

**LBA16**

**KEYNOTE-355: Final results from a randomized, double-blind phase III study of first-line pembrolizumab + chemotherapy vs placebo + chemotherapy for metastatic TNBC**

J. Cortés<sup>1</sup>, D.W. Cescon<sup>2</sup>, H.S. Rugo<sup>3</sup>, S-A. Im<sup>4</sup>, M. Md Yusof<sup>5</sup>, C. Gallardo<sup>6</sup>, O. Lipatov<sup>7</sup>, C.H. Barrios<sup>8</sup>, J. Perez-Garcia<sup>9</sup>, H. Iwata<sup>10</sup>, N. Masuda<sup>11</sup>, M. Torregroza Otero<sup>12</sup>, E. Gokmen<sup>13</sup>, S. Loi<sup>14</sup>, Z. Guo<sup>15</sup>, X. Zhou<sup>15</sup>, V. Karantza<sup>15</sup>, W. Pan<sup>15</sup>, P. Schmid<sup>16</sup>

<sup>1</sup> International Breast Cancer Center (IBCC), Quiron Group, Madrid and Barcelona, Spain; Vall d'Hebron Institute of Oncology, Barcelona, Spain; Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain, <sup>2</sup> Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada, <sup>3</sup> Department of Hematology/Oncology, University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA, <sup>4</sup> Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea, <sup>5</sup> Cancer Center, Pantai Hospital, Kuala Lumpur, Malaysia, <sup>6</sup> Oncology Institute, Arturo Lopez Perez Foundation, Santiago, Chile, <sup>7</sup> Department of Oncology, Republican Clinical Oncology Dispensary, Republic of Bashkortostan, Russian Federation, <sup>8</sup> Oncology Research Unit, Hospital São Lucas, PUCRS, Porto Alegre, Brazil, <sup>9</sup> International Breast Cancer Center (IBCC), Quiron Group, Barcelona, Spain, <sup>10</sup> Department of Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan, <sup>11</sup> Department of Surgery, Breast Oncology, National Hospital Organization Osaka National Hospital, Osaka, Japan, <sup>12</sup> Hematology & Oncology, Oncomedica S.A., Monteria, Colombia, <sup>13</sup> Medical Faculty, Ege University Medical School, Izmir, Turkey, <sup>14</sup> Division of Cancer Research, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; The Sir Peter MacCallum Department of Medical Oncology, University of Melbourne, Parkville, VIC, Australia, <sup>15</sup> Merck Research Laboratories, Merck & Co., Inc., Kenilworth, NJ, USA <sup>16</sup> Barts Cancer Institute, Centre for Experimental Cancer Medicine, London, UK

**Background**

A prior interim analysis of KEYNOTE-355 (NCT02819518) showed that first-line pembrolizumab (pembro) + chemotherapy (chemo) significantly improved PFS vs placebo (pbo) + chemo in patients (pts) with metastatic TNBC whose tumors expressed PD-L1 (CPS ≥10) (HR, 0.65, 95% CI, 0.49–0.86; one-sided *P*=0.0012 [*P*-value boundary, 0.00411]). We present final results for the dual primary endpoint of OS and other study endpoints.

**Methods**

847 pts with de novo metastasis or ≥6 mo DFI were randomized 2:1 to pembro + chemo (nab-paclitaxel, paclitaxel, or gemcitabine-carboplatin) or pbo + chemo for up to 35 administrations of pembro/pbo or until progression/intolerable toxicity. Pts were stratified by chemo type (taxane or gemcitabine-carboplatin), PD-L1 status (CPS ≥1 or <1) and prior (neo)adjuvant treatment with same-class chemo (yes or no). Dual primary endpoints are PFS (RECIST v1.1 by BICR) and OS in pts with PD-L1+ tumors (CPS ≥10 and ≥1) and all pts (ITT). ORR is a secondary endpoint. AEs were monitored throughout the study and graded per NCI CTCAE v4.0.

**Results**

As of June 15, 2021, median follow-up was 44.1 mo. Pembro + chemo significantly improved OS vs chemo alone in pts with CPS ≥10 tumors (Table). The *p*-value boundary for a significant OS benefit of pembro + chemo in pts with CPS ≥1 tumors was not met and formal testing in ITT was not performed. The benefit of pembro + chemo on PFS was consistent with the prior results. Pembro + chemo improved ORR in pts with CPS ≥10 tumors. For all endpoints, the pembro treatment effect increased with PD-L1 enrichment. Grade 3-5 treatment-related AE rates were 68.1% with pembro + chemo (2 deaths) vs 66.9% with chemo (0 deaths).

