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Pembrolizumab versus placebo as adjuvant therapy for resected stage IIB or IIC melanoma: 5-year follow-up of the phase III KEYNOTE-716 study

J.J. Luke¹, G.V. Long², M.A. Khattak³, P. Rutkowski⁴, M. Del Vecchio⁵, F. Spagnolo⁶, J. Mackiewicz⁷, L. de la Cruz Merino⁸, J. Pigozzo⁹, J.M. Kirkwood¹⁰, C. Robert¹¹, M.S. Carlino¹², D. Schadendorf¹³, F. De Galitiis¹⁴, A.T. Odeleye-Ajakaye¹⁵, T. Hoki¹⁶, M. Kalabis¹⁷, A.M.M. Eggermont¹⁸, P.A. Ascierto¹⁹

¹ Immunotherapy and Drug Development Center, UPMC Hillman Cancer Center and University of Pittsburgh, Pittsburgh, United States of America, ² Faculty of Medicine and Health, The University of Sydney, and Mater and Royal North Shore Hospitals, Melanoma Institute Australia, The University of Sydney, Royal North Shore and Mater Hospitals, Sydney, Australia, ³ Oncology, Fiona Stanley Hospital and Edith Cowan University, Perth, Australia, ⁴ Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, ⁵ Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, ⁶ Medical Oncology, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, ⁷ Department of Medical and Experimental Oncology, Poznan University of Medical Sciences Sciences and Greater Poland Cancer Center, Poznan, Poland, ⁸ Clinical Oncology, Instituto de Biomedicina de Sevilla (IBiS)/Hospital Universitario Virgen Macarena/Consejo Superior de Investigaciones Científicas (CSIC)/Universidad de Sevilla, Seville, Spain, ⁹ Medical Oncology, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy, ¹⁰ Medicine, UPMC Hillman Cancer Center and University of Pittsburgh, Pittsburgh, United States of America, ¹¹ Dermatology, Gustave Roussy, Villejuif and Paris-Saclay University, Villejuif, France, ¹² Medical Oncology department, Melanoma Institute Australia, The University of Sydney, and Westmead and Blacktown Hospitals, Westmead, Australia, ¹³ Department of Dermatology - Hautklinik, University Hospital Essen and German Cancer Consortium Partner Site and National Center for Tumor Diseases (NCT)-West, Campus Essen, Research Alliance Ruhr, Research Center One Health, and University Duisburg-Essen, Essen, Germany, ¹⁴ Oncology, Dermopathic Institute of the Immaculate (IDI) IRCCS, Rome, Italy, ¹⁵ BARDS, Merck & Co., Inc., Rahway, United States of America, ¹⁶ Oncology, Merck & Co., Inc., Rahway, United States of America, ¹⁷ Global Clinical Development, Oncology, Merck & Co., Inc., Rahway, United States of America, ¹⁸ Cancer Medicine, University Medical Center Utrecht, Utrecht, Netherlands, and Comprehensive Cancer Center Munich of the Technical University Munich and the Ludwig Maximilian University, Utrecht, Netherlands¹⁹ Department of Skin Cancer, Cancer Immunotherapy and Development Therapeutics, Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy

Background

Adjuvant pembrolizumab (pembro) significantly prolonged RFS and DMFS vs placebo in participants (pts) with resected high-risk stage II melanoma in KEYNOTE-716 (NCT03553836). At the final DMFS analysis (median study follow-up, 39.4 mo), pembro continued to demonstrate a DMFS and RFS benefit. Here, we report 5-year follow-up data.

Methods

Pts aged ≥12 y with resected stage IIB or IIC melanoma were randomly assigned 1:1 to pembro 200 mg (2 mg/kg up to 200 mg for pts <18 y) or placebo IV Q3W for 17 cycles (part 1). Pts with recurrence after placebo or >6 mo after 17 cycles of pembro could crossover to or be rechallenged with pembro (part 2). RFS was the primary end point. DMFS and safety were secondary. Progression/recurrence-free survival 2 (PRFS2; time to PD beyond initial recurrence, second recurrence, or death) and time to subsequent therapy (TTST) were exploratory.

