Conclusions: Pembro continues to show improvements in OS vs chemo as 1L treatment for metastatic NSCLC with PD-L1 TPS ≥50%. Despite the high crossover rate, 5-year OS was approximately doubled among pts who received pembro (31.9% vs 16.3%). Fewer pts who received pembro experienced grade 3−5 AEs vs those who received chemo. Long-term OS and durable responses were observed with pembro monotherapy.

Clinical trial identification: NCT02142738.

Editorial acknowledgement: Medical writing assistance was provided by Rozena Varghese, PharmD, CMPP, of ICON plc (North Wales, PA, USA). This assistance was funded by the study sponsor, 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: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Disclosure: J.R. Brahmer: Advisory/Consultancy: Merck. D. Rodriguez-Abreu: Honoraria (self), Advisory/Consultancy: BMS; Honoraria (self), Advisory/Consultancy: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self), Advisory/Consultancy: Boehringer Ingelheim; Honoraria (self), Advisory/Consultancy: Eli Lilly; Honoraria (self), Advisory/Consultancy: Roche; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self), Advisory/Consultancy: Pfizer. A.G. Robinson: Advisory/Consultancy, Research grant/Funding (institution): Merck; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Roche; Research grant/Funding (institution): Pfizer . R. Hui: Advisory/Consultancy, Speaker Bureau/Expert testimony: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: BMS; Advisory/Consultancy: Eli Lilly; Advisory/Consultancy, Speaker Bureau/Expert testimony: Novartis; Advisory/Consultancy, Speaker Bureau/Expert testimony: Roche. N. Peled: Honoraria (self), Research grant/Funding (self): AstraZeneca; Honoraria (self), Research grant/Funding (self): Boehringer Ingelheim; Honoraria (self), Research grant/Funding (self): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (self): Eli Lilly; Honoraria (self), Research grant/Funding (self): Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Honoraria (self), Research grant/Funding (self): Novartis; Honoraria (self), Research grant/Funding (self): Pfizer; Honoraria (self), Research grant/Funding (self): NovellusDx; Honoraria (self), Research grant/Funding (self): Foundation Medicine; Honoraria (self), Research grant/Funding (self): Guardant360. S. Cuffe: Travel/Accommodation/Expenses: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Travel/Accommodation/Expenses: Roche; Travel/Accommodation/Expenses: Bristol-Myers Squibb; Travel/Accommodation/Expenses: Pfizer; Travel/Accommodation/Expenses: Amgen. M. O'Brien: Advisory/Consultancy: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: AbbVie; Advisory/Consultancy: Pierre Fabre; Advisory/Consultancy: Boehringer Ingelheim; Speaker Bureau/Expert testimony: Roche. K. Hotta: Honoraria (self), Research grant/Funding (institution): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (institution): Eli Lilly; Honoraria (self), Research grant/Funding (institution): AstraZeneca; Honoraria (self): Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Honoraria (self): Ono; Honoraria (self): Kayaku; Honoraria (self): Taiho; Honoraria (self): Chugai. T.A. Leal: Advisory/Consultancy: Takeda; Advisory/Consultancy: Novocure; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Genentech; Advisory/Consultancy: Inivata; Advisory/Consultancy: Merck; Advisory/Consultancy: PharmaMar; Advisory/Consultancy: EMD Serono. J.W. Riess: Research grant/Funding (institution): Merck Sharp & Dohme Corp; Research grant/Funding (self): Spectrum; Research grant/Funding (institution): Revolution Medicines; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): GlaxoSmithKline; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Honoraria (self): Blueprint Medicines; Honoraria (self): Medtronic; Advisory/Consultancy: Boehringer Ingelheim. E. Jensen: Full/Part-time employment: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. B. Zhao: Full/Part-time employment: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. M.C. Pietanza: Full/Part-time employment: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. M. Reck: Honoraria (self), Advisory/Consultancy: Amgen; Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self), Advisory/Consultancy: Bristol-Myers Squibb; Honoraria (self), Advisory/Consultancy: Boehringer Ingelheim; Honoraria (self), Advisory/Consultancy: Celgene; Honoraria (self), Advisory/Consultancy: Merck; Honoraria (self), Advisory/Consultancy: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; Honoraria (self), Advisory/Consultancy: Eli Lilly; Honoraria (self), Advisory/Consultancy: Pfizer; Honoraria (self), Advisory/Consultancy: AbbVie; Honoraria (self), Advisory/Consultancy: Roche; Honoraria (self), Advisory/Consultancy: Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2284

