Meet The Professor Current and Future Role of Immunotherapy in the Management of Lung Cancer

> Stephen V Liu, MD Associate Professor of Medicine Georgetown University Hospital Washington, DC



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Dr Love — Disclosures

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ONCOLOGY TODAY WITH DR NEIL LOVE

Key Presentations on Lung Cancer from the 2021 ASCO Annual Meeting



DR JOEL NEAL STANFORD UNIVERSITY









Dr Joel Neal Key Presentations on Lun Oncology Today with Dr Neil Love —

(30)

(15)

Meet The Professor Management of BRAF-Mutant Melanoma

Monday, November 29, 2021 5:00 PM – 6:00 PM ET

> Faculty Jason J Luke, MD



Meet The Professor Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

> Tuesday, November 30, 2021 5:00 PM – 6:00 PM ET

> > Faculty A Oliver Sartor, MD



Meet The Professor Optimizing the Management of Acute Myeloid Leukemia

Wednesday, December 1, 2021 5:00 PM – 6:00 PM ET

Faculty Andrew H Wei, MBBS, PhD



Meet The Professor Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Thursday, December 2, 2021 5:00 PM – 6:00 PM ET

> Faculty Hope S Rugo, MD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of ER-Positive Breast Cancer

> Tuesday, December 7, 2021 8:00 PM – 9:45 PM ET

Faculty

Aditya Bardia, MD, MPH Joyce O'Shaughnessy, MD Kevin Kalinsky, MD, MS

> Moderator Erika Hamilton, MD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

> Wednesday, December 8, 2021 8:00 PM – 10:00 PM ET

Faculty

Carey K Anders, MD Sara Virginia F Borges, MD, MMSc Ian I

Sara Hurvitz, MD Ian E Krop, MD, PhD

Moderator Lisa Carey, MD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Triple-Negative Breast Cancer

> Thursday, December 9, 2021 8:00 PM – 9:45 PM ET

FacultyRita Nanda, MDMelinda Telli, MDPeter Schmid, FRCP, MD, PhD

Moderator Hope S Rugo, MD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Chronic Lymphocytic Leukemia

> Friday, December 10, 2021 7:30 AM – 9:30 AM ET

Faculty

Nitin Jain, MD Anthony R Mato, MD, MSCE John M Pagel, MD, PhD Jennifer Woyach, MD

Moderator John N Allan, MD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Hodgkin and Non-Hodgkin Lymphoma

> Friday, December 10, 2021 11:30 AM – 1:30 PM ET

Faculty

Jeremy Abramson, MD Martin Dreyling, MD, PhD Loretta J Nastoupil, MD Gilles Salles, MD, PhD

Moderator Ann S LaCasce, MD, MMSc



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Multiple Myeloma

> Friday, December 10, 2021 3:15 PM – 5:15 PM ET

Faculty

Larry D Anderson Jr, MD, PhDIrene M Ghobrial, MDMorie A Gertz, MD, MACPPeter Voorhees, MD

Moderator Robert Z Orlowski, MD, PhD



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

> Friday, December 10, 2021 7:00 PM – 9:00 PM ET

Faculty

Alice S Mims, MD, MSCR Alexander Perl, MD Richard M Stone, MD Geoffrey L Uy, MD

Moderator Harry Paul Erba, MD, PhD



Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.



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Matthew Gubens, MD, MS University of California, San Francisco San Francisco, California



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Kapisthalam (KS) Kumar, MD Florida Cancer Specialists and Research Institute New Port Richey, Florida


Meet The Professor with Dr Liu

MODULE 1: Adjuvant and Neoadjuvant Immunotherapy in Non-Small Cell Lung Cancer (NSCLC)

MODULE 2: Case Presentations

- Dr Patel: A 57-year-old man with metastatic NSCLC and no actionable mutations
- Dr Shameem: A 66-year-old woman with newly diagnosed adenocarcinoma of the lung PD-L1 65%
- Dr Kumar: A 70-year-old man with localized NSCLC and no actionable mutations PD-L1 90%
- Dr Gupta: A 60-year-old woman with extensive-stage small cell lung cancer
- Dr Gubens: A 72-year-old woman with Stage IIIB adenocarcinoma of the lung and an EGFR L858R tumor mutation — PD-L1 40%
- Dr Kumar: A 75-year-old man with newly diagnosed metastatic NSCLC MET amplification, PD-L1 90%

MODULE 3: Thoughts for the Future

MODULE 4: Journal Club with Dr Liu

MODULE 5: Appendix – Key Data Sets



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Recent Advances in Adjuvant Systemic Treatment of Solid Tumors

| Disease | Agent or regimen | | | | |
|----------|--------------------------|--------------------------|--------------------------|------------------|--|
| NSCLC | Atezolizumab (10-15-21) | Osimertinib (12-18-20) | Durvalumab (2-16-18) | Nivolumab/Chemo* | |
| Breast | Abemaciclib (10-13-21) | Olaparib | Pembrolizumab (7-26-21) | T-DM1 (5-3-19) | |
| Upper GI | Nivolumab (5-20-21) | | | | |
| RCC | Pembrolizumab (11-17-21) | | | | |
| Bladder | Nivolumab (8-19-21) | Pembrolizumab (1-8-2020) | | | |
| Ovarian | Olaparib (12-19-18) | Niraparib (4-29-20) | Olaparib/Bevacizumab (5- | -8-20) | |
| Melanoma | Nivolumab (12-20-17) | Pembrolizumab (2-15-19) | Dabrafenib/Trametinib (4 | -30-18) | |
| Prostate | Abiraterone (+LHRH) | | | | |

*Neoadjuvant therapy



FDA Approves Atezolizumab as Adjuvant Treatment for NSCLC Press Release: October 15, 2021

"The Food and Drug Administration approved atezolizumab for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.

