Expert Second Opinion: The Emerging Role of Immunotherapy and Targeted Treatment in Localized Non-Small Cell Lung Cancer

A Live Webinar Held as a Satellite CME/MOC Symposium During the IASLC 2021 World Conference on Lung Cancer Worldwide Virtual Event

Sunday, September 12, 2021
11:15 PM – 12:15 AM ET

Faculty
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Jarushka Naidoo, MB BCH, MHS
Harvey I Pass, MD
Heather Wakelee, MD

Moderator
Neil Love, MD
Faculty

Edward B Garon, MD, MS
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Director, Thoracic Oncology Program
Director, Signal Transduction and Therapeutics Research Program
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Department of Cardiothoracic Surgery
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Chief, Division of Oncology
Stanford University School of Medicine
Deputy Director, Stanford Cancer Institute
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Faculty Presenter
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Consultant Medical Oncologist
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Dublin, Ireland
Adjunct Assistant Professor of Oncology
Johns Hopkins University
Baltimore, Maryland

Moderator
Neil Love, MD
Research To Practice
Miami, Florida
Commercial Support

This activity is supported by an educational grant from Genentech, a member of the Roche Group.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.
## Dr Garon — Disclosures

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<td>Lilly, Merck, Mirati Therapeutics, Neon Therapeutics, Novartis</td>
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# Dr Naidoo — Disclosures

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Dr Pass — Disclosures

No relevant conflicts of interest to disclose
## Dr Wakelee — Disclosures

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We Encourage Clinicians in Practice to Submit Questions

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How to answer poll questions

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Expand chat submission box

Drag the white line above the submission box up to create more space for your message.
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Increase chat font size

Press Command (for Mac) or Control (for PC) and the + symbol. You may do this as many times as you need for readability.
ONCOLOGY TODAY
WITH DR NEIL LOVE

Key Presentations on Lung Cancer from the 2021 ASCO Annual Meeting

DR JOEL NEAL
STANFORD UNIVERSITY
What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty
Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator
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Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator
Neil Love, MD
Meet The Professor
Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Tuesday, September 14, 2021
5:00 PM – 6:00 PM ET

Faculty
Neeraj Agarwal, MD

Moderator
Neil Love, MD
Meet The Professor
Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 16, 2021
5:00 PM – 6:00 PM ET

Faculty
Loretta J Nastoupil, MD

Moderator
Neil Love, MD
Meet The Professor
Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty
Philip A Philip, MD, PhD, FRCP

Moderator
Neil Love, MD
Meet The Professor

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

Wednesday, September 22, 2021
5:00 PM – 6:00 PM ET

Faculty
Sara M Tolaney, MD, MPH

Moderator
Neil Love, MD
Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.
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Agenda

Introduction: Tumor Board Discussions Since ASCO 2021?

Module 1: Immunotherapy in Surgically Resectable Non-Small Cell Lung Cancer
- Case: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type
- Case: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%
- Case: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%
- Key relevant data sets

Module 2: Adjuvant Treatment of NSCLC with a Driver Mutation
- Case: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation
- Case: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation
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- Key relevant data sets
Adjuvant Chemotherapy

Jessica A. Hellyer, MD, Heather A. Wakelee, MD*

KEYWORDS
- Adjuvant • Chemotherapy • Targeted agents

KEY POINTS
- Standard of care for resectable, early-stage lung cancer is 4 cycles of adjuvant chemotherapy.
- Chemotherapy regimens have equitable efficacy, although in practice platinum plus pemetrexed is used most often for nonsquamous non–small cell lung cancer (NSCLC) due to favorable toxicity profile, with recent support for this approach from the JIPANG trial.
- Adjuvant immunotherapy is under investigation and discussed separately.
- Targeted therapies currently are not standard-of-care adjuvant treatment in driver mutation–positive early-stage NSCLC, but several trials are under way examining their use.
IO in the Surgically Resectable Patient

Jamie E. Chaft, MD
Memorial Sloan Kettering Cancer Center
USA
We need to move beyond perioperative chemotherapy...

5.3% survival benefit at 5 years

HR = 0.89, \( P < 0.005 \)

Chasing Progress in Metastatic NSCLC
What about adjuvant IO?