LBA52 EMPOWER-Lung 1: Phase III first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

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Background: EMPOWER-Lung 1 is a multicentre, open-label, global, phase III study of cemiplimab, an anti−PD-1, in patients (pts) with treatment-naïve stage IIIB, IIIC, or IV squamous or non-squamous NSCLC with PD-L1 expressed in ≥50% of tumour cells.

Methods: Pts were randomised 1:1 to receive cemiplimab 350 mg Q3W IV or investigator's choice of chemo. Crossover (CO) from chemo to cemiplimab was allowed following progression. The primary endpoints were overall survival (OS) and progression-free survival (PFS) per blinded Independent Review Committee. A prespecified interim analysis was performed after 50% of OS events. Data are presented per intention-to-treat (ITT) and in a PD-L1 ≥50% ITT population which comprised only pts with PD-L1 ≥50% by 22C3 per instruction for use (after recommended retesting in some pts). Data cut-off was 1 March 2020.

Results: In the ITT population (median follow-up: 13.1 months), median OS was 22.1 months (95% CI: 17.7−not evaluable [NE]) with cemiplimab (n=356) vs 14.3 months (95% CI: 11.7−19.2) with chemo (n=354; HR, 0.68; 95% CI: 0.53−0.87; P=0.002). Median PFS was 6.2 months (95% CI: 4.5−8.3) with cemiplimab vs 5.6 months (95% CI: 4.5−6.1) with chemo (HR, 0.59; 95% CI: 0.49−0.72; P<0.0001). In the PD-L1 ≥50% ITT population (median follow-up: 10.8 months), median OS was not reached (95% CI: 17.9−NE) with cemiplimab (n=283) vs 14.2 months (95% CI: 11.2−17.5) with chemo (n=280; HR, 0.57; 95% CI: 0.42−0.77; P=0.0002). Median PFS was 8.2 months (95% CI: 6.1−8.8) with cemiplimab vs 5.7 months (95% CI: 4.5−6.2) with chemo (HR, 0.54; 95% CI: 0.43−0.68; P<0.0001). CO rate to cemiplimab was 73.9%. In the ITT population, cemiplimab was associated with higher response rate (36.5% vs 20.6%), longer median duration of response (21.0 months vs 6.0 months) and lower rates of Grade ≥3 adverse events regardless of attribution (37.2% vs 48.5%) compared to chemo.

Conclusions: In this study, 1L cemiplimab monotherapy significantly improved OS and PFS vs chemo in pts with advanced NSCLC with PD-L1 ≥50%, despite high CO rate, providing rationale for cemiplimab as a new treatment option for this patient population.

Clinical trial identification: NCT03088540.

Editorial acknowledgement: Medical writing support was provided by Emmanuel Ogunnowo, PhD of Prime, Knutsford, UK, funded by Regeneron Pharmaceuticals, Inc., and Sanofi.

Legal entity responsible for the study: Regeneron Pharmaceuticals, Inc. and Sanofi.

Funding: Regeneron Pharmaceuticals, Inc. and Sanofi.