Today, the FDA also approved the VENTANA PD-L1 (SP263) Assay (Ventana Medical Systems, Inc.) as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with atezolizumab.

The major efficacy outcome measure was disease-free survival (DFS) as assessed by the investigator in the primary efficacy analysis population (n=476) of patients with stage II-IIIA NSCLC with PD-L1 expression on ≥1% of tumor cells (PD-L1 ≥1% TC). Median DFS was not reached (95% CI: 36.1, NE) in patients on the atezolizumab arm compared with 35.3 months (95% CI: 29.0, NE) on the BSC arm (HR 0.66; 95% CI: 0.50, 0.88; p=0.004)."



IMpower010: Phase III Trial of Adjuvant Atezolizumab After Chemotherapy in Resected Stage IB-IIIA NSCLC



Stratification factors

- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status^a: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints

- Investigator-assessed DFS tested hierarchically:
 - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
 - All-randomized stage II-IIIA population
 - ITT population (stage IB-IIIA)

Key secondary endpoints

- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations



IMpower010: Disease-Free Survival (DFS) in the PD-L1 TC ≥1% Stage II-IIIA Population (Primary Endpoint)





IMpower010: Efficacy Summary

| Clinical Endpoint | Atezolizumab | BSC | HR (p-value) |
|--|---------------|---------|---------------|
| PD-L1 TC ≥ 1%, Stage II-IIIA (n = 248;228) | | | |
| Median DFS | Not estimable | 35.3 mo | 0.66 (0.0039) |
| 2-year DFS rate | 75% | 61% | - |
| 3-year DFS rate | 60% | 48% | - |
| All randomized Stage II-IIIA (n = 442;440) | | | |
| Median DFS | 42.3 mo | 35.3 mo | 0.79 (0.020) |
| 2-year DFS rate | 70% | 62% | - |
| 3-year DFS rate | 56% | 50% | - |
| ITT population (n = 507;598) | | | |
| Median DFS | Not estimable | 37 mo | 0.81 (0.040) |
| 2-year DFS rate | 71% | 64% | - |
| 3-year DFS rate | 58% | 53% | - |

Overall survival data in the ITT population were immature and not formally tested.



Felip E et al. *Lancet* 2021;398(10308):1344-57.

IMpower010: DFS in NSCLC ≥5cm (7th ed. St II-III) Key Subsets



| SP263 PD-L1 status | | | |
|--------------------------|-----|------------------------------|-------------------|
| TC≥50% | 229 | ·• | 0.43 (0.27, 0.68) |
| TC≥1% | 476 | | 0.66 (0.49, 0.87) |
| TC<1% | 383 | | 0.97 (0.72, 1.31) |
| EGFR mutation status | | | |
| Yes | 109 | | 0.99 (0.60, 1.62) |
| No | 463 | | 0.79 (0.59, 1.05) |
| Unknown | 310 | | 0.70 (0.49, 1.01) |
| ALK rearrangement status | | | |
| Yes | 31 | · | 1.04 (0.38, 2.90) |
| No | 507 | | 0.85 (0.66, 1.10) |
| Unknown | 344 | | 0.66 (0.46, 0.93) |
| | 0.1 | 1.0 HR | 10.0 |
| | At | ezolizumab better BSC better | . 9 |

No obvious benefit in:

- Never smokers
- PD-L1 negative
- EGFR/ALK+

Adapted from Wakelee H et al. ASCO 2021;Abstract 8500



Chaft JE. IASLC 2021; Abstract PL05.04

IMpower010: Safety Summary

| | Atezolizumab group (n=495) | Best supportive care group (n=495) |
|---|-------------------------------|---------------------------------------|
| Adverse event | | |
| Any grade | 459 (93%) | 350 (71%) |
| Grade 3-4 | 108 (22%) | 57 (12%) |
| Serious | 87 (18%) | 42 (8%) |
| Grade 5 | 8 (2%)* | 3 (1%)† |
| Led to dose interruption of atezolizumab | 142 (29%) | |
| Led to atezolizumab discontinuation | 90 (18%) | |
| Immune-mediated adverse events | | |
| Any grade | 256 (52%) | 47 (9%) |
| Grade 3-4 | 39 (8%) | 3 (1%) |
| Required the use of systemic corticosteroids‡ | 60 (12%) | 4 (1%) |
| Led to discontinuation | 52 (11%) | 0 |

Data are n (%). *Interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukaemia (all four events related to atezolizumab), and pneumothorax, cerebrovascular accident, arrhythmia, and acute cardiac failure. †Pneumonia; pulmonary embolism; and cardiac tamponade and septic shock in the same patient. ‡Atezolizumab-related.



CheckMate 816 Met a Primary Endpoint of Improved Event-Free Survival with Neoadjuvant Nivolumab in Combination with Chemotherapy Press Release — November 8, 2021

"The Phase 3 CheckMate-816 trial met the primary endpoint of improved event-free survival (EFS) in patients with resectable stage IB to IIIA non-small cell lung cancer (NSCLC). In a prespecified interim analysis, nivolumab plus chemotherapy showed a statistically significant and clinically meaningful improvement in EFS compared to chemotherapy alone when given before surgery. This combination previously showed a significant improvement of pathologic complete response (pCR), the trial's other primary endpoint. The safety profile of nivolumab plus chemotherapy was consistent with previously reported studies in NSCLC. CheckMate-816 is the first Phase 3 trial with an immunotherapy-based combination to demonstrate a statistically significant and clinically meaningful benefit as a neoadjuvant treatment for patients with non-metastatic nonsmall cell lung cancer."

https://news.bms.com/news/details/2021/Neoadjuvant-Opdivo-nivolumab-Plus-Chemotherapy-Significantly-Improves-Event-Free-Survival-in-Patients-with-Resectable-Non-Small-Cell-Lung-Cancer-in-Phase-3-CheckMate--816-Trial/default.aspx



CheckMate 816: Phase III Trial of Neoadjuvant Nivolumab with Chemotherapy for Newly Diagnosed, Resectable, Stage IB-IIIA NSCLC





CheckMate 816: Coprimary Endpoint pCR



• pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)



CheckMate 816: Depth of Pathological Regression in Primary Tumor by Stage



with chemo, respectively

^aResponse-evaluable patients.