- >4,650 patients enrolled
- All studies enrolled after SOC chemo
- All studies enrolled irrespective of PD-L1, however subsets planned
- Only 1 study powered for OS

Chaft JE. IASLC 2021;Abstract PL05.04
# Ongoing Adjuvant PD-1/PD-L1 IO trials

<table>
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<td>Pembrolizumab</td>
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Courtesy of Heather Wakelee, MD
Abstract 8500

**IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)**

Heather A. Wakelee,1 Nasser Altorki,2 Caicun Zhou,3 Tibor Csőszi,4 Ihor O. Vynnychenko,5 Oleksandr Goloborodko,6 Alexander Luft,7 Andrey Akopov,8 Alex Martinez-Martí,9 Hirotugu Kenmotsu,10 Yuh-Min Chen,11 Antonio Chella,12 Shunichi Sugawara,13 Fan Wu,14 Jing Yi,15 Yu Deng,15 Mark McCleland,15 Elizabeth Bennett,15 Barbara J. Gililiz,15 Enriqueuta Felip16

Abstract CT003

**Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer in the phase 3 CheckMate 816 trial**

Patrick M. Forde,1 Jonathan Spicer,2 Shun Lu,3 Mariano Provencio,4 Tetsuya Mitsudomi,5 Mark M. Awad,6 Enriqueuta Felip,7 Stephen Broderick,1 Julie Braher,1 Scott J. Swanson,6 Keith Kerr,8 Changli Wang,9 Gene B. Saylors,10 Fumihiro Tanaka,11 Hiroyuki Ito,12 Ke-Neng Chen,13 Cecile Dorange,14 Junliang Cai,14 Joseph Fiore,14 Nicolas Girard15
Neoadjuvant/Adjuvant Immunotherapy for Curing Nondriver Genes

PD-(L)1 Checkpoint inhibitors:
- **Neoadjuvant:** Improve surgical and pathologic outcomes
- **Adjuvant:** Improve DFS in stage II-IIIA with PD-L1 expression

Becoming new Standard of Care for Early Stage NSCLC without a driver mutation

Likely will lead to improved cure rates
Agenda

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• Key relevant data sets
Case Presentation: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type

- Incidental finding of a 7-cm right-sided lung mass with no other areas of metastatic disease after she presents to the ER after a motor vehicle accident
- NGS: No actionable mutations; PD-L1 assay: Negative
- Resection → Stage IIA, T3N02a

Questions

- When do you think mature data in terms of overall survival will be available for IMpower010?
- May we use the 22C3 assay for assessing PD-L1 status for patients where administration of atezolizumab is planned?
- Are there any data available on patients who have relapsed after atezolizumab, what are the patterns of relapse? Does administering immunotherapy early change the natural history of lung cancer in some way?
ctDNA as a biomarker for treatment selection

Dr Jarushka Naidoo
Case Presentation: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%

- Smoker who attends a lung cancer screening clinic is found to have a 4-cm right-sided lung mass on non-contrast CT
  - PET-CT identifies an FDG-avid right hilar lymph node, squamous NSCLC
  - Stage IIA, T2bN1
  - PD-L1: 15%

Questions

- Does PD-L1 score matter when deciding between a neoadjuvant and adjuvant approach for a patient? What are the cut-off values?
- What role does TMB play in your decision-making?
Role of surgery after neoadjuvant therapy

Dr Jarushka Naidoo
Case Presentation: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%

- Multiple medical comorbidities, ECOG PS 2
- He undergoes right upper lobe lobectomy for a Stage IB adenocarcinoma
- PD-L1 assay: 10%
- He has a slow postoperative recovery and returns for next appointment 10 weeks later

Questions
- What adjuvant treatment would you have recommended for this patient?
- From IMpower010, what do we know about the efficacy of atezolizumab in the Stage IB patient population?
- For this patient with multiple medical comorbidities in a poor performance status, should we think about adapting the algorithm and giving the patient atezolizumab alone and forgoing the chemotherapy?
Considerations for Future Studies

• IO clearly has a role in early-stage lung cancer!
• Adenocarcinoma and Squamous cell carcinoma are different diseases and should be studied separately
• NGS is needed to understand impact of all drivers, not just EGFR and ALK, particularly in the adjuvant setting where time to test is ample
• We need to compare preop IO to postop IO, not default to give both as 4 randomized phase 3 studies are doing
**Phase 3 IMpower010 Study: Schema**

**Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7**
- Stage IB tumors ≥4 cm
- ECOG PS 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

**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)

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

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

**Atezolizumab**
- 1,200 mg Q21D
- 16 cycles

**Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine**
- 1-4 cycles
- N = 1,280

**BSC**

**Survival follow-up**

**No crossover**

N = 1,005

Wakelee HA. ASCO 2021; Abstract 8500
IMpower010: DFS in the PD-L1 TC ≥1%
Stage II-IIIA Population (Primary Endpoint)

Wakelee HA. ASCO 2021; Abstract 8500
IMpower010: DFS in the All-Randomized Stage II-IIIA Population (Primary Endpoint)