Disclosure: A. Sezer: Research grant/Funding (institution): Roche; Research grant/Funding (self): MSD Oncology; Research grant/Funding (self): Regeneron Pharmaceuticals, Inc.; Research grant/Funding (self): Novartis; Travel/Accommodation/Expenses: Bristol-Myers Squibb; Research grant/Funding (institution): Merck Serono; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Lily; Research grant/Funding (institution): Johnson & Johnson; Research grant/Funding (institution): Sanofi. M. Gümüş: Honoraria (institution), outside the submitted work: Roche; Honoraria (institution), outside the submitted work: Merck Sharp & Dohme; Honoraria (institution), outside the submitted work: Gen İlaç; Honoraria (institution), outside the submitted work: Novartis. N. Rizvi: Advisory/Consultancy, outside the submitted work: AbbVie; Advisory/Consultancy, outside the submitted work: Apricity; Advisory/Consultancy, outside the submitted work: AstraZeneca; Advisory/Consultancy, outside the submitted work: Boehringer; Advisory/Consultancy, outside the submitted work: Calithera; Advisory/Consultancy, outside the submitted work: Dracen; Advisory/Consultancy, outside the submitted work: Editas; Advisory/Consultancy, outside the submitted work: EMD Sorono; Advisory/Consultancy, outside the submitted work: G1 Therapeutics; Advisory/Consultancy, outside the submitted work: Genentech; Advisory/Consultancy, outside the submitted work: Gilead; Advisory/Consultancy, outside the submitted work: GSK; Advisory/Consultancy, outside the submitted work: Illumina; Advisory/Consultancy, outside the submitted work: Lilly; Advisory/Consultancy, outside the submitted work: Merck; Advisory/Consultancy, outside the submitted work: Neogenomics; Advisory/Consultancy, outside the submitted work: Novartis; Advisory/Consultancy, Shareholder/Stockholder/Stock options, outside the submitted work: Brooklyn ImmunoTherapeutics; Advisory/Consultancy, outside the submitted work: Takeda; Advisory/Consultancy, Shareholder/Stockholder/Stock options, outside the submitted work: Bellicum; Licensing/Royalties, Patent (pending) filed by MSKCC, in the form of royalties, on

"determinants of cancer response to immunotherapy, (PCT/US2015/062208)" licensed to Personal Genome Diagnostics: Personal Genome Diagnostics; Shareholder/Stockholder/Stock options, outside the submitted work: Gritstone. S. Li, S. Lee, G. Gullo: Shareholder/Stockholder/Stock options, Full/Part-time employment: Regeneron Pharmaceuticals, Inc. I. Lowy, P. Rietschel: Shareholder/Stockholder/Stock options, Licensing/Royalties, Full/Part-time employment, Patents pending: Regeneron Pharmaceuticals, Inc. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2285

LBA53 Precision immuno-oncology for advanced non-small cell lung cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): A first analysis of the PIONeeR study

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Background: PIONeeR aims to predict response/resistance to PD1/L1 ICIs in advanced NSCLC pts through comprehensive agnostic multiparametric and longitudinal biomarkers assessment. These ICIs significantly improve long-term outcome in 20% of advanced NSCLC pts but to date, no robust biomarker predicts primary or secondary resistance.

Methods: Advanced NSCLC pts with available archived tumor tissue treated with either nivolumab, pembrolizumab or atezolizumab, alone (2nd line min) or combined with chemotherapy (1st line), were systematically re-biopsied and blood-sampled at 6wks (V2) of treatment. ORR was assessed by RECIST 1.1 every 6wks. Quantification of circulating and tumor infiltrating immune cells and PD-L1 mediated inhibition (Immunoscore® IC) were performed by FACS and multiplex IHC coupled to digital pathology respectively. Endothelial activation, blood soluble factors, PK and TMB through WES were also assessed.

Results: The first 100 pts are mainly male (64%), smokers (91-8%), <65yrs (55%), with an ECOG PS0/1 (97%), treated in 2nd line setting (86%). Tumors were mainly ADC (57%) with ≥1% PDL1 expression in 38% of the cases. 21% were still on treatment at data cut-off. V2 biopsy was available in 46% of cases; 33 pts progressed before the 6wks milestone, and 13 pts were considered as responders. Median PFS was 2.99 months (mo) [95%CI: 2.43 − 4.83] and median OS was 11.01 mo [95%CI: 8.21 - NA]. At baseline (VS), PD-L1 tumor cell percentage was significantly higher in responders, as well as tumor infiltration by cytotoxic lymphocytes (cTILs) (median: 160 vs 410 cells/mm^2). Five non-responders presented high cTILs densities (up to 1800 cells/mm^2), associated either to no PDL1 expression, high infiltration of Treg cells in the tumor or weak PD1 expression on cTILs. High immune cell densities at the periphery and in the tumor were associated with survival. Immune cell infiltration and PD-L1+ cell density increased from VS to V2, as well as proximity between these cells. Massive PK variability among patients was found.