CheckMate 816: Treatment-Related Adverse Events in ≥15% of Patients





In general, what would you estimate to be the 5-year risk of disease recurrence for an otherwise healthy 65-year-old patient with NSCLC and PD-L1 TPS = 50% in each of the following scenarios:

| Disease stage | No adjuvant treatment | Adjuvant chemotherapy | Adjuvant chemotherapy + anti-PD-1/PD-L1 antibody | Treatment |
|------------------|--------------------------|--------------------------|---|--|
| IB | 25% | 25% | 20% | None |
| IIA | 35% | 30% | 20% | Cisplatin/pemetrexed → atezolizumab |
| IIB | 50% | 45% | 20% | Cisplatin/pemetrexed → atezolizumab |
| IIIA | 60% | 55% | 30% | Cisplatin/pemetrexed → atezolizumab |

How long have you been in oncology practice (after fellowship)?

- 1. Less than 5 years
- 2. 5-10 years
- 3. 11-20 years
- 4. 21-30 years
- 5. 31-40 years
- 6. 41-50 years
- 7. More than 50 years



If you were a patient with <u>Stage IB</u> NSCLC with a <u>PD-L1 TPS of 50%</u> and cost were not an issue, what would be your preference?

- 1. Chemotherapy
- 2. Chemotherapy \rightarrow atezolizumab
- 3. Atezolizumab
- 4. No systemic treatment
- 5. Other



If you were a patient in this situation with a <u>PD-L1 TPS of 50%</u> and cost were not an issue, what would be your preference?

- 1. Chemotherapy
- 2. Chemotherapy \rightarrow atezolizumab
- 3. Atezolizumab
- 4. No systemic treatment
- 5. Other



In what situations, if any, are you currently recommending neoadjuvant chemotherapy (with or without an anti-PD-1/PD-L1 antibody) for your patients with non-small cell lung cancer (NSCLC)?

"Resectable N2+ NSCLC"



Based on available data and your clinical experience, does neoadjuvant immunotherapy (alone or with chemotherapy) increase the risk of surgical complications in patients with NSCLC?

1. Yes

<mark>2. No</mark>

3. I'm not sure

4. It is too early to tell



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Case Presentation – Dr Patel: A 57-year-old man with metastatic NSCLC and no actionable mutations



Dr Sandip Patel

- Diagnosed with metastatic NSCLC
- On baseline O² due to COPD
- Chemoimmunotherapy initiated with decrease in oxygen requirement and improvement in lean muscle mass within 6 weeks
- CT: Nearly 50% increase in size of multiple mediastinal lymph nodes in the chest
- Therapy continued with patient monitoring for 6 to 8 weeks
- Follow-up CT: 50% decrease of multiple mediastinal lymph nodes



Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic <u>nonsquamous lung cancer</u>, no identified targetable mutations and a PD-L1 <u>TPS of 0%</u>?

- 1. Chemotherapy
- 2. Chemotherapy + bevacizumab
- 3. Pembrolizumab
- 4. Atezolizumab
- 5. Cemiplimab
- 6. Carboplatin/pemetrexed/pembrolizumab
- 7. Atezolizumab/carboplatin/nab paclitaxel
- 8. Atezolizumab/carboplatin/paclitaxel/bevacizumab
- 9. Ipilimumab/nivolumab
- 10. Ipilimumab/nivolumab + chemotherapy
- 11. Other





Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic <u>squamous lung cancer</u>, no identified targetable mutations and a PD-L1 <u>TPS of 0%</u>?

- 1. Chemotherapy
- 2. Pembrolizumab
- 3. Atezolizumab
- 4. Cemiplimab
- 5. Carboplatin/paclitaxel/pembrolizumab
- 6. Carboplatin/nab paclitaxel/pembrolizumab
- 7. Ipilimumab/nivolumab
- <mark>8. Ipilimumab/nivolumab + chemotherapy</mark>
- 9. Other



Faculty Survey November 2021

Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic <u>squamous lung cancer</u>, no identified targetable mutations and a PD-L1 <u>TPS of 10%</u>?

- 1. Chemotherapy
- 2. Pembrolizumab
- 3. Atezolizumab
- 4. Cemiplimab
- 5. Carboplatin/paclitaxel/pembrolizumab
- 6. Carboplatin/nab paclitaxel/pembrolizumab
- 7. Ipilimumab/nivolumab
- <mark>8. Ipilimumab/nivolumab + chemotherapy</mark>
- 9. Other



Faculty Survey November 2021

Case Presentation – Dr Shameem: A 66-year-old woman with newly diagnosed adenocarcinoma of the lung – PD-L1 65%



Dr Raji Shameem

- Never smoker presents with progressive shortness of breath
- Chest CT: Right hilar lung mass extending into the mediastinal subcarinal space, large right pleural effusion
- CT guided biopsy: Adenocarcinoma, PD-L1 65%
- Carboplatin/pemetrexed/pembrolizumab with pembrolizumab held after cycle 1
- Liquid and tumor tissue NGS testing ordered
 - Liquid NGS: NTRK mutation
 - Tumor tissue: Notable for PD-L1 65%, NTRK fusion reported to be negative
- Chemotherapy plus pembrolizumab continued, patient faring well

Questions

• Which NTRK inhibitor would the faculty typically use, entrectinib or larotrectinib? Do any data indicate that one would have better CNS activity?



