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EPICS Congress Coverage: ASCO 2021 – Focus on Lung Cancer

Friday, June 11, 2021
10.00 AM – 2.00 PM EDT/16.00 – 20.00 CEST (4-hour meeting)

Chair: Corey J. Langer, MD, FACP

Faculty

- Julie Brahmer, MD – Sidney Kimmel Cancer Center at Johns Hopkins
- Enriqueta Felip, MD, PhD – Vall d'Hebron University Hospital
- Marina Garassino, MD – University of Chicago Medicine
- David Jablons, MD – University of California San Francisco
- Natasha Leighl, MD – Princess Margaret Cancer Centre, University Health Network
- Paul Paik, MD – Memorial Sloan Kettering Cancer Center
- Lynette Sholl, MD – Dana-Farber Cancer Institute
- David Spigel, MD – Sarah Cannon Cancer Center

AGENDA

Time (EDT)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM (5 min)	Welcome and Introductions	Corey J. Langer, MD, FACP
10.05 AM – 10.20 AM (15 min)	**Immunotherapy in Stage I–III NSCLC** *Resectable* • 8500: IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIA non-small cell lung cancer (NSCLC). Wakelee et al • 8503: Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). Spicer et al • 8517: Residual ctDNA after treatment predicts early relapse in patients with early-stage NSCLC. Gale et al	David Jablons, MD

	Unresectable Stage III • 8511: Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial. Spigel et al • 8512: KEYNOTE-799: Phase 2 trial of pembrolizumab plus platinum chemotherapy and radiotherapy for unresectable, locally advanced, stage 3 NSCLC. Jabbour et al • TPS8584 Randomized phase III Trial of MEDI4736 (durvalumab) as concurrent and consolidative therapy or consolidative therapy alone for unresectable stage 3 NSCLC: A trial of the ECOG-ACRIN Cancer Research Group (EA5181). Varlotto et al	
10.20 AM – 10.45 AM (25 min)	**Discussion** • Which approach should be standard for perioperative IO – adjuvant or neoadjuvant? • Should chemotherapy be part of neoadjuvant regimens? • Do the current data from phase III trials warrant a change in practice? • Will surrogate endpoints be enough to influence therapeutic decision-making, or will survival data dictate standard of practice? • Have any predictive biomarkers emerged for perioperative IO? • Please comment on the role of ctDNA (abstract 8517) in selecting patients for early stage NSCLC treatment • What patients will be candidates for IO in adjuvant? For IO in neoadjuvant? Please comment on biomarker (driver mutations, PD-L1 status) as well as disease stage (IB, II, IIIA) • Should we continue to investigate other approaches for IO in unresectable stage III NSCLC (eg, with CRT)? Is concurrent preferable to sequential? • Please comment on the potential role of EA5181 vs PACIFIC-2 regarding concurrent CRT-IO	
10.45 AM – 11.00 AM (15 min)	**Immunotherapy in Stage IV NSCLC** • 9000: First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell	Marina Garassino, MD

	lung cancer (NSCLC): Two-year update from CheckMate 9LA. Reck et al • 9016: Nivolumab (NIVO) plus ipilimumab (IPI) versus chemotherapy (chemo) as first-line (1L) treatment for advanced non-small cell lung cancer (NSCLC): 4-year update from CheckMate 227. Paz-Ares et al • 9001: Outcomes of anti-PD-(L1) therapy in combination with chemotherapy versus immunotherapy (IO) alone for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score 1-49%: FDA pooled analysis. Akinboro et al • 9085: Cemiplimab monotherapy as first-line (1L) treatment of patients with brain metastases from advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥ 50%: EMPOWER-Lung 1 subgroup analysis. Ozguroglu et al • 9046: Results from a phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic non-small cell lung carcinoma. Clay et al • 2504: COM701 with or without nivolumab: Results of an ongoing phase 1 study of safety, tolerability and preliminary antitumor activity in patients with advanced solid malignancies (NCT03667716). Vaena et al • 2583: AdvanTIG-105: Phase 1 dose-escalation study of anti-TIGIT monoclonal antibody ociperlimab (BGB-A1217) in combination with tislelizumab in patients with advanced solid tumors. Frentzas et al	
11.00 AM – 11.25 AM (25 min)	**Discussion** • Do long-term data reveal an advantage for targeting both PD-1 and CTLA-4? Is there any cohort of patients who benefit from nivo-ipi ahead of KEYNOTE-189/407? • How to view CM-227 (nivo-ipi) data in the context of KN-598 (pembro-ipi)? • How do you choose IO-chemo or IO mono for those patients with PD-L1 >50%? Please comment on Dr Peters' presentation at ESMO plenary	

