LBA44 Overall survival at 4 years of follow-up in a phase III trial of nivolumab plus ipilimumab combination therapy in advanced melanoma (CheckMate 067)

F.S. Hodi[1], V. Chiarion-Sileni[2], R. Gonzalez[3], J.J. Grob[4], P. Rutkowski[5], C.L. Cowey[6], C. Lao[7], D. Schadendorf[8], J. Wagstaff[9], R. Dummer[10], P.F. Ferrucci[11], M. Smylie[12], A.G. Hill[13], D. Hogg[14], I. Marquez-Rodas[15], J. Jiang[16], J. Rizzo[17], J. Larkin[18], J. Wolchok[19]

[1]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA, [2]Melanoma and Esophageal Cancer Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy, [3]Division of Medical Oncology, University of Colorado Cancer Center, Denver, CO, USA, [4]Service de Dermatologie, Aix Marseille University, and APHM Hospital CHU Timone, Marseille, France, [5]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Institute - Oncology Center, Warsaw, Poland, [6]Melanoma and Genitourinary Oncology Program, Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA, [7]Oncology, University of Michigan, Ann Arbor, MI, USA, [8]Department of Dermatology - Hautklinik, University of Essen, Essen and German Cancer Consortium, Essen, Germany, [9]Medical Oncology, The College of Medicine, Swansea University, Swansea, UK, [10]Dermatology, Universitäts Spital, Zurich, Switzerland, [11]Oncology, European Institute of Oncology, Milan, Italy, [12]Department of Oncology, Cross Cancer Institute, Edmonton, AL, Canada, [13]Medical Oncology, Tasman Oncology Research, Southport, Australia, [14]Medical Oncology & Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [15]Medical Oncology, General University Hospital Gregorio Marañón, Madrid, Spain, [16]Global Biometric Sciences, Bristol-Myers Squibb, Princeton, NJ, USA, [17]Oncology Clinical Development, Bristol-Myers Squibb, Princeton, NJ, USA, [18]Medicine, The Royal Marsden Hospital NHS Foundation Trust, London, UK, [19]Melanoma & Immunotherapeutics, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA

Background: Previous results from the CheckMate 067 study demonstrated a significant improvement in objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) with nivolumab plus ipilimumab (NIVO+IPI) and NIVO alone vs IPI alone in patients (pts) with advanced melanoma. Here, we report a 4-year update from CheckMate 067, representing the longest follow-up of a phase 3 study evaluating checkpoint inhibitor combination therapy.

Methods: Treatment-naive pts (N = 945) were randomized 1:1:1 to (1) NIVO 1 mg/kg Q3W + IPI 3 mg/kg Q3W for 4 doses, followed by NIVO 3 mg/kg Q2W, (2) NIVO 3 mg/kg Q2W + placebo, or (3) IPI 3 mg/kg Q3W for 4 doses + placebo. Randomization was stratified by PD-L1 status, BRAF mutation status, and M stage. Pts were treated until progression or unacceptable toxicity. Co-primary endpoints were PFS and OS. Secondary endpoints included ORR and safety. While the study was not powered to compare the NIVO-containing groups, secondary objectives also included descriptive efficacy evaluations between NIVO+IPI and NIVO.

Results: At a minimum follow-up of 48 months, NIVO+IPI and NIVO continued to show a higher ORR and improved PFS and OS vs IPI (Table). Time from randomization to subsequent systemic therapy was longest with NIVO+IPI. Among pts alive at 4 years, 71% (113/159), 50% (69/138), and 39% (32/82) in the NIVO+IPI, NIVO, and IPI groups, respectively, were treatment free (off study treatment and had not received subsequent systemic therapy). No new safety signals were observed.