Case Presentation – Dr Shameem: A 66-year-old woman with newly diagnosed adenocarcinoma of the lung – PD-L1 65% (continued)



Dr Raji Shameem

| Blood Tumor Mutational Burden - 13 Muts/Mb | | Atezolizumab | 1 | Avelumab |
|---|----------------|---|--|--|
| | | Cemiplimab | 1 | |
| | | Durvalumab | 1 | |
| | | Nivolumab | 1 | |
| | | Pembrolizumab | 1 | |
| 10 Trials see p. 18 | | | | |
| Microsatellite status - MSI-High N Detected | vot | MSI-High not detected. N (see Appendix section). | lo evidence of | microsatellite instability in this sample |
| | | | | |
| Tumor Fraction - 47% | | Tumor fraction is an estir (ctDNA) present in a cell- aneuploid instability. | nate of the per -free DNA (cfD | centage of circulating-tumor DNA NA) sample based on observed |
| Tumor Fraction - 47% | VAF % | Tumor fraction is an estir (ctDNA) present in a cell aneuploid instability. THERAPIES WITH CLINIC (IN PATIENT'S TUMO | nate of the per -free DNA (cfD CAL BENEFIT DR TYPE) | centage of circulating-tumor DNA NA) sample based on observed THERAPIES WITH CLINICAL BENEFI (IN OTHER TUMOR TYPE) |
| Tumor Fraction - 47% GENOMIC FINDINGS NTRK3 - NTRK3-KLHL20 | VAF % 0.86% | Tumor fraction is an estin (ctDNA) present in a cell aneuploid instability. THERAPIES WITH CLINI (IN PATIENT'S TUMO Entrectinib | nate of the per- free DNA (cfD CAL BENEFIT DR TYPE) 2A | Centage of circulating-tumor DNA INA) sample based on observed THERAPIES WITH CLINICAL BENEFI (IN OTHER TUMOR TYPE) None |
| Tumor Fraction - 47% GENOMIC FINDINGS NTRK3 - NTRK3-KLHL20 rearrangement | VAF % 0.86% | Tumor fraction is an estin (ctDNA) present in a cell- aneuploid instability. THERAPIES WITH CLINIC (IN PATIENT'S TUMO Entrectinib Larotrectinib | nate of the per -free DNA (cfD CAL BENEFIT DR TYPE) 2A 2A | centage of circulating-tumor DNA NA) sample based on observed THERAPIES WITH CLINICAL BENEFI (IN OTHER TUMOR TYPE) None |
| Tumor Fraction - 47% GENOMIC FINDINGS NTRK3 - NTRK3-KLHL20 rearrangement 5 Trials see p. 20 | VAF % 0.86% | Tumor fraction is an estir (ctDNA) present in a cell aneuploid instability. THERAPIES WITH CLINIC (IN PATIENT'S TUMO Entrectinib Larotrectinib | nate of the per- free DNA (cfD CAL BENEFIT DR TYPE) 2A 2A | Centage of circulating-tumor DNA NA) sample based on observed THERAPIES WITH CLINICAL BENEFI (IN OTHER TUMOR TYPE) None |

Liquid NGS results



Case Presentation – Dr Shameem: A 66-year-old woman with newly diagnosed adenocarcinoma of the lung – PD-L1 65% (continued)



| THERAPY CONSIDERATIONS FOR NON-SMALL CELL LUNG CANCER | | | | | | |
|---|---|--|----------------------------------|--|--|--|
| | Markers | Therapies in Non-Small Cell Lung Cancer | Therapies in Other Tumor Types | | | |
| FDA (Level 1) | PD-L1 (IHC_22C3) 65% TPS | cemipilimab ¹ , pembrolizumab ^{2,3} | None | | | |
| Guidelines (Level 2) | No mark for t | ers associated with guideline-indicated therapy he tumor type tested or other tumor types wer | y considerations e identified | | | |
| a) | PIK3CA c.2702G>T (C901F) PTEN c.388C>G (R130G) TP53 c.817C>T (R273C) | | | | | |
| Trial Ma (Level | ADORA2A 60% CD137 76% CD39 79% IDO1 99% PD-L1 81% | | | | | |
| | PERTINENT NEGATI | VE RESULTS FOR NON-SMALL CELL | LUNG CANCER | | | |
| | (Tested markers for FDA-ap | proved or guideline-indicated therapies th | at were not positive) | | | |
| ive Results | ALK fusion BRAF V600 EGFR exon 19 deletion EGFR exon 20 insertion EGFR mutation | HER2 (ERBB2) mutation KRAS mutation MET amp/exon 14 NTRK fusion RET fusion | ROS1 fusion | | | |
| Negat | MSI Inconclusive TMB 8.6/Mb (Intermediate) | | | | | |



Dr Raji Shameem



Case Presentation – Dr Kumar: A 70-year-old man with localized NSCLC and no actionable mutations – PD-L1 90%



Dr KS Kumar

- Clinically unresectable, received neoadjuvant cisplatin/pemetrexed with good response
- Underwent surgical resection
 - All nodes negative, residual tumor was 0.6 cm
- NGS: No actionable mutations, PD-L1 = 90%

Questions

- Would the faculty consider this patient to be a candidate for anti-PD-L1 therapy?
- If you had seen the patient initially, would you have considered neoadjuvant anti-PD-1/PD-L1 therapy?