Results

A total of 976 pts were enrolled (pembro, n = 487; placebo, n = 489). Median study follow-up at data cutoff (Feb 13, 2025) was 64.7 mo (range, 51.4-76.7). 62 of 149 pts (41.6%) in the pembro arm and 83 of 218 (38.1%) in the placebo arm with an RFS event received subsequent therapy, most commonly combination anti-PD-1/anti-CTLA-4 (22.1% and 18.8%). Efficacy is presented in the table. Treatment-related AEs occurred in 399/483 pts (82.6%) in the pembro arm and 311/486 (64.0%) in the placebo arm; 84 (17.4%) and 25 (5.1%), respectively, were grade 3 or 4. Immune-mediated AEs and infusion reactions occurred in 185/483 pts (38.3%) in the pembro arm and 46/486 pts (9.5%) in the placebo arm; 53 (11.0%) and 6 (1.2%), respectively, were grade 3 or 4. No grade 5 immune-mediated AEs or infusion reactions occurred. Table: 1611P

	Overall		Stage IIB		Stage IIC	
	Pembro n = 487	Placebo n = 489	Pembro n = 309	Placebo n = 316	Pembro n = 171	Placebo n = 169
RFS, HR (95% CI), mo	0.62 (0.50-0.76)		0.61 (0.46-0.80)		0.62 (0.44-0.86)	

	Overall		Stage IIB		Stage IIC	
	Pembro n = 487	Placebo n = 489	Pembro n = 309	Placebo n = 316	Pembro n = 171	Placebo n = 169
5-y RFS, %	67.1	52.4	70.4	56.9	62.2	45.4
DMFS, HR (95% CI), mo	0.59 (0.46-0.77)		0.63 (0.45-0.89)		0.55 (0.36-0.82)	
5-y DMFS, %	78.7	66.6	80.4	70.7	76.0	60.1
PRFS2, HR (95% CI), mo	0.72 (0.55-0.94)		0.74 (0.51-1.07)		0.69 (0.45-1.04)	
5-y PRFS2, %	81.1	73.3	84.9	77.6	75.4	66.8
TTST, HR (95% CI), mo	0.65 (0.52-0.80)		0.64 (0.49-0.84)		0.62 (0.44-0.87)	
5-y TTST, %	67.5	55.2	70.2	58.7	64.3	49.5

Conclusions

After a median follow-up of ≥5 years, pembro continued to prolong RFS and DMFS. Of pts treated with pembro, 67.1% were without disease recurrence at 5 years vs 52.4% with placebo. PRFS2 and TTST results were promising. These findings support the use of adjuvant pembro for high-risk stage II melanoma.

Clinical trial identification

NCT03553836.