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Atezolizumab

N = 442

Median DFS (95% CI), mo
42.3 (36-NE)

Stratified HR (95% CI)
0.79 (0.64-0.96)

Stratified log-rank P
.02

BSC

N = 440

Median DFS (95% CI), mo
35.3 (30.4-46.4)

Median follow-up: 32.2 mo (range = 0-57.5)

Wakelee HA. ASCO 2021; Abstract 8500
IMpower010: DFS in NSCLC ≥5cm (7th ed. St II-III) Key Subsets

No obvious benefit in:
- Never smokers
- PD-L1 negative
- EGFR/ALK+

Adapted from Wakelee H et al. ASCO 2021;Abstract 8500
IMpower010: early OS data at interim DFS analysis

OS data were immature at this pre-planned DFS interim analysis
OS in the ITT population was not formally tested
A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population

Wakelee HA. ASCO 2021; Abstract 8500
IMpower010: Characterization of Stage IB-IIIA NSCLC Patients by Type and Extent of Therapy Prior to Adjuvant Atezolizumab

Nasser Altorki,1 Enriqueta Felip,2 Caicun Zhou,3 Eric Vallieres,4 Vladimir Moiseyenko,5 Alexey Smolin,6 Achim Rittmeyer,7 Roman Vereshchako,8 Maurice Perol,9 Wolfgang Schutte,10 Jian Fang,11 Min Tao,12 Encarnacao Teixeira,13 Young-Chul Kim,14 Virginia McNally,15 Fan Wu,16 Yu Deng,17 Elizabeth Bennett,17 Barbara Gitlitz,17 Heather Wakelee18

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# IMpower010: PD-L1 TC ≥1% Stage II-IIIA Population DFS by Disease and Treatment Characteristics

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>HR (95% CI)</th>
<th>Atezolizumab</th>
<th>BSC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>476</td>
<td>0.66 (0.50, 0.88)</td>
<td>NE</td>
<td>35.3</td>
</tr>
<tr>
<td><strong>Disease stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IIA</td>
<td>161</td>
<td>0.73 (0.43, 1.24)</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>83</td>
<td>0.77 (0.35, 1.69)</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>232</td>
<td>0.62 (0.42, 0.90)</td>
<td>42.3</td>
<td>26.7</td>
</tr>
<tr>
<td><strong>Regional lymph node status (pN)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>106</td>
<td>0.88 (0.45, 1.74)</td>
<td>36.7</td>
<td>NE</td>
</tr>
<tr>
<td>N+</td>
<td>370</td>
<td>0.62 (0.46, 0.85)</td>
<td>NE</td>
<td>31.4</td>
</tr>
<tr>
<td>N1</td>
<td>194</td>
<td>0.59 (0.36, 0.97)</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>N2</td>
<td>176</td>
<td>0.66 (0.44, 0.99)</td>
<td>32.3</td>
<td>21.3</td>
</tr>
<tr>
<td><strong>Type of surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>359</td>
<td>0.63 (0.45, 0.87)</td>
<td>NE</td>
<td>33.4</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>85</td>
<td>0.83 (0.43, 1.58)</td>
<td>36.1</td>
<td>NE</td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>24</td>
<td>0.78 (0.18, 3.33)</td>
<td>36.7</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Chemotherapy regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin-docetaxel</td>
<td>71</td>
<td>0.60 (0.30, 1.23)</td>
<td>36.1</td>
<td>18.0</td>
</tr>
<tr>
<td>Cisplatin-gemcitabine</td>
<td>75</td>
<td>1.14 (0.50, 2.61)</td>
<td>36.1</td>
<td>NE</td>
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<tr>
<td>Cisplatin-vinorelbine</td>
<td>161</td>
<td>0.55 (0.33, 0.92)</td>
<td>NE</td>
<td>34.2</td>
</tr>
<tr>
<td>Cisplatin-pemetrexed</td>
<td>169</td>
<td>0.66 (0.42, 1.06)</td>
<td>NE</td>
<td>31.4</td>
</tr>
</tbody>
</table>

Clinical cutoff: January 21, 2021. a Per SP283 assay.
b Stratified for all patients; unstratified for all other subgroups.
c Subgroups with ≤10 patients are not shown.