Case Presentation – Dr Gupta: A 60-year-old woman with extensive-stage small cell lung cancer



Dr Ranju Gupta

- August 2020: Diagnosed with extensive stage small cell lung cancer, symptomatic with mediastinal adenopathy
- Cisplatin/etoposide/atezolizumab x 4 → atezolizumab maintenance

Questions

- What second-line treatment options are available for this patient when her disease progresses?
- Would there still be a role for prophylactic cranial radiation if the patient had stable disease for 6 months or more?



In general, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage small cell lung cancer (SCLC)?

- 1. Carboplatin/etoposide
- 2. Carboplatin/etoposide + trilaciclib
- 3. Cisplatin/etoposide
- 4. Cisplatin/etoposide + trilaciclib
- 5. Carboplatin/etoposide + atezolizumab
- 6. Carboplatin/etoposide + atezolizumab + trilaciclib
- 7. Carboplatin/etoposide + durvalumab
- 8. Carboplatin/etoposide + durvalumab + trilaciclib
- 9. Cisplatin/etoposide + durvalumab
- 10. Cisplatin/etoposide + durvalumab + trilaciclib
- 11. Carboplatin/irinotecan
- 12. Cisplatin/irinotecan
- 13. Other

Faculty Survey November 2021



In what situations if any, do you administer trilaciclib to patients with extensive-stage SCLC who are receiving platinum/etoposide- or topotecan-containing regimens to reduce the incidence of chemotherapy-induced myelosuppression?

"I have not used trilaciclib but might consider it if multi-lineage myelosuppression was noted with topotecan."



The benefits and risks of adding durvalumab to platinum/etoposide and of adding atezolizumab to carboplatin/etoposide are very similar, and from a clinical point of view selecting between the 2 regimens as first-line treatment for a patient with extensive-stage SCLC can be considered a "coin flip."

<mark>1. Agree</mark>

2. Disagree

3. I'm not sure



In general, what is your preferred second-line treatment for a patient with extensive-stage SCLC with metastases and disease progression on chemotherapy/atezolizumab?

- 1. Topotecan or irinotecan
- 2. Lurbinectedin
- 3. Nivolumab/ipilimumab
- 4. Pembrolizumab
- 5. Nivolumab
- 6. Other



Case Presentation – Dr Gubens: A 72-year-old woman with Stage IIIB adenocarcinoma of the lung and an EGFR L858R tumor mutation – PD-L1 40%

- Never smoker presents with progressive cough
- RUL mass, 2.4-cm, with R hilar and mediastinal LAD
- CT guided biopsy: Adenocarcinoma, PD-L1 40%
- NGS: EGFR L858R mutation
- Definitive chemoradiation therapy, with good radiographic response

Question

• Would you consider consolidation durvalumab in this patient with an EGFR activating mutation?



Dr Matt Gubens



Case Presentation – Dr Gubens: A 72-year-old woman with Stage IIIB adenocarcinoma of the lung and an EGFR L858R tumor mutation – PD-L1 40% (continued)



Dr Matt Gubens

- Never smoker presents with progressive cough
- RUL mass, 2.4-cm, with R hilar and mediastinal LAD
- CT guided biopsy: Adenocarcinoma, PD-L1 40%
- NGS: EGFR L858R mutation
- Definitive chemoradiation therapy, with good radiographic response
- Discussed PACIFIC data with consolidation durvalumab with patient's 2 physician daughters
- Consolidation durvalumab x 6 months \rightarrow Abnormal thyroid function tests (TSH: 20, T4: 11)
 - Initiated levothyroxine 88 mcg and continued durvalumab
 - One month later: Fasting glucose 317, A1C 7.3 \rightarrow Immune-related insuline-dependent diabetes
- Durvalumab discontinued, but 24 months later no evidence of recurrence


What would you most likely recommend as consolidation treatment for a patient with locally advanced NSCLC who has completed chemoradiation therapy and is found to have an EGFR activating mutation?

1. Durvalumab

<mark>2. Osimertinib</mark>

3. Durvalumab + osimertinib

4. Durvalumab followed by osimertinib

5. Other



Case Presentation – Dr Kumar: A 75-year-old man with newly diagnosed metastatic NSCLC – MET amplification, PD-L1 90%



Dr KS Kumar

- Diagnosed with NSCLC with extensive mediastinal lymphadenopathy, TTF1-positive
- Quickly progressed with SVC syndrome
- Palliative radiation initiated with patient's condition improved
- MET amplification detected, PD-L1 90%

Questions

- Should this patient receive the available MET inhibitor given that he has a MET amplification and not a MET exon 14 skipping mutation?
- Should chemotherapy combined with an IO be his first-line therapy?



Meet The Professor with Dr Liu

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- Dr Shameem: A 66-year-old woman with newly diagnosed adenocarcinoma of the lung PD-L1 65%
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- Dr Gupta: A 60-year-old woman with extensive-stage small cell lung cancer
- Dr Gubens: A 72-year-old woman with Stage IIIB adenocarcinoma of the lung and an EGFR L858R tumor mutation — PD-L1 40%
- Dr Kumar: A 75-year-old man with newly diagnosed metastatic NSCLC MET amplification, PD-L1 90%

MODULE 3: Thoughts for the Future

MODULE 4: Journal Club with Dr Liu

MODULE 5: Appendix – Key Data Sets



Thoughts for the Future

- Choice of immunotherapy regimen
 - Interval between dosing
- Immunotherapy combinations
 - Anti-PD-1/PD-L1 antibody/tyrosine kinase inhibitor
 - Immunotherapy/immunotherapy
 - Other investigational approaches



