Squibb; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Merck Serono; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: MSD; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Novartis; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: Pierre Fabre; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Roche; Travel/Accommodation/Expenses: OncoSec. E.G.E. de Vries: Advisory/Consultancy: Daiichi Sankyo; Advisory/Consultancy: NSABP; Advisory/Consultancy: Sanofi; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Bayer; Research grant/Funding (institution): Chugai Pharma; Research grant/Funding (institution): CytomX Therapeutics; Research grant/Funding (institution): G1 Therapeutics; Research grant/Funding (institution): Genentech; Research grant/Funding (institution): Nordic Nanavector; Research grant/Funding (institution): Radius Health; Research grant/Funding (institution): Regeneron; Research grant/Funding (institution): Roche; Research grant/Funding (institution): Servier; Research grant/Funding (institution): Synthon; Non-remunerated activity/ies, Chair ESMO Cancer Medicines Working Group: ESMO; Non-remunerated activity/ies, Chair RECIST committee: RECIST; Non-remunerated activity/ies, Member ESMO-MCBS working group: ESMO-MCBS. C.U. Blank: Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): Bristol-Myers Squibb; Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): Novartis; Research grant/Funding (institution): NanoString; Honoraria (institution), Advisory/Consultancy: MSD; Honoraria (institution), Advisory/Consultancy: Roche; Honoraria (institution), Advisory/Consultancy: GSK; Honoraria (institution), Advisory/Consultancy: AZ; Honoraria (institution), Advisory/Consultancy: Pfizer; Honoraria (institution), Advisory/Consultancy: Lilly; Honoraria (institution), Advisory/Consultancy: GenMab; Honoraria (institution), Advisory/Consultancy: Pierre Fabre; Honoraria (self), Advisory/Consultancy: Third Rock Ventures; Shareholder/Stockholder/Stock options: Uniti Cars; Shareholder/Stockholder/Stock options: Immagene BV. M. Jalving: Honoraria (institution): Merck; Honoraria (institution): Bristol-Myers Squibb; Honoraria (institution): Novartis; Honoraria (institution): Pierre Fabre; Honoraria (institution): Tesaro; Honoraria (institution): AstraZeneca. All other authors have declared no conflicts of interest.

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1081MO Efficacy of ipilimumab plus nivolumab or ipilimumab plus fotemustine vs fotemustine in patients with melanoma metastatic to the brain: Primary analysis of the phase III NIBIT-M2 trial

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Background: Brain metastases (BM) represent a high-unmet medical need, in which the therapeutic potential of immune-checkpoint(s) (ICI) is being actively investigated. Temozolomide and fotemustine (FTM) have been the therapeutic mainstay of melanoma (MM) patients (pts) with BM for over two decades. The Italian Network for Tumor Biotherapy (NIBIT)-M1 trial firstly demostrated signs of activity of ipilimumab (Ipi) combined with FTM in a subset of 20 MM pts with active BM (Di Giacomo, *Lancet Oncol*, 2012), with a 3-year survival rate of 28% (Di Giacomo, *Annals Oncol*, 2015). Two subsequent phase II studies reported the efficacy of Ipi combined with nivolumab (Nivo) in MM pts with asymptomatic BM (Twabi, *NEJM 2018*; Long, *Lancet Oncol* 2018). We here report the results of the primary analysis of the NIBIT-M2 study, the first phase III trial that explored the efficacy of Ipi *plus* Nivo in MM pts with BM.

Methods: The NIBIT-M2 is a phase III, multicenter, open-label study in MM pts with active, untreated, and asymptomatic BM. *BRAF* wilde type or mutant pts were randomized to receive FTM (ARM A), the combination of Ipi and FTM (ARM B), or the combination of Ipi and Nivo (ARM C). Primary objective was overall survival (OS); among secondary were intracranial (*i*) objective response rate (*i*ORR), *i* disease control rate (*i*DCR), and progression free survival (PFS).

Results: From January 2013 to September 2018, 96 MM pts were enrolled, 80 randomized, and 76 were treated: 23 in ARM A, 26 in ARM B, and 27 in ARM C. With a median follow-up of 39 months (mo), median OS was 8.5 mo (CI, 95%: 4.8-12.2) for ARM A, 8.2 mo (CI, 95%: 2.0-14.3) for ARM B, and 29.2 mo (CI, 95%: not yet evaluable) for ARM C. The *i*ORR was 0%, 19.2% and 44.4% in ARM A, B, and C, respectively. The *i*DCR was 26.1%, 34.6% and 55.6% in ARM A, B, and C, respectively. Median PFS was 3.0 mo (CI, 95%: 2.3-3.6), 3.3 mo (CI, 95%: 1.2-5.4), and 8.4 mo (CI,95%: 4.2-12.7), in ARM A, B, and C, respectively.

Conclusions: Unlike Ipi *plus* FTM, Ipi *plus* Nivo significantly (p=0.009) improves the long-term survival of MM pts with BM, compared to FTM. Ipi *plus* Nivo should represent the treatment of choice in first line MM pts with BM.

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1082MO 5-year characterization of complete responses in patients with advanced melanoma who received nivolumab plus ipilimumab (NIVO+IPI) or NIVO alone

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Background: 5-year outcomes of patients (pts) with a CR to NIVO+IPI or NIVO alone and factors associated with continued CR or relapse are unknown. The current pooled analysis addresses these key questions, including a 12-mo CR landmark analysis used to decrease the time guarantee bias.

Methods: In this post hoc analysis, 5-yr data were pooled from the phase III CheckMate 066 and 067 studies and the phase II CheckMate 069 study of pts with treatment-naive, advanced melanoma. Analyzed pts received either the approved regimen of NIVO+IPI followed by NIVO monotherapy or NIVO monotherapy. Characteristics and outcomes of pts with a CR (by RECIST) were investigated, including 12-mo landmark survival analyses to determine the likelihood of being alive at 5-y among pts in CR by 12 mo (to mitigate the time guarantee bias).

Results: Minimum follow-up was 60 mo since randomization of the last pt in each study; pooled median mo of follow-up was 63 for NIVO+IPI (n=409) and 64 for NIVO (n=526). CRs were demonstrated in 96 (23%) NIVO+IPI pts and 102 (19%) NIVO pts; of CR pts alive at 5 yrs, 75/79 (95%) and 85/91 (93%) had not received subsequent systemic therapy. Baseline characteristics significantly associated with CR (Table) were M stage (NIVO+IPI), PD-L1 $\geq$ 5% (NIVO), normal lactate dehydrogenase (LDH; both) and fewer disease sites (both). Median duration of CR and median time to subsequent systemic therapy were not reached in either group. Median mo (Q1, Q3) to CR was 9.1 (2.8, 23.1) for NIVO+IPI and 11.8 (5.8, 26.5) for NIVO alone. In pts in CR at 12-mo, 5-y OS for NIVO+IPI and NIVO respectively was 85% and 86%; PFS was 84% and 82%.