**Conclusions**

Pembro + chemo showed a statistically significant and clinically meaningful improvement in OS vs chemo alone in pts with previously untreated locally recurrent inoperable or metastatic TNBC whose tumors expressed PD-L1 (CPS ≥10). No new safety signals were identified. Table: LBA16

	CPS ≥10		CPS ≥1		ITT	
	P + Cn = 220	Cn = 103	P + Cn = 425	Cn = 211	P + Cn = 566	Cn = 281
OS, mo, median <sup>a</sup> (95% CI)						
23.0 (19.0 – 26.3)	16.1 (12.6 – 18.8)	17.6 (15.5 – 19.5)	16.0 (12.8 – 17.4)	17.2 (15.3 – 19.0)	15.5 (13.9 – 17.2)	

	CPS ≥10		CPS ≥1		ITT	
	P + Cn = 220	Cn = 103	P + Cn = 425	Cn = 211	P + Cn = 566	Cn = 281
OS, HR <sup>b</sup> (95% CI)	0.73 <sup>c</sup> (0.55 – 0.95)	0.86 <sup>d</sup> (0.72 – 1.04)	0.89 (0.76 – 1.05)			
PFS, mo, median <sup>a</sup> (95% CI)	9.7 (7.6 – 11.3)	5.6 (5.3 – 7.5)	7.6 (6.6 – 8.0)	5.6 (5.4 – 7.4)	7.5 (6.3 – 7.7)	5.6 (5.4 – 7.2)
PFS, HR <sup>b</sup> (95% CI)	0.66 (0.50 – 0.88)	0.75 (0.62 – 0.91)	0.82 (0.70 – 0.98)			
ORR, %(95% CI)	52.7 (45.9 – 59.5)	40.8 (31.2 – 50.9)	44.9 (40.1 – 49.8)	38.9 (32.2 – 45.8)	40.8 (36.7 – 45.0)	37.0 (31.4 – 42.9)

<sup>a</sup>From Kaplan-Meier method. <sup>b</sup>From a stratified Cox model. <sup>c</sup> $P=0.0093$ ; boundary of  $P=0.0113$  met. <sup>d</sup> $P=0.0563$ ; boundary of  $P=0.0172$  not met.

## Clinical trial identification

NCT02819518.

## Editorial acknowledgement

Medical writing and/or editorial assistance was provided by Christine McCrary Sisk. This assistance was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