FDA-Approved Immunotherapy Monotherapy Options for First-Line Therapy

| Monotherapy | FDA approval | Pivotal study | Histologic type | HR (OS) |
|---|---------------------|--------------------------------|---|---------|
| Pembrolizumab ^{1,2} (q3wk or q6wk) | 4/11/19 10/24/16 | KEYNOTE-042 KEYNOTE-024 | PD-L1 TPS ≥1% | 0.63 |
| Atezolizumab ³ (q2wk, q3wk or q4wk) | 5/18/20 | IMpower110 | PD-L1 TPS ≥50, EGFR and/or ALK wt | 0.59 |
| Cemiplimab ⁴ (q3wk) | 2/22/21 | EMPOWER-Lung 1 (Study 1624) | PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt | 0.57 |



¹ Mok. Lancet 2019. ² Reck. J Clin Oncol 2019. ³ Herbst. N Engl J Med 2020. ⁴ Sezer. Lancet 2021.

EMPOWER-Lung 1: Phase III Trial of Cemiplimab Monotherapy for First-Line Treatment of NSCLC with PD-L1 ≥50%

Overall Survival

Progression-Free Survival





Sezer A et al. Lancet 2021;397:592-604.

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

| Combination regimen | FDA approval | Pivotal study | Histologic type | HR (OS) |
|---|--------------|---------------|-------------------------------------|---------|
| Pembrolizumab (q3wk or q6wk) + Platinum and pemetrexed ¹ | 8/20/18 | KEYNOTE-189 | Nonsquamous | 0.56 |
| Pembrolizumab (q3wk or q6wk) + Carboplatin, paclitaxel or <i>nab</i> paclitaxel ² | 10/30/18 | KEYNOTE-407 | Squamous | 0.71 |
| Atezolizumab (q3wk) + Carboplatin and paclitaxel and bevacizumab ³ | 12/6/18 | IMpower150 | Nonsquamous | 0.80 |
| Atezolizumab (q3wk) + Carboplatin and <i>nab</i> paclitaxel ⁴ | 12/3/19 | IMpower130 | Nonsquamous | 0.79 |
| <mark>Nivolumab (q2wk) +</mark> Ipilimumab⁵ | 5/15/20 | CheckMate 227 | PD-L1 TPS ≥1, EGFR and/or ALK wt | 0.76 |
| Nivolumab (q3wk) + Ipilimumab and chemotherapy ⁶ | 5/26/20 | CheckMate 9LA | EGFR and/or ALK wt | 0.72 |

¹ Rodriguez-Abreu. *Ann Oncol* 2021. ² Paz-Ares. *J Thorac Oncol* 2020. ³ Socinski *J Thorac Oncol* 2021. ⁴ West. *Lancet Oncol* 2019. ⁵ Paz-Ares. ASCO 2021; Abstract 9016. ⁶ Reck. ASCO 2021; Abstract 9000.



EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



Key secondary: PFS and ORR

Additional secondary: DOR, BOR, safety, and PRO

Two interim analyses were prespecified per protocol Second interim analysis (14 June 2021) presented here



EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC





Gogishvili M et al. ESMO 2021; Abstract LBA51.

EMPOWER-Lung 3: Progression-Free Survival





Gogishvili M et al. ESMO 2021; Abstract LBA51.

Thoughts for the Future

- Choice of immunotherapy regimen
 - Interval between dosing
- Immunotherapy combinations
 - Anti-PD-1/PD-L1 antibody/tyrosine kinase inhibitor
 - Immunotherapy/immunotherapy
 - Other investigational approaches



KEYNOTE-146: Phase IB/II Trial of Lenvatinib/Pembrolizumab in Advanced Solid Cancers

| Efficacy in the Metastatic NSCLC Population | | | | |
|---|-----------------|-----|---------------|------------|
| Ν | Line of Therapy | ORR | Median DOR | Median PFS |
| 21 | Any | 33% | 10.9 mo | 5.9 mo |

DOR = duration of response

| Summary of Treatment-Related AEs (TREAs): All Patients | | | | |
|--|-----------|--|--|--|
| Parameter | (N = 137) | | | |
| Serious AEs | 26% | | | |
| TREAs leading to pembrolizumab dose interruption | 45% | | | |
| TREAs leading to pembrolizumab discontinuation | 15% | | | |
| TREAs leading to lenvatinib dose reduction and/or interruption | 85% | | | |
| TREAs leading to lenvatinib discontinuation | 13% | | | |



Taylor MH et al. *J Clin Oncol* 2020;38:154-63.

KEYNOTE-146: Maximum Change in Target Lesion Size (All Patients)





Taylor MH et al. J Clin Oncol 2020;38:154-63.

Ongoing LEAP Phase III Trials in NSCLC

| Trial ID | N | Patient population | Line of therapy | Treatment |
|----------|-----|--|--------------------|---|
| LEAP-006 | 726 | Previously untreated metastatic nonsquamous NSCLC | 1L | Pemetrexed + Platinum chemo + Pembrolizumab + Lenvatinib Pemetrexed + Platinum chemo + Pembrolizumab + Placebo |
| LEAP-007 | 620 | Previously untreated, advanced (Stage IV), PD-L1 positive (TPS ≥1%) NSCLC | 1L | Lenvatinib + Pembrolizumab Placebo + Pembrolizumab |
| LEAP-008 | 405 | Metastatic NSCLC that progressed during/after platinum doublet chemotherapy or on treatment with anti-PD-1/PD-L1 monoclonal antibody as monotherapy or combination therapy | ≥2L | Lenvatinib + Pembrolizumab SOC chemo Lenvatinib |



COSMIC-021 (Cohort 7): Best Change from Baseline with Cabozantinib/Atezolizumab for Metastatic NSCLC



Patient Population

- Patients with radiographic progression on or after one prior ICI treatment
- ≤2 lines of prior systemic anticancer therapy for metastatic NSCLC
- No EGFR mutations, ALK or ROS1 rearrangements, or BRAF V600E mutation



Neal JW et al. ASCO 2020; Abstract 9610.