Conclusions: Immune cells quantification and characterization add value to clinical factors to predict advanced NSCLC response/resistance to ICIs.

Clinical trial identification: NCT03493581, Release date: February 2018.

Legal entity responsible for the study: Assistance Publique Hôpitaux de Marseille (AP-HM).

Funding: French National Research Agency (ANR-17-RHUS-0007).

Disclosure: F. Barlesi: Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): ACEA; Research grant/Funding (institution): Amgen; Honoraria (self), Research grant/Funding (institution): AstraZeneca; Honoraria (self), Research grant/Funding (institution): Bayer; Honoraria (self), Research grant/Funding (institution): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (institution): Boehringer-Ingelheim; Research grant/Funding (institution): Eisai; Honoraria (self), Research grant/Funding (institution): Eli Lilly Oncology; Honoraria (self), Research grant/Funding (institution): F. Hoffmann-La Roche Ltd.; Research grant/Funding (institution): Genentech; Research grant/Funding (institution): Ipsen; Research grant/Funding (institution): Ignyta; Research grant/Funding (institution): Innate Pharma; Research grant/Funding (institution): Loxo; Research grant/Funding (institution): MedImmune; Honoraria (self), Research grant/Funding (institution): Novartis; Honoraria (self), Research grant/Funding (institution): Merck; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self), Research grant/Funding (institution): Pierre Fabre; Honoraria (self), Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): Sanofi-Aventis; Honoraria (self), Research grant/Funding (institution): Takeda. F. Monville: Full/Part-time employment: HalioDx. J. le treut: Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Boehringer; Honoraria (self): Roche. C. Audigier-Valette: Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: Boehringer Ingelheim; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: BMS; Advisory/Consultancy, Travel/Accommodation/Expenses: Lilly; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: Novartis; Honoraria (institution), Advisory/Consultancy, Travel/Accommodation/Expenses: Roche; Honoraria (institution), Advisory/Consultancy: MSD; Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy: AbbVie; Advisory/Consultancy: FoundationOne; Advisory/Consultancy: Takeda. S. Garcia: Travel/Accommodation/Expenses: MSD. J. Ciccolini: Research grant/Funding (institution), Travel/Accommodation/Expenses: AstraZeneca; Research grant/Funding (institution): Institut Roche; Honoraria (self): Pierre Fabre; Honoraria (self): BMS; Honoraria (self): Novartis; Honoraria (self): Lilly; Honoraria (self): Ipsen. P. Outters: Full/Part-time employment: HalioDx. J. Mazieres: Honoraria (self), Research grant/Funding (self): Roche; Honoraria (self), Research grant/Funding (self): AstraZeneca; Honoraria (self), Research grant/Funding (self): Pierre Fabre; Honoraria (self): Takeda; Honoraria (self), Research grant/Funding (self): BMS; Honoraria (self): MSD; Honoraria (self): Hengrui; Honoraria (self): Blueprint; Honoraria (self): Daiichi; Honoraria (self): Novartis. M. Pérol: Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Roche; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: AstraZeneca; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Eli Lilly; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: MSD; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: BMS; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Boehringer Ingelheim; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Honoraria (self), Advisory/Consultancy: Novartis; Honoraria (self), Speaker Bureau/Expert testimony: Amgen; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Takeda; Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Chugai. E. Vivier: Shareholder/Stockholder/Stock options, Full/Part-time employment, Officer/Board of Directors: Innate Pharma. J. Fieschi: Officer/Board of Directors: HalioDx. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2286