared no conflicts of interest.