	• How do you treat PD-L1 1%–49% (single-agent IO vs chemo-IO)? • Is there a cohort in the 1%–49% group that we can identify by biomarker that would benefit with single-agent IO vs chemo? • Are the current PD-L1 cutoffs (1%, 50%) sufficient, or do we need to get more granular, especially for ≥50% or 1%–49%? • Are there other biomarkers besides PD-L1 for IO? Can we integrate TMB? • What is your clinical assessment of cemiplimab in patients with brain mets? Squamous histology? • Given the positive outcome of relatlimab (antibody inhibiting LAG-3) in melanoma (RELATIVITY-047 first-line melanoma, #9503), how do we reconcile regarding the need to enhance LAG-3 activity in NSCLC by eftilagimod (LAG-3 agonist)?	
11.25 AM – 11.40 AM (15 min)	***EGFR* (Common Mutations): Resectable and Metastatic** *Resectable* • 8501: Adjuvant gefitinib versus cisplatin/vinorelbine in Japanese patients with completely resected, EGFR-mutated, stage II-III non-small cell lung cancer (IMPACT, WJOG6410L): A randomized phase 3 trial. Tada et al • 8502: CTONG1103: Final overall survival analysis of the randomized phase 2 trial of erlotinib versus gemcitabine plus cisplatin as neoadjuvant treatment of stage IIIA-N2 EGFR-mutant non–small cell lung cancer. Wu et al *Metastatic* • 9081: Update analysis of NEJ009: Gefitinib alone (G) versus gefitinib plus chemotherapy (GCP) for non-small cell lung cancer with mutated EGFR. Miyauchi et al • 9006: Amivantamab in combination with lazertinib for the treatment of osimertinib-relapsed, chemotherapy-naïve EGFR mutant (EGFRm) non-small cell lung cancer (NSCLC) and potential biomarkers for response. Bauml et al	David Spigel, MD

	• 9007: Efficacy and safety of patritumab deruxtecan (HER3-DXd) in EGFR inhibitor-resistant, EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC). Janne et al • 9013: Randomized phase III trial of aumolertinib (HS-10296, Au) versus gefitinib (G) as first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) and EGFR exon 19 del or L858R mutations (EGFRm). Lu et al • 9124: Effect of continuing osimertinib with chemotherapy in the post-progression setting on progression-free survival among patients with metastatic epidermal growth factor receptor (EGFR) positive non-small cell lung cancer. Patil et al	
11.40 AM – 12.00 PM (20 min)	**Discussion** • Is osimertinib the SOC for adjuvant therapy in resected, *EGFR* mutation-positive NSCLC? What about patients with stage IB disease? • Do you test patients with resectable NSCLC for oncogenic drivers other than EGFR? • What is the role of first-line combinations with chemotherapy or antiangiogenic agents? • What are your current testing practices with patients who progress on osimertinib (testing vs no testing; tissue vs liquid, tissue + liquid)? • What is your preferred management approach post-osimertinib? Is there a role for continuing TKI? • Will there be a role for amivantamab or patritumab frontline? • Is there any way to differentiate aumolertinib from osimertinib?	
12.00 PM – 12.05 PM (5 min)	**BREAK**	
12.05 PM – 12.15 PM (10 min)	***EGFR* (Exon 20 and Other Uncommon Mutations)** • 9014: Mobocertinib (TAK-788) in EGFR exon 20 insertion (ex20ins)+ metastatic NSCLC (mNSCLC): Additional results from platinum-pretreated patients (pts) and EXCLAIM cohort of phase 1/2 study. Ramalingam et al • 9052: Amivantamab compared with real-world therapies in patients with NSCLC with EGFR Exon 20 insertion mutations who have	Natasha Leighl, MD