Altorki N et al. IASLC 2021;Abstract PL02.05
**IMpower010: All-Randomized Stage II-IIIA Population DFS by Disease and Treatment Characteristics**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>Median DFS, mo</th>
<th>HR (95% CI)</th>
<th>Atezolizumab</th>
<th>BSC</th>
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<tbody>
<tr>
<td><strong>Disease stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>882</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IIA</td>
<td>295</td>
<td></td>
<td>0.79 (0.64, 0.96)</td>
<td>42.3</td>
<td>35.3</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>174</td>
<td></td>
<td>0.68 (0.46, 1.00)</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>413</td>
<td></td>
<td>0.81 (0.61, 1.06)</td>
<td>37.1</td>
<td>46.4</td>
</tr>
<tr>
<td><strong>Regional lymph node status (pN)</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>229</td>
<td>32.3</td>
<td>0.88 (0.57, 1.35)</td>
<td>NE</td>
<td>46.4</td>
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<tr>
<td>N+</td>
<td>653</td>
<td></td>
<td>0.76 (0.60, 0.96)</td>
<td>42.3</td>
<td>31.4</td>
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<tr>
<td>N1</td>
<td>348</td>
<td></td>
<td>0.67 (0.47, 0.95)</td>
<td>NE</td>
<td>36.0</td>
</tr>
<tr>
<td>N2</td>
<td>305</td>
<td></td>
<td>0.83 (0.61, 1.13)</td>
<td>30.2</td>
<td>24.1</td>
</tr>
<tr>
<td><strong>Type of surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>675</td>
<td>42.3</td>
<td>0.77 (0.61, 0.97)</td>
<td>42.3</td>
<td>32.0</td>
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<tr>
<td>Pneumonectomy</td>
<td>150</td>
<td></td>
<td>0.91 (0.56, 1.47)</td>
<td>36.1</td>
<td>42.1</td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>47</td>
<td></td>
<td>1.02 (0.35, 2.98)</td>
<td>36.7</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Chemotherapy regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin-docetaxel</td>
<td>124</td>
<td></td>
<td>0.72 (0.42, 1.23)</td>
<td>36.1</td>
<td>37.3</td>
</tr>
<tr>
<td>Cisplatin-gemcitabine</td>
<td>138</td>
<td></td>
<td>0.76 (0.56, 1.57)</td>
<td>36.1</td>
<td>46.4</td>
</tr>
<tr>
<td>Cisplatin-vinorelbine</td>
<td>271</td>
<td></td>
<td>0.67 (0.46, 0.99)</td>
<td>NE</td>
<td>37.0</td>
</tr>
<tr>
<td>Cisplatin-pemetrexed</td>
<td>349</td>
<td></td>
<td>0.84 (0.61, 1.16)</td>
<td>42.3</td>
<td>31.4</td>
</tr>
</tbody>
</table>

Clinical cutoff: January 21, 2021.

* Stratified for all patients; unstratified for all other subgroups.

* Subgroups with ≤10 patients are not shown.

Altorki N et al. IASLC 2021;Abstract PL02.05
IMpower010: ITT (All-Randomized Stage IB-IIIA) Population DFS by Disease and Treatment Characteristics

Altorki N et al. IASLC 2021;Abstract PL02.05
Neoadjuvant PD-1 Blockade in Resectable Lung Cancer

CheckMate 816 Phase III study design

Key eligibility criteria
- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
- ECOG PS 0-1
- No known sensitizing EGFR mutations or ALK alterations

Stratified by stage (IB/II vs IIIA), PD-L1 (≥ 1% vs < 1%), and sex

N = 358
R 1:1

Primary endpoints
• pCR by BIPR
• EFS by BICR

Key secondary endpoints
• MPR by BIPR
• OS
• Time to death or distant metastases

Key exploratory endpoints included
• ORR by BICR
• Feasibility of surgery; peri- and post-operative surgery-related AEs

Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

a NCT02998528; this study included an exploratory arm: NIVO 3 mg/kg Q2W (3 cycles) + ipilimumab 1 mg/kg (cycle 1 only). Data from this arm are not included in this presentation; b Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); c Included patients with PD-L1 expression status not evaluable and indeterminate; d NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; e Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin.


Spicer J. ASCO 2021;Abstract 8503
CheckMate 816: MPR Rate in the ITT Population

MPR Rate, %

<table>
<thead>
<tr>
<th>Group</th>
<th>n/N</th>
<th>MPR Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivo + Chemo</td>
<td>66/179</td>
<td>36.9%</td>
</tr>
<tr>
<td>Chemo</td>
<td>16/179</td>
<td>8.9%</td>
</tr>
</tbody>
</table>

Difference: 27.9%

OR = 5.70 (95% CI, 3.16-10.26)

Spicer J. ASCO 2021;Abstract 8503
CheckMate 816: pCR Rate (Primary Endpoint)

- The addition of nivo to chemo increased pCR from 2.2% with chemo alone to 24% with chemo + nivo ($P < .0001$)
- pCR was assessed by central pathologists who were blinded to trial arms

**pCR Rate With Neoadjuvant Nivo + Chemo vs Chemo**

- pCR rate in the exploratory nivo + ipi arm (ITT) was 20.4% (95% CI, 13.4-29.0)

Forde PM et al. AACR 2021. Abstract CT003.