## Legal entity responsible for the study

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

## Funding

Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

## Disclosure

J. Cortés: Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: Celgene; Financial Interests, Personal, Advisory Role: Celestial; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Biothera Pharmaceutical; Financial Interests, Personal, Advisory Role: Merus; Financial Interests, Personal, Advisory Role: Seattle Genetics; Financial Interests, Personal, Advisory Role: Daiichi Sankyo; Financial Interests, Personal, Advisory Role: Erytech; Financial Interests, Personal, Advisory Role: Athenex; Financial Interests, Personal, Advisory Role: Polyphor; Financial Interests, Personal, Advisory Role: Lilly; Financial Interests, Personal, Advisory Role: Servier; Financial Interests, Personal, Advisory Role: Merck Sharp & Dohme; Financial Interests, Personal, Advisory Role: GSK; Financial Interests, Personal, Advisory Role: Leuko; Financial Interests, Personal, Advisory Role: Bioasis; Financial Interests, Personal, Advisory Role: Clovis Oncology; Financial Interests, Personal, Advisory Role: Boehringer Ingelheim; Financial Interests, Personal, Advisory Role: Kyowa Kirin; Financial Interests, Personal, Advisory Role: 4D Pharma PLC; Financial Interests, Personal, Funding: Roche; Financial Interests, Personal, Funding: Novartis; Financial Interests, Personal, Funding: Celgene; Financial Interests, Personal, Funding: Eisai; Financial Interests, Personal, Funding: Pfizer; Financial Interests, Personal, Funding: Samsung Bioepis; Financial Interests, Personal, Funding: Lilly; Financial Interests, Personal, Funding: Merck Sharp & Dohme; Financial Interests, Personal, Funding: Daiichi Sankyo; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Institutional, Research Grant: Ariad Pharmaceuticals; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Baxalta GMBH/Servier Affaires; Financial Interests, Institutional, Research Grant: Bayer Healthcare; Financial Interests, Institutional, Research Grant: Eisai; Financial Interests, Institutional, Research Grant: F. Hoffmann-La Roche; Financial Interests, Institutional, Research Grant: Guardanth Health; Financial Interests, Institutional, Research Grant: Merck Sharp & Dohme; Financial Interests, Institutional, Research Grant: Pfizer; Financial Interests, Institutional, Research Grant: Piquor Therapeutics; Financial Interests, Institutional, Research Grant: Puma C; Financial Interests, Institutional, Research Grant: Queen Mary University of London; Financial Interests, Personal, Stocks/Shares: MedSIR; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Roche; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Novartis; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Eisai; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Pfizer; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Daiichi Sankyo. D.W. Cescon: Financial Interests, Institutional, Research Grant: Pfizer; Financial Interests, Institutional, Funding: GlaxoSmithKline, Inivata, Merck, Pfizer, Roche; Non-Financial Interests, Institutional, Funding: GlaxoSmithKline, Inivata, Merck, Pfizer, Roche; Financial Interests, Personal, Principal Investigator: GlaxoSmithKline, Merck, Pfizer, Roche; Financial Interests, Personal, Advisory Role: AstraZeneca, Dynamo Therapeutics, Exact Sciences, Gilead, GlaxoSmithKline, Merck, Novartis, Pfizer, Puma Biotechnology, Roche. H.S. Rugo: Financial Interests, Institutional, Research Grant: Pfizer, Merck, Novartis, Lilly, Roche, Daiichi, Seattle Genetics, MacroGenics, Sermonix, Boehringer Ingelheim, Polyphor, AstraZeneca, Ayala, Gilead; Financial Interests, Personal, Other, Honoraria: Puma, Mylan, Samsung. S. Im: Financial Interests, Personal, Invited Speaker: Novartis; Non-Financial Interests, Personal, Member of the