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L. de la Cruz Merino: Financial Interests, Personal and Institutional, Invited Speaker: Bristol Myers Squibb, Merck & Co., Inc., Roche; Financial Interests, Personal and Institutional, Speaker's Bureau: Bristol Myers Squibb, Merck & Co., Inc.; Financial Interests, Personal and Institutional, Funding: Bristol Myers Squibb, Merck & Co., Inc., ROCHE; Financial Interests, Personal and Institutional, Principal Investigator: Bristol Myers Squibb, Merck & Co., Inc., Roche; Financial Interests, Personal and Institutional, Advisory Board: Merck & Co., Inc.; Financial Interests, Personal and Institutional, Research Grant: Merck & Co., Inc., Roche; Financial Interests, Personal and Institutional, Project Lead: ROCHE; Financial Interests, Personal, Invited Speaker: GILEAD, ABBVIE; Financial Interests, Personal, Advisory Board: Gilead; Financial Interests, Personal, Principal Investigator: Gilead. J. Pigozzo: Other, Personal, Advisory Board: MSD; Other, Personal, Principal Investigator: MSD, BMS, Regeneron. J.M. Kirkwood: Financial Interests, Personal, Advisory Board: Ankyra Therapeutics, Bristol Myers Squibb, Iovance Biotherapeutics, Istari Oncology, Jazz Pharmaceuticals, Inc., Merck & Co., Inc., Mural Oncology, Natera, Inc., Novartis Pharmaceuticals, OncoCyte Corporation, Regeneron Pharmaceuticals, Inc., Replimune, Inc., Scopus BioPharma, Takeda; Financial Interests, Personal, Other, Data Safety Monitoring Board: Axio Research, LLC, IQVIA, Lytix Biopharma AS; Financial Interests, Personal, Advisory Role: Boxer Capital, CytomX Therapeutics, Engage Health Media, iOnctura, Lumira Capital Investment Management, Magnolia Innovation, LLC, PathAI, Inc., Pfizer, Inc., Piper Sandler & Co., PyrOjas Corporation, Valar Labs, Inc, Zola Therapeutics; Financial Interests, Personal, Other, Leader of Consensus Conference: DermTech; Financial Interests, Institutional, Principal Investigator: Amgen, Inc., Bristol Myers Squibb, Checkmate Pharmaceuticals, Harbour BioMed, Immvira Pharma Co, Immunocore, Ltd., Iovance Biotherapeutics, Lion Biotechnologies, Inc., Lytix Biopharma AS, Novartis Pharmaceuticals, Takeda, Verastem, Inc.. C. Robert: Financial Interests, Personal, Advisory Board: Pierre Fabre, Sanofi, BMS, MSD, Novartis, Merck, Roche, Pfizer, Sun Pharma, Ultimovacs, Regeneron, Egle, Philogen, Maat Pharma, Pierre Fabre; Financial Interests, Personal, Other, Steering Committee: Novartis, Regeneron, Pfizer, IO Biotech; Financial Interests, Personal, Invited Speaker: Sanofi, BMS, MSD, Novartis. M.S. Carlino: Financial Interests, Personal, Advisory Board: Amgen, Bristol Myers Squibb, Eisai, Ideaya, Merck Sharpe & Dohme, Medison, Moderna, Nektar, Novartis, Oncosec, Pierre Fabre, Qbiotic, Regeneron, Roche, Merck KGaA, Sanofi, Strand therapeutics. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, MSD, Merck Serono, Regeneron; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Regeneron, Philogen, BioAlta, Daiichi Sanyko, BioNTech, Immatics, CureVac, Formycon, Replimune, SunPharma, Skyline Dx, IOVance, Ipsen, IOBioTech, Boehringer-Ingelheim; Financial Interests, Institutional, Coordinating PI: Novartis, BMS, MSD, Pierre Fabre, Immatics; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Personal, Steering Committee Member: MSD; Financial Interests, Institutional, Local PI: Philogen, Immunocore, Regeneron, Biontech Rna Pharmaceuticals GMBH, Replimune, IO Biotech; Non-Financial Interests, Member of Board of Directors: EORTC-MG; Non-Financial Interests, Leadership Role, Founding member and SC chair: European Melanoma Registry (EuMelaReg). F. De Galitiis: Financial Interests, Personal and Institutional, Invited Speaker: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme; Financial Interests, Personal and Institutional, Advisory Board: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme; Financial Interests, Personal and Institutional, Principal Investigator: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme. A.T. Odeleye-Ajakaye: Financial Interests, Institutional, Full or part-time Employment: Merck & Co., Inc; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc. T. Hoki, M. Kalabis: Financial Interests, Personal, Full or part-time Employment: Merck & Co., Inc.; Financial Interests, Personal, Stocks or ownership: Merck & Co., Inc.: A.M.M. Eggermont: Financial Interests, Personal, Other, Data safety monitoring board: Boehringer Ingelheim, BioNTech, IQVIA, Pfizer, T3Pharma; Financial Interests, Personal, Advisory Board: Agenus, Boehringer Ingelheim, BioInvent, BioNTech, Catalym, Egle, Eurobio, Imcheck, IO Biotech, IQVIA, Merck&Co, MSD, Pfizer, Oncolytics, Pierre Fabre, QBiotics, Regeneron, Sairopa, Secarna, SkylineDX, Thermosome, T3Pharma, Trained Immunity Discovery; Financial Interests, Personal, Speaker's Bureau: MSD; Financial Interests, Personal, Stocks or ownership: IO Biotech, Oncolytics, Sairopa, SkylineDX. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, Novartis, Merck Serono, Sun Pharma, Sanofi, Sandoz, Immunocore, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant, Advisory Role and Travel support: MSD, Pierre Fabre; Financial Interests, Personal, Other, Consultant and Advisory Role. 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