Courtesy of Brendan M Stiles, MD
CheckMate 816: Pathological Regression

- Surgical specimens had a median of 10% residual tumor cells after chemo + nivo vs 74% after chemo alone

- Median viable tumor cells were 10% in the nivo + chemo arm and 74% in the chemo arm

Forde PM et al. AACR 2021. Abstract CT003.
CheckMate 816: Type Of Surgery by Baseline Stage of Disease

**Lobectomy**
- NIVO + chemo
- Chemo

<table>
<thead>
<tr>
<th>BL stage</th>
<th>All</th>
<th>IB/II</th>
<th>IIIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>115/149</td>
<td>33/52</td>
<td>74/94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>77</th>
<th>74</th>
<th>79</th>
</tr>
</thead>
<tbody>
<tr>
<td>61</td>
<td>64</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>

**Pneumonectomy**
- NIVO + chemo
- Chemo

<table>
<thead>
<tr>
<th>BL stage</th>
<th>All</th>
<th>IB/II</th>
<th>IIIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>25/149</td>
<td>9/55</td>
<td>16/94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>17</th>
<th>17</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>
Neoadjuvant pembrolizumab for early stage non-small cell lung cancer

Jair Bar¹, Damien Urban¹, Ilanit Redinsky¹, Aliza Ackerstein¹, Sameh Daher¹, Iris Kamer¹, Amir Onn², Tiberiu Shulimzon², Michael Peled², Nona Zeitlin³, Ran Kremer³, Stephen Raskin⁴, Alon Ben-Nun³, Marina Perelman⁵, Efrat Ofek⁵

¹Institute of Oncology, Sheba Medical Center, Tel HaShomer, Ramat Gan, Israel, ²Institute of Pulmonology, Sheba Medical Center, Ramat Gan, Israel, ³Thoracic Surgery, Sheba Medical Center, Ramat Gan, Israel, ⁴Radiology Department, Sheba Medical Center, Ramat Gan, Israel, ⁵Pathology Department, Sheba Medical Center, Ramat Gan, Israel
# Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

<table>
<thead>
<tr>
<th>TRAE grade ≥ 3</th>
<th>AE leading to surgery deferral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pt. #19</strong></td>
<td><strong>Pt. #19</strong></td>
</tr>
<tr>
<td>72 yo male, past-light smoker. PMHx: CAF</td>
<td>72 yo male, past-light smoker. PMHx: CAF</td>
</tr>
<tr>
<td>Myositis grade 3 (day 9)</td>
<td>Myositis grade 3 (day 9)</td>
</tr>
<tr>
<td>Myocarditis grade 3 (day 22)</td>
<td>Myocarditis grade 3 (day 22)</td>
</tr>
<tr>
<td><strong>Pt. #29</strong></td>
<td><strong>Pt. #18</strong></td>
</tr>
<tr>
<td>62 yo female, heavy smoker</td>
<td>71 yo male, past heavy smoker. PMHx: DM2, HTN, diverticulosis</td>
</tr>
<tr>
<td>Encephalitis grade 3 (day 124)</td>
<td>Myocardial infarct (day 21)</td>
</tr>
<tr>
<td>Hepatitis grade 3 (day 171)</td>
<td></td>
</tr>
</tbody>
</table>

All in the expansion cohort

Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

Pathology: remaining viable tumor cells

Major Pathologic Response

Gray bars: Cohort 1 (single pembro dose)

Bar J et al. IASLC 2021;Abstract OA11.01
Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

Recommended Phase 2 Dose/Schedule

- No DLT in the escalation cohorts
- MPR was observed only in patients with a time interval from treatment initiation to surgery ≥ 5 weeks
- Recommended dose/schedule:

  
  - Exploratory: among the patients treated by this dose/schedule (n=16)
    - MPR 44% (7 of 16)
    - pCR 19% (3 of 16)

Bar J et al. IASLC 2021;Abstract OA11.01
Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

**TAKE HOME MESSAGES**

- Neoadjuvant Pembrolizumab was safe, with an 8% rate of grade 3-4 TRAE, with no apparent relation to treatment-surgery interval.
- Outcome in the entire study cohort:
  - 27% rate of MPR (7 of 26)
  - 12% rate of pCR (3 of 26)
- Longer interval from treatment to surgery was associated with higher rate of MPR.
- Two doses of neoadjuvant pembrolizumab at a three-week interval, followed by surgery at two weeks or later, is the RP2D/S.
- Exploratory look at the patients treated by the RP2D/S reveals:
  - MPR 44% (7 of 16)
  - pCR 19% (3 of 16)
# Ongoing Phase 3 NEO-Adj PD-(L)1 NSCLC IO