COSMIC-021 (Cohort 7): Immune-Related Adverse Events with Cabozantinib/Atezolizumab for Metastatic NSCLC

| | NSCLC Cohort 7 (N=30) | | | |
|--|--------------------------|---------|--|--|
| | Any Grade | Grade 3 | | |
| Any AE, n (%) | 6 (20) | 0 | | |
| Hyperthyroidism | 1 (3.3) | 0 | | |
| Hypothyroidism | 1 (3.3) | 0 | | |
| Lipase increased | 1 (3.3) | 0 | | |
| Myocarditis* | 1 (3.3) | 0 | | |
| Pain | 1 (3.3) | 0 | | |
| Pneumonitis* | 1 (3.3) | 0 | | |
| Rash | 1 (3.3) | 0 | | |
| *One patient experienced grade 5 pneumonitis and myocarditis; pneumonitis was assessed as the cause of death | | | | |



Enrollment Completed in Phase 3 CONTACT-01 Pivotal Trial of Cabozantinib in Combination with an Immune Checkpoint Inhibitor in Previously Treated Metastatic Non-Small Cell Lung Cancer Press Release: November 9, 2021

"Enrollment is now completed for CONTACT-01, the global, phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab in patients with metastatic non-small cell lung cancer (NSCLC) who have been previously treated with an immune checkpoint inhibitor and platinum-containing chemotherapy.

CONTACT-01 is a global, multicenter, randomized, phase 3, open-label study that enrolled 366 patients who were randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. The primary endpoint of the trial is overall survival. Secondary endpoints include progression-free survival, objective response rate and duration of response. Results from cohort 7 of the phase 1b COSMIC-021 trial informed the CONTACT-01 trial design."



CONTACT-01 Phase III Study Design



Primary endpoint: Overall survival **Secondary endpoints:** PFS, ORR, DOR, others

www.clinicaltrials.gov. NCT04471428. Accessed November 2021.



POSEIDON: First-Line Durvalumab with Tremelimumab and Chemotherapy for Advanced NSCLC

PFS







Johnson ML et al. WCLC 2021;Abstract PL02.01

Background: TIGIT Pathway

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory receptor expressed on multiple immune cells, including T cells and NK cells¹⁻³
- TIGIT inhibits T cells and NK cells by binding to its ligand PVR on tumor cells and antigen-presenting cells (APCs)
- TIGIT expression strongly correlates with PD-1 expression, especially in tumor-infiltrating T cells in lung cancer
- <u>Hypothesis</u>: Anti-TIGIT antibodies, which prevent TIGIT from binding to its ligand, could restore the anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies



Figure adapted from Manieri et al. Trends Immunology 2017

NK, natural killer; PVR, poliovirus receptor

¹ Manieri et al. Trends Immunology 2017; ² Rotte et al. Annals of Oncology 2018; ³ Yu et al. Nature Immunology 2009

PRESENTED AT: 2020 ASCO #ASCOO Sides are the prop

PRESENTED BY: Melissa Johnson



Background: Tiragolumab, an Anti-TIGIT Antibody

PRESENTED BY:

Melissa Johnson

Tiragolumab is a fully human IgG1/kappa ٠ anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR



In preclinical models, combination treatment with anti-TIGIT and anti-PD-L1 antibodies synergistically improves tumor control and prolongs survival in mice¹



Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

PRESENTED AT:

CITYSCAPE Study Design

1L Stage IV NSCLC

- EGFR/ALK wild-type
- Tumor PD-L1 TPS ≥ 1% by 22C3 IHC by local or central assay

N=135

Stratification Factors:

- PD-L1 TPS (1-49% vs ≥ 50%)
- Histology (Non-Squamous vs Squamous)
- Tobacco use (yes vs no)



- Co-Primary Endpoints: ORR and PFS
- Key Secondary Endpoints: Safety, DOR, OS, Patient-reported outcomes (PROs)
- Exploratory Endpoints: Efficacy analysis by PD-L1 status

DOR = duration of response; IHC = immunohistochemistry; ORR = confirmed overall response rate; OS = overall survival; PD = progressive disease; PFS = progression free survival ; q3w = every 3 weeks; R = randomized; TPS = tumor proportion score

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PRESENTED BY: Melissa Johnson

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Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

CITYSCAPE Updated Confirmed Overall Response Rate (ORR)





Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

CITYSCAPE Updated Investigator-Assessed PFS: ITT



PRESENTED BY: Melissa Johnson

ITT= intention-to-treat; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab

#ASCO20

Follow data cutoff: 02 December 2019

2020ASCO lides are the property of the outho

Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

PRESENTED AT:



CITYSCAPE Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%



Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

CITYSCAPE Updated Investigator-Assessed PFS: PD-L1 TPS 1-49%



Follow data cutoff: 02 December 2019

PRESENTED BY: Melissa Johnson

Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.

PRESENTED AT: 2020

#ASCO20



CITYSCAPE <u>Updated</u> Immune-Mediated Adverse Events



Rodriguez-Abreu D et al. ASCO 2020; Abstract 9503.