Board of Directors: Translational Research in Oncology; Financial Interests, Institutional, Research Grant: AstraZeneca, Daewoong, Eisai, Pfizer, Roche; Non-Financial Interests, Personal, Advisory Role: AstraZeneca, Amgen, Daichi Sankyo, Eli Lilly, Eisai, GSK, Hanmi, MSD, Novartis, Pfizer, Roche. M. Md Yusof: Non-Financial Interests, Personal and Institutional, Invited Speaker: Eli Lilly, Roche, Novartis, MSD, AstraZeneca, Eisai, MSD, Zuellig Pharma, GSK, Mundi Pharma; Financial Interests, Institutional, Funding: Mundi Pharma; Financial Interests, Institutional, Principal Investigator: MSD, Novartis, Genentech, Astella, AstraZeneca; Non-Financial Interests, Personal and Institutional, Advisory Role: Eli Lilly, Roche, Novartis, MSD, AstraZeneca, Eisai, MSD, Zuellig Pharma, GSK, Mundi Pharma; Non-Financial Interests, Personal, Leadership Role: Malaysian Oncological Society. C. Gallardo: Non-Financial Interests, Personal, Expert Testimony: AstraZeneca; Financial Interests, Personal, Speaker's Bureau: MSD, Roche, AstraZeneca, Novartis; Financial Interests, Personal, Advisory Board: MSD, Roche, AstraZeneca, Novartis; Financial Interests, Institutional, Principal Investigator: MSD, BMS, AstraZeneca. C.H. Barrios: Financial Interests, Personal, Invited Speaker: Boehringer-Ingelheim, GSK, Novartis, Pfizer, Roche/Genentech, Eisai, Bayer, MSD, AstraZeneca, Zodiac, Lilly, Sanofi; Financial Interests, Personal, Advisory Board: Boehringer-Ingelheim, GSK, Novartis, Pfizer, Roche/Genentech, Eisai, Bayer, MSD, AstraZeneca, Zodiac, Lilly, Sanofi; Financial Interests, Personal, Stocks/Shares: Biomarker, Tummi, MEDSir; Financial Interests, Institutional, Research Grant: Pfizer, Novartis, Amgen, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Roche/Genentech, Lilly, Sanofi, Taiho Pharmaceutical, Mylan, Merrimack, Merck, AbbVie, Astellas Pharma, BioMarin, Bristol Myers Squibb, Daiichi Sankyo, Abraxis Biosciences, AB Sc; Financial Interests, Personal, Advisory Role: Boehringer-Ingelheim, GSK, Novartis, Pfizer, Roche/Genentech, Eisai, Bayer, MSD, AstraZeneca, Zodiac, Lilly, Sanofi. J. Perez-Garcia: Financial Interests, Personal, Advisory Board: Roche, Lilly, Daiichi Sankyo, AstraZeneca. H. Iwata: Financial Interests, Personal, Advisory Board: Chugai, AstraZeneca, Lilly, Pfizer, Daiichi Sankyo, Kyowa Hakko Kirin, MSD; Financial Interests, Institutional, Funding: Chugai, AstraZeneca, Lilly, Pfizer, Daiichi Sankyo, Kyowa Hakko Kirin, MSD, Sanofi, Novartis, Bayer, Nihon kayaku, Boehringer Ingelheim; Non-Financial Interests, Personal, Principal Investigator: Chugai, AstraZeneca, Lilly, Pfizer, Daiichi Sankyo, Kyowa Hakko Kirin, MSD, Sanofi, Novartis, Bayer, Nihon kayaku, Boehringer Ingelheim; Financial Interests, Personal, Advisory Role: Chugai, AstraZeneca, Lilly, Pfizer, Daiichi Sankyo, Kyowa Hakko Kirin, MSD. N. Masuda: Financial Interests, Personal, Speaker's Bureau: Chugai, AstraZeneca, Pfizer, Eli-Lilly, Eisai; Non-Financial Interests, Personal, Member of the Board of Directors: JBCS (Japanese Breast Cancer Society), JBCRG (Japan Breast Cancer Research Group Association); Financial Interests, Institutional, Research Grant: Chugai, AstraZeneca, Kyowa-Kirin, MSD, Novartis, Pfizer, Eli-Lilly, Eisai, Sanofi, Daiichi Sankyo. E. Gokmen: Financial Interests, Personal and Institutional, Invited Speaker: Roche, Pfizer, BMS, Astellas, AstraZeneca, GEN, Amgen, Novartis; Financial Interests, Personal, Advisory Board: Roche, Pfizer, BMS, AstraZeneca, Novartis, GEN; Financial Interests, Personal, Stocks/Shares: Radius Health, Immunogen, 9 Meters. S. Loi: Non-Financial Interests, Personal, Expert Testimony: Seattle Genetics, Novartis, Bristol Meyers Squibb, Merck, AstraZeneca, Roche-Genentech; Financial Interests, Institutional, Expert Testimony: Aduro Biotech, Novartis, GlaxoSmithKline, Roche-Genentech, AstraZeneca, Silverback Therapeutics, G1 Therapeutics, PUMA Biotechnologies, Pfizer, Gilead Therapeutics, Seattle Genetics, Bristol Meyers Squibb; Financial Interests, Personal, Advisory Board: Akamara Therapeutics; Financial Interests, Institutional, Research Grant: Novartis, Bristol Meyers Squibb, Merck, Puma Biotechnology, Eli Lilly, Nektar Therapeutics AstraZeneca, Roche-Genentech, Seattle Genetics. Z. Guo: Financial Interests, Personal, Full or part-time Employment: Merck & Co., Inc.; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc. X. Zhou: Financial Interests, Personal, Full or part-time Employment: Merck & Co., Inc. V. Karantza: Financial Interests, Personal, Full or part-time Employment: Merck & Co., Inc.; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc. W. Pan: Financial Interests, Personal, Full or part-time Employment: Merck & Co., Inc.; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc. P. Schmid: Financial Interests, Personal, Advisory Board: AstraZeneca, Bayer, Boehringer, Ingelheim, Merck, Novartis, Pfizer, Puma, Roche, Eisai, Celgene; Financial Interests, Personal, Full or part-time Employment, Spouse: Roche; Financial Interests, Institutional, Research Grant: Astellas, AstraZeneca, Genentech, Novartis, Oncogenex, Roche, Medivation. All other authors have declared no conflicts of interest.