<table>
<thead>
<tr>
<th>Drug</th>
<th>N</th>
<th>Stages</th>
<th>Description</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivo + platinum Chemo (ipi/nivo closed) CheckMate 816</td>
<td>350</td>
<td>Stage IB–IIIA, resectable NSCLC</td>
<td>Neo-adjuvant, no adjuvant</td>
<td>MPR / RFS</td>
</tr>
<tr>
<td>Atezo + platinum Chemo IMpower030</td>
<td>374</td>
<td>Stage II–IIIB (T3N2), resectable NSCLC</td>
<td>Neo-adjuvant chemo-ICI, then adjuvant IO</td>
<td>MPR / RFS</td>
</tr>
<tr>
<td>Pembro + platinum-doublet Chemo KEYNOTE-671</td>
<td>786</td>
<td>Stage IIB–IIIA, resectable NSCLC</td>
<td>Neo-adjuvant chemo-ICI then adjuvant IO</td>
<td>RFS / OS</td>
</tr>
<tr>
<td>Durva + platinum-doublet Chemo</td>
<td>300</td>
<td>Stage II–IIIA, resectable NSCLC</td>
<td>Neo-adjuvant chemo-ICI then adjuvant IO</td>
<td>MPR</td>
</tr>
</tbody>
</table>

Courtesy of Heather Wakelee, MD
Agenda

Introduction: Tumor Board Discussions Since ASCO 2021?

Module 1: Immunotherapy in Surgically Resectable Non-Small Cell Lung Cancer
- Case: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type
- Case: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%
- Case: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%
- Key relevant data sets

Module 2: Adjuvant Treatment of NSCLC with a Driver Mutation
- Case: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation
- Case: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation
- Key relevant data sets
Case Presentation: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation

- S/p resection of a right hilar lesion and mediastinal lymph node dissection, which revealed a 5-cm lung adenocarcinoma with involvement of station 4R lymph nodes
- Stage III, pT2aN2
- PD-L1 assay: < 1%
- NGS: EGFR L858R mutation

Question
- What treatment approach would you recommended for this patient?
Case Presentation: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation (continued)

• S/p resection of a right hilar lesion and mediastinal lymph node dissection, which revealed a 5-cm lung adenocarcinoma with involvement of station 4R lymph nodes
• Stage III, pT2aN2
• PD-L1 assay: < 1%
• NGS: EGFR L858R mutation

Questions
• What treatment approach would you recommended for this patient?
• Would postoperative radiotherapy have been appropriate for this patient?
Case Presentation: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation

- Never smoker who presents to PCP with sudden onset dyspnea and is diagnosed with Stage IIIA, T2bN2 NSCLC
- NGS: ALK rearrangement
- PD-L1 assay: 50%
- Tumor is deemed resectable by the thoracic surgeon

Question
- What treatment option would you recommend for this patient?
- How do you interpret the PD-L1 score in a patient who is also positive for an ALK rearrangement?
- In light of the PACIFIC trial, what is your perspective on whether or not Stage III disease should undergo resection?
ADAURA: Disease-Free Survival by Stage

**ADAURA: Adjuvant Osimertinib in Resected Stage IB-IIIA EGFR+ NSCLC**

### DFS by stage

<table>
<thead>
<tr>
<th></th>
<th>Stage IB</th>
<th>Stage II</th>
<th>Stage IIIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2 year DFS rate, % (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osimertinib</td>
<td>87 (77, 93)</td>
<td>91 (82, 95)</td>
<td>88 (79, 94)</td>
</tr>
<tr>
<td>Placebo</td>
<td>73 (62, 81)</td>
<td>56 (45, 65)</td>
<td>32 (23, 42)</td>
</tr>
<tr>
<td><strong>Overall HR (95% CI)</strong></td>
<td>0.50 (0.25, 0.96)</td>
<td>0.17 (0.06, 0.31)</td>
<td>0.12 (0.07, 0.20)</td>
</tr>
</tbody>
</table>

- In the osimertinib arm, 2 year DFS rates were consistent across stages IB, II, and IIIA disease.
- Maturity (overall population: stage IB / II / IIIA) 29%: osimertinib events 12%, placebo events 46%

**DFS benefit increases consistently with stage**

*OS remains very immature (5% maturity)*

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Courtesy of Zofia Piotrowska, MD, MHS