	progressed after platinum doublet chemotherapy. Minchom et al • 9008: Preliminary safety and efficacy results from phase 1 studies of DZD9008 in NSCLC patients with EGFR Exon20 insertion mutations. Yang et al • 9077: Safety and activity of CLN-081 (TAS6417) in NSCLC with EGFR Exon 20 insertion mutations (Ins20). Piotrowska et al • 9093: CNS activity of poziotinib in NSCLC with exon 20 insertion mutations. Le et al • 9068: Neratinib efficacy in a subgroup of patients with EGFR exon 18-mutant non-small cell lung cancer (NSCLC) and central nervous system (CNS) involvement: Findings from the SUMMIT basket trial. Goldman et al	
12.15 PM – 12.35 PM (20 min)	**Discussion** • What is your current first-line approach for patients with *EGFR* exon 20 insertions? Do these patients also not benefit from IO? • Is amivantamab now SOC for *EGFR* exon 20 insertions? • If approved, what would be the role of mobocertinib for exon 20 insertions post-platinum? • Is there a need for more awareness of different types of *EGFR* exon 20 aberrations (insertions, point mutations)?	
12.35 PM – 12.45 PM (10 min)	**Oncogenic Mutations** *KRAS* • 9003: Overall survival and exploratory subgroup analyses from the phase 2 CodeBreaK 100 trial evaluating sotorasib in pretreated KRAS p.G12C mutated non-small cell lung cancer. Skoulidis et al • 9025: Anti PD-(L)1 in KRAS mutant advanced nsclcs: A meta-analysis of randomized controlled trials. Landre et al • 9088: Chemo-immunotherapy outcomes of KRAS-G12C mutant lung cancer compared to other molecular subtypes of KRAS-mutant lung cancer. Arbour et al *HER2* • 9015: Combination of trastuzumab, pertuzumab and docetaxel in patients with advanced non-small cell lung cancer (NSCLC) harboring HER2	Enriqueta Felip, MD, PhD

	mutation: Final results from the IFCT-1703 R2D2 trial. Mazieres et al *MET (Exon 14 and Other Alterations)* • 9020: Capmatinib in MET exon 14-mutated, advanced NSCLC: Updated results from the GEOMETRY mono-1 study. Wolf et al • 9111: Capmatinib efficacy in patients with NSCLC identified as METex14 using an NGS-based liquid biopsy assay: Results from the GEOMETRY mono-1 study. Heist et al • 9012: METex14 ctDNA dynamics & resistance mechanisms detected in liquid biopsy (LBx) from patients (pts) with METex14 skipping NSCLC treated with tepotinib. Paik et al • 9084: Intracranial activity of tepotinib in patients (pts) with MET exon 14 (METex14) skipping NSCLC enrolled in VISION. Patel et al • 9021: Tepotinib in patients (pts) with advanced non-small cell lung cancer (NSCLC) with MET amplification. Le et al	
12.45 PM – 1.05 PM (20 min)	**Discussion** • How would you compare the efficacy and safety of sotorasib and adagrasib? • If sotorasib is approved in second line, would this become your SOC in patients with *KRAS* G12C? • Is there a role for KRAS inhibitors in newly diagnosed patients? • What is your perspective on the dose selected for both KRAS inhibitors, given Amgen's latest announcement to test sotorasib 240 mg QD vs 960 mg tested in the pivotal trial? • How do you view the role of KRAS inhibitors in first-line and early NSCLC? Can we combine safely with IO? • Is there a best approach emerging for *HER2* mutations – antibodies, ADCs, TKIs? • What is your first-line approach for patients with *MET* exon 14 mutations? • What is the status of *MET* amplification as a target? What is the best definition of "*MET* amplified"? Is tissue the only biopsy source to assess this?	