Table: LBA44

	NIVO+IPI (N = 314)	NIVO (N = 316)	IPI (N = 315)
ORR, % (95% CI)	58 (53–64)	45 (39–50)	19 (15–24)
Median PFS, mo (95% CI)	11.5 (8.7–19.3)	6.9 (5.1–10.2)	2.9 (2.8–3.2)
4-year PFS rates, % (95% CI)	37 (31–42)	31 (25–36)	9 (6–13)
Median OS, mo (95% CI)	NR (38.2–NR)	36.9 (28.3–NR)	19.9 (16.9–24.6)
4-year OS rates, % (95% CI)	53 (47–58)	46 (41–52)	30 (25–35)
BRAF mutant	62 (52–71)	50 (39–59)	33 (24–42)
BRAF wild-type	49 (42–55)	45 (38–52)	28 (22–35)
PD-L1 <5%	52 (45–58)	45 (38–52)	28 (22–35)
PD-L1 ≥5%	61 (48–71)	54 (42–64)	36 (25–47)
Median time from randomization to subsequent systemic therapy, mo (95% CI)	NR	25.2 (16.0–43.2)	8.1 (6.5–8.7)

Conclusions: Long-term survival was achieved with NIVO+IPI and NIVO alone in pts with advanced melanoma. Descriptive analyses suggest higher survival rates with NIVO+IPI, and a higher proportion of pts treatment free, than with NIVO alone. First-line NIVO+IPI may reduce the need for subsequent therapy or prolong the time to subsequent therapy when needed.

Clinical trial identification: NCT01844505.

Editorial acknowledgement: Professional medical writing and editorial assistance were provided by Melissa Kirk, PhD, and Cara Hunsberger at StemScientific, an Ashfield Company, funded by Bristol-Myers Squibb.

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

Funding: Bristol-Myers Squibb.

Disclosure: F.S. Hodi: Consultant: Merck. V. Chiarion-Sileni: Advisory boards: Bristol-Myers Squibb, Roche, MSD, Novartis, Merck Serono. R. Gonzalez: Grants and fees: BMS, Roche; Grants: Merck, Amgen, Incyte, Novartis, Checkmate Pharmaceuticals, Boston Biomedical, Takeda, Syndax, Reata, Array Biopharma, Dynavax, Prometheus, Eisai, Celldex New Link Genetics. J.J. Grob: Personal fees, advisory boards: Bristol-Myers Squibb, MSD, Roche, Novartis, Merck, Amgen, Pierre Fabre. P. Rutkowski: Personal fees, advisory board member: Blueprint Medicines; Personal fees, honoraria: Novartis, BMS, MSD, Roche, Amgen, Pfizer; Non-financial support: MSD. C.L. Cowey: Grants and personal fees, clinical research support, advisory board membership: Bristol-Myers Squibb. C. Lao: Research support: Bristol-Myers Squibb. D. Schadendorf: Grants and personal fees: BMS; Personal fees: Amgen, Boehringer Ingelheim, Leo Pharma, Roche, MSD, Incyte, Regeneron, 4SC, AstraZeneca, Immunocore, Pierre Fabre, Merck-EMD, Pfizer, Philogen, Array. J. Wagstaff: Grants, personal fees and consulting fees: Pfizer, Bristol-Myers Squibb, Roche, Merck, Astellas, Johnson and Johnson, AstraZeneca, Bayer. R. Dummer: Personal and consultancy fees: Novartis, Merck Sharp & Dhome, Bristol-Myers Squibb, Roche, Amgen, Taekda, Pierre Fabre. P.F. Ferrucci: Personal fees, non-financial support, advisory boards, travel: MSD, Bristol-Myers Squibb, Roche, Novartis. M. Smylie: Personal fees and honoraria: Bristol-Myers Squibb, Merck, Novartis, Roche. A.G. Hill: Personal fees, non-financial support, travel fees, honoraria: Bristol-Myers Squib; Non-financial support, travel fees: Merck. D. Hogg: Personal fees, advisory boards: Bristol-Myers Squibb, Merck, Novartis, Roche, EMD Serono. I. Marquez-Rodas: Personal and consulting fees: Novartis, Roche, Amgen, Pierre Fabre, Bristol-Myers Squibb, Merck. J. Jiang, J. Rizzo: Employee of Bristol-Myers Squibb. J. Larkin: Consulting fees, personal fees and grants: Eisai, Bristol-Myers Squibb, MSD, GlaxoSmithKline, Kymab, Pfizer, Novartis, Roche/Genentech, Secarna, Pierre Fabre, EUSA Pharma. J. Wolchok: Grants/fees, stock ownership at various companies, including: BMS, Ono, Celgene, Merck, Genentech, Apricity, Potenza, Tizona, Adaptive Biotech, and more. [see manuscript for full disclosure]