Herbst R et al. ASCO 2020; Wu TL et al. NEJM 2020
Osimertinib Adjuvant Therapy in Patients (pts) with Resected EGFR Mutated (EGFRm) NSCLC (ADAURA): Central Nervous System (CNS) Disease Recurrence

Tsuboi M et al.
ESMO 2020;Abstract LBA1.
ADAURA: Sites of Disease Recurrence

Tsuboi M et al. ESMO 2020;Abstract LBA1.
**ADAURA: CNS DFS Events**

- Overall, 45 patients (osimertinib n=6, placebo n=39) had CNS DFS events

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Osimertinib n=339</th>
<th>Placebo n=343</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS DFS events:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS recurrence</td>
<td>4 (1%)</td>
<td>33 (10%)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (1%)</td>
<td>6 (2%)</td>
</tr>
</tbody>
</table>
ADAURA: CNS DFS in Overall Population

Tsuboi M et al. ESMO 2020;Abstract LBA1.
5-YEAR SURVIVAL OUTCOMES WITH DURVALUMAB AFTER CHEMORADIOThERAPY IN UNRESECTABLE STAGE III NSCLC – AN UPDATE FROM THE PACIFIC TRIAL

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June 4th, 2021

ASCO 2021; Abstract 8511
PACIFIC: Study Design

- Unresectable Stage III NSCLC without progression after definitive platinum-based cCRT* (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumor tissue for PD-L1 testing

Patients enrolled irrespective of PD-L1 status
N = 713 randomized

**Durvalumab**
10 mg/kg q2w for up to 12 months
N = 476

2:1 randomization, stratified by age, sex, and smoking history

**Placebo**
q2w for up to 12 months
N = 237

Primary endpoints
- PFS (BICR) using RECIST v1.1
- OS

Key secondary endpoints
- ORR, DoR, and TTDM (BICR) using RECIST v1.1
- Safety
- Patient-reported outcomes

- Updated analyses of OS and PFS, assessed ~5 years after the last patient was randomized (data cutoff: 11 January 2021; exploratory, post-hoc analysis)
  - Treatment effects were estimated using stratified log-rank tests in the ITT population
  - Medians and yearly landmark rates were estimated using the Kaplan–Meier method
PACIFIC: Updated Progression-Free Survival (ITT)

Spigel DR et al. ASCO 2021;Abstract 8511.
**PACIFIC: Updated Overall Survival (ITT)**

No. of events/total no. of patients (%) & Median OS (95% CI), months
\hline
Durvalumab & 264/476 (55.5) & 47.5 (38.1–52.9) \\
Placebo & 155/237 (65.4) & 29.1 (22.1–35.1) \\
\hline
**Stratified HR (95% CI): 0.72 (0.59–0.89)**

Stratified HR from the primary analysis (95% CI):1,2 0.68 (0.53–0.87)

Spigel DR et al. ASCO 2021;Abstract 8511.
AFT-16 Phase II Trial

• Median PFS = 23.7 mo
• OS at 18 mo = 84%
• 1 pt each with Gr 3 pneumonitis/pneumonia/colitis, Gr 4 Guillain Barre
• PFS 12 and 18 mo from end CRT was 78% and 72% vs 56% and 44% in PACIFIC

Ross HJ, ASCO 2021; Abstract 8513.
KEYNOTE-799 Phase II Trial

KEYNOTE-799 (NCT03631784)

Study Population
- Age ≥18 years
- Stage IIIA–C, unresectable, locally advanced, pathologically confirmed, previously untreated NSCLC
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- Adequate pulmonary function
- No prior systemic immunosuppressive therapy within 7 days

N = 216

Primary Objectives
- ORR per RECIST v1.1 by BICR
- Patients who develop grade ≥3 pneumonitis

Secondary Objectives
- PFS per RECIST v1.1 by BICR, OS, safety

COHORT A (Squamous and Nonsquamous NSCLC)
- Pembrolizumab 200 mg Q3W + Paclitaxel 200 mg/m² Q3W / Carboplatin AUC6 Q3W
- Pembrolizumab 200 mg Q3W + Paclitaxel 45 mg/m² QW / Carboplatin AUC2 QW / Thoracic radiotherapy

COHORT B (Nonsquamous NSCLC Only)
- Pembrolizumab 200 mg Q3W
- Pembrolizumab 200 mg Q3W

Cycle 1
- Pembrolizumab 200 mg Q3W + Pemetrexed 500 mg/m² Q3W / Cisplatin 75 mg/m² Q3W

Cycles 2–3
- Pembrolizumab 200 mg Q3W + Pemetrexed 500 mg/m² Q3W / Cisplatin 75 mg/m² Q3W / Thoracic radiotherapy

Cycles 4–17
- Pembrolizumab 200 mg Q3W

Statistical Analysis Details
- Efficacy and safety assessed in all patients as-treated

AUC, area under the concentration-time curve; BICR, blinded independent central review.