1.05 PM – 1.15 PM (10 min)	**Oncogenic Fusions** *ALK* • 9011: Early circulating tumor (ct) DNA dynamics and efficacy of lorlatinib: Analysis from the CROWN study. Soo et al *ROS1* • 9040: Phase II study of brigatinib in ROS1 positive non-small cell lung cancer (NSCLC) patients previously treated with crizotinib: Barossa cohort 2. Daga et al *NTRK* • 9109: Long-term efficacy and safety of larotrectinib in patients with TRK fusion-positive lung cancer. Lin et al *RET* • 9065: Updated overall efficacy and safety of selpercatinib in patients (pts) with RET fusion+ non-small cell lung cancer (NSCLC). Besse et al • 9032: Response to selpercatinib versus prior systemic therapy in patients (pts) with RET fusion+ non-small-cell lung cancer (NSCLC). Drilon et al • 9089: Safety and efficacy of pralsetinib in patients with advanced RET fusion-positive non-small cell lung cancer: Update from the ARROW trial. Curigliano et al • 3008: BOS172738, a highly potent and selective RET inhibitor, for the treatment of RET-altered tumors including RET-fusion+ NSCLC and RET-mutant MTC: Phase 1 study results. Schoffski et al	Paul Paik, MD
1.15 PM – 1.35 PM (20 min)	**Discussion** • Is alectinib the first-line SOC for ALK, or would you consider first-line use of brigatinib, ensartinib, or lorlatinib, if available in this setting? Do any of these agents potentially displace alectinib? • Which is SOC for *ROS1* – crizotinib or entrectinib (or agnostic)? • What is your first-line approach for patients with an *NTRK* or *RET* fusion? • Is there any role for combinations of TKIs + chemotherapy for oncogenic fusions?	

	• What is your approach for subsequent lines of therapy?	
1.35 PM – 1.40 PM (5 min)	**Other Targets in NSCLC/SCLC** • 9058: TROPION-PanTumor01: Dose analysis of the TROP2-directed antibody-drug conjugate (ADC) datopotamab deruxtecan (Dato-DXd, DS-1062) for the treatment (Tx) of advanced or metastatic non-small cell lung cancer (NSCLC). Meric-Bernstam et al • 8510: Updated results from a phase 1 study of AMG 757, a half-life extended bispecific T-cell engager (BiTE) immuno-oncology therapy against delta-like ligand 3 (DLL3), in small cell lung cancer (SCLC). Owonikoko et al • TPS8588 A phase I, open-label, dose-escalation trial of BI 764532, a DLL3/CD3 bispecific antibody, in patients (pts) with small cell lung carcinoma (SCLC) or other neuroendocrine neoplasms expressing DLL3. Wermke et al • 8562: The clinical efficacy of olaparib monotherapy or combination with ceralasertib (AZD6738) in relapsed small cell lung cancer. Park et al	Julie Brahmer, MD
1.40 PM – 1.55 PM (15 min)	**Discussion** • What is your assessment of the TROPION data? • What is your assessment of bispecific agents (eg, AMG 757) to target DLL3 in SCLC? Is BI 764532 differentiated from AMG 757? • How do you manage patients with ES-SCLC who progress after first-line chemo-IO? • Is lurbinectedin SOC for R/R SCLC, in light of the ATLANTIS trial outcome? • Please comment on the role of DNA damage repair agents for SCLC (and NSCLC)	
1.55 PM – 2.00 PM (5 min)	Wrap-up Comments and Adjourn	Corey J. Langer, MD, FACP