Meet The Professor with Dr Liu

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- Dr Kumar: A 75-year-old man with newly diagnosed metastatic NSCLC MET amplification, PD-L1 90%

MODULE 3: Thoughts for the Future

MODULE 4: Journal Club with Dr Liu

MODULE 5: Appendix – Key Data Sets



Journal Club with Dr Liu

- Reuss JE et al. Antibody drug conjugates in lung cancer: State of the current therapeutic landscape and future developments. *Clin Lung Cancer* 2021;[Online ahead of print]
- Jonna S et al. Effect of prior therapy on tumor mutational burden in NSCLC. Transl Lung Cancer Res 2021;10(3):1231-8.
- Farid S, Liu SV. Chemo-immunotherapy as first-line treatment for small-cell lung cancer. Ther Adv Med Oncol 2020;12:1758835920980365.
- Montenegro GB et al. Immunotherapy in lung cancer. J Surg Oncol 2021;123(3):718-29.



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Practical Considerations with the Use of Anti-PD-1/PD-L1 Antibodies for the Management of Localized and Locally Advanced NSCLC



Select Ongoing Phase III Trials of Immunotherapy in the Neoadjuvant Setting

| Trial identifier | Ν | Patient population | Study arms |
|------------------------------|-----|--|---|
| IMpower030 (NCT03456063) | 453 | Resectable Stage II, IIIA, or select IIIB (T3N2 only) NSCLC Squamous or non-squamous histology | Atezolizumab + platinum-based chemotherapy Placebo + platinum- based chemotherapy |
| KEYNOTE-671 (NCT03425643) | 786 | Resectable Stage II, IIIA, and resectable IIIB (T3-4N2) NSCLC | Pembrolizumab + platinum-based chemotherapy Placebo + platinum- based chemotherapy |
| AEGEAN (NCT03800134) | 800 | Resectable Stage IIA to select (ie, N2) Stage IIIB NSCLC | Durvalumab + platinum- based chemotherapy Placebo + platinum- based chemotherapy |



Select Ongoing Phase III Trials of Immunotherapy in the Adjuvant Setting

| Trial identifier | Ν | Patient population | Study arms |
|---|-------|---|---|
| BR31 (NCT02273375) | 1,360 | Stage IB (≥ 4cm in the longest diameter), II or IIIA after complete resection | DurvalumabPlacebo |
| KEYNOTE-091/ PEARLS (NCT02504372) | 1,177 | Stage IB with T ≥ 4 cm, II-IIIA NSCLC after complete surgical resection with or without adjuvant chemotherapy | PembrolizumabPlacebo |
| ANVIL (NCT02595944) | 903 | Complete surgical resection of stage IB (≥ 4 cm), II or IIIA NSCLC with adjuvant chemotherapy Negative for ALK translocation and EGFR exon 19 del or exon 21 L858R mutation | NivolumabPlacebo |



PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC





Spigel DR et al. ASCO 2021; Abstract 8511.

PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC





PACIFIC-R: Real-World Study of Durvalumab After Chemoradiation Therapy for Patients with Unresectable Stage III NSCLC

- International observational study (N = 1155)
- Median PFS: 22.5 months
- Median duration of durvalumab treatment: 11 months

| Summary of Safety and Pneumonitis | N = 1155 |
|--|----------|
| Discontinuation of durvalumab due to AE | 17.5% |
| Discontinuation of durvalumab due to pneumonitis | 13.8% |
| Temporary | 5.1% |
| Permanent | 8.7% |
| Any-grade pneumonitis and/or ILD | 18.5% |
| Moderate severity | 8.8% |
| Life-threatening | 0.2% |
| Fatal | 0.1% |


FDA Approves Durvalumab for Fixed-Dose Use in NSCLC, Bladder Cancer Indications

Press Release: November 20, 2020

"The FDA has approved durvalumab for an additional dosing option, a fixed dose of 1500 mg every 4 weeks, in the approved indications of unresectable stage III non-small cell lung cancer after chemoradiation and previously treated advanced bladder cancer.

This new dosing option is consistent with the dosing for the agent that has been approved in extensive-stage small cell lung cancer (ES-SCLC); this will serve as an alternative option for patients who weigh more than 30 kg rather than the weight-based dosing of 10 mg/kg that is administered every 2 weeks.

The regulatory decision was based on data from several clinical trials examining the agent, including the phase 3 PACIFIC trial (NCT02125461), which supported the 2-week, weight-based dosing in patients with unresectable stage III NSCLC, and the phase 3 CASPIAN trial (NCT03043872), which examined a 4-week, fixed-dose during maintenance treatment in patients with ES-SCLC."



Phase II KEYNOTE-799 Trial of Pembrolizumab with Concurrent Chemoradiation Therapy in Unresectable Stage III NSCLC — Coprimary Endpoints: Overall Response Rate (ORR) and Grade 3 or Higher Pneumonitis

| | Cohort A (Squamous and nonsquamous) (n = 112) | Cohort B (Nonsquamous only) (n = 102) |
|--------------------------|--|--|
| ORR | 70.5% | 70.6% |
| Pts with response ≥12 mo | 79.7% | 75.6% |
| ≥Grade 3 pneumonitis | 8.0% | 6.9% |



Jabbour SK et al. JAMA Oncol 2021;7(9):1351-9.

Role of Immunotherapy in Small Cell Lung Cancer (SCLC)



IMpower133: Updated OS in Extensive-Stage SCLC (ES-SCLC) Treated with First-Line Atezolizumab, Carboplatin and Etoposide



CASPIAN: Three-Year Updated OS in ES-SCLC Treated with First-Line Durvalumab, Platinum and Etoposide





Paz-Ares LG et al. Ann Oncol. 2021;32(suppl 5):S1283-46.

Meet The Professor Management of BRAF-Mutant Melanoma

Monday, November 29, 2021 5:00 PM – 6:00 PM ET

> Faculty Jason J Luke, MD

> > Moderator Neil Love, MD



Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