*60 Gy in 30 daily 2-Gy fractions. †Treatment continued until cycle 17 was completed or until documented disease progression, unacceptable AEs, intercurrent illness that prevents further administration of treatment, or study withdrawal. Pembrolizumab therapy was discontinued permanently in patients who develop grade ≥3 or recurrent grade 2 pneumonitis.

Jabour SK et al. ASCO 2021;Abstract 8512
### Efficacy Outcomes

<table>
<thead>
<tr>
<th>Total Population</th>
<th>Cohort A (Squamous and Nonsquamous)</th>
<th>Cohort B (Nonsquamous)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 112</td>
<td>n = 102</td>
</tr>
<tr>
<td><strong>ORR, % (95% CI)</strong></td>
<td>70.5 (61.2–78.8)</td>
<td>70.6 (60.7–79.2)</td>
</tr>
<tr>
<td>CR</td>
<td>4 (3.6)</td>
<td>5 (4.9)</td>
</tr>
<tr>
<td>PR</td>
<td>75 (67.0)</td>
<td>67 (65.7)</td>
</tr>
<tr>
<td>SD</td>
<td>20 (17.9)</td>
<td>23 (22.5)</td>
</tr>
<tr>
<td>PD</td>
<td>1 (0.9)</td>
<td>0</td>
</tr>
<tr>
<td>Not evaluable*/No assessment\b</td>
<td>2 (1.8) / 10 (8.9)</td>
<td>0 / 7 (6.9)</td>
</tr>
<tr>
<td><strong>DOR, median (range),\c mo</strong></td>
<td>NR (1.7+ to 19.7+)</td>
<td>NR (1.8+ to 21.4+)</td>
</tr>
<tr>
<td>DOR ≥12 mo,\c %</td>
<td>79.7</td>
<td>75.6</td>
</tr>
<tr>
<td><strong>PFS,\c median (95% CI), mo</strong></td>
<td>NR (16.6–NR)</td>
<td>NR (NR–NR)</td>
</tr>
<tr>
<td>12-mo PFS rate, %</td>
<td>67.1</td>
<td>71.6</td>
</tr>
<tr>
<td><strong>OS,\c median (95% CI), mo</strong></td>
<td>NR (NR–NR)</td>
<td>NR (21.9–NR)</td>
</tr>
<tr>
<td>12-mo OS rate, %</td>
<td>81.3</td>
<td>87.0</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>PD-L1 Status</th>
<th>TPS &lt;1% (n = 21)</th>
<th>TPS ≥1% (n = 66)</th>
<th>TPS &lt;1% (n = 28)</th>
<th>TPS ≥1% (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR, n (%)</strong></td>
<td>14 (66.7)</td>
<td>50 (75.8)</td>
<td>20 (71.4)</td>
<td>29 (72.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Histology</th>
<th>Nonsquamous (n = 39)</th>
<th>Squamous (n = 73)</th>
<th>Nonsquamous (n = 102)</th>
<th>Squamous (n = 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR, n (%)</strong></td>
<td>27 (69.2)</td>
<td>52 (71.2)</td>
<td>72 (70.6)</td>
<td>NA</td>
</tr>
</tbody>
</table>

**DOR**, duration of response; **NR**, not reached; **TPS**, tumor proportion score. \*\* indicates no PD by the time of last disease assessment.

\*Postbaseline assessment available but not evaluable or CR/PR/SD <6 weeks from first dose. \c No postbaseline assessment available for response evaluation. \c Kaplan-Meier estimate.


Jabbour SK et al. ASCO 2021;Abstract 8512
"The registrational clinical trial (GEMSTONE-301 study) of the anti-PD-L1 monoclonal antibody sugemalimab in patients with stage III NSCLC met its primary endpoint at a planned interim analysis reviewed by the independent Data Monitoring Committee. The findings showed that sugemalimab as a consolidation therapy brought statistically significant and clinically meaningful improvement in the Blinded Independent Central Review assessed PFS in patients with locally advanced/unresectable NSCLC without disease progression after concurrent or sequential chemoradiotherapy. Investigator assessed PFS showed consistent results as those of the primary endpoint. Sugemalimab was well-tolerated with no new safety signals. Subgroup analyses demonstrated that sugemalimab was associated with clinical benefit regardless of whether patients received concurrent or sequential chemoradiotherapy prior to sugemalimab."
What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

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11:00 AM – 12:30 PM ET

Faculty
Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator
Neil Love, MD
Thank you for joining us!

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