Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty
Corey J Langer, MD
Anne S Tsao, MD, MBA

Moderator
Neil Love, MD
YiR Immunotherapy and Other Nontargeted Approaches for Lung Cancer Faculty

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Director of Thoracic Oncology
Abramson Cancer Center
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Vice President, Faculty and Academic Affairs
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Clinical Medical Director ad Interim, Thoracic and Orthopaedic Center
Director, Mesothelioma Program
The University of Texas MD Anderson Cancer Center
Houston, Texas
Commercial Support

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Dr Love — Disclosures

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Companies/Institutions</th>
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<tbody>
<tr>
<td><strong>Advisory Committee</strong></td>
<td>AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Exelixis Inc, Genentech, a member of the Roche Group, Merck, Novocure Inc, Regeneron Pharmaceuticals Inc, Takeda Pharmaceuticals USA Inc</td>
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<tr>
<td><strong>Data and Safety Monitoring Board/Committee</strong></td>
<td>Lilly, Oncocyte</td>
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</tbody>
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## Dr Tsao — Disclosures

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

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty
Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator
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Chronic Lymphocytic Leukemia

Tuesday, January 25, 2022
5:00 PM – 6:00 PM ET

Faculty
Lindsey Roeker, MD
Jeff Sharman, MD

Moderator
Neil Love, MD
Promising Investigational Agents and Strategies for Patients with Metastatic Non-Small Cell Lung Cancer Who Experience Disease Progression on Immune Checkpoint Inhibitor Therapy

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5:00 PM – 6:00 PM ET

Faculty
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Neil Love, MD
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Acute Myeloid Leukemia and Myelodysplastic Syndromes

Thursday, January 27, 2022
5:00 PM – 6:00 PM ET

Faculty
Daniel A Pollyea, MD, MS
Gail J Roboz, 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.
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Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma
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Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

- KEYNOTE-091: Adjuvant pembrolizumab
- IMpower010: Adjuvant atezolizumab – FDA indication
- CheckMate 816: Neoadjuvant nivolumab/chemotherapy
- PACIFIC: Durvalumab consolidation
- PACIFIC R
- COAST: Durvalumab-based consolidation
Phase III KEYNOTE-091 Trial Meets One of Its Dual Primary Endpoints of DFS for the Adjuvant Treatment of Stage IB-IIIA NSCLC
Press Release: January 10, 2022

“The European Organisation for Research and Treatment of Cancer (EORTC) and the European Thoracic Oncology Platform (ETOP) today announced that the Phase 3 KEYNOTE-091 trial, also known as EORTC-1416-LCG/ETOP-8-15 – PEARLS, investigating pembrolizumab, met one of its dual primary endpoints of disease-free survival (DFS) for the adjuvant treatment of patients with stage IB-IIIA non-small cell lung cancer (NSCLC) following surgical resection regardless of PD-L1 expression. Based on an interim analysis review conducted by an independent Data Monitoring Committee, adjuvant treatment with pembrolizumab resulted in a statistically significant and clinically meaningful improvement in DFS compared with placebo in the all-comer population of patients with stage IB-IIIA NSCLC.

At the interim analysis, there was also an improvement in DFS for patients whose tumors express PD-L1 (tumor proportion score [TPS] ≥50%) treated with pembrolizumab compared to placebo; however, this dual primary endpoint did not meet statistical significance per the pre-specified statistical plan. The trial will continue to analyze DFS in patients whose tumors express high levels of PD-L1 (TPS ≥50%) and evaluate overall survival (OS), a key secondary endpoint.”

Resectable NSCLC: Adjuvant Immunotherapy

**IMpower010: study design**

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

**No crossover**

- Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine
  - 1-4 cycles
  - N=1280

- Atezolizumab 1200 mg q21d 16 cycles
  - N=1005

- Survival follow-up

**Stratification factors**
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status:
  - 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

**Safety**
- Consistent with prior data.
- 7.9% grade 3-4 imAE with atezolizumab

**imAEs occurring in ≥1% of patients**

<table>
<thead>
<tr>
<th></th>
<th>Atezolizumab (n=495)</th>
<th>BSC (n=495)</th>
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</thead>
<tbody>
<tr>
<td>Any grade</td>
<td>Any grade</td>
<td></td>
</tr>
<tr>
<td>51.7%</td>
<td>9 (5.5%)</td>
<td></td>
</tr>
<tr>
<td>39 (7.9%)</td>
<td>11 (2.2%)</td>
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<tr>
<td>47 (9.5%)</td>
<td>0</td>
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<tr>
<td>1344.0</td>
<td>22 (4.4%)</td>
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</tr>
<tr>
<td>1357.0</td>
<td>10 (2.0%)</td>
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<tr>
<td>16 (3.2%)</td>
<td>21 (4.2%)</td>
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</tr>
<tr>
<td>86 (17.4%)</td>
<td>7 (1.4%)</td>
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<tr>
<td>4 (0.8%)</td>
<td>100 (%)</td>
<td></td>
</tr>
<tr>
<td>6 (1.2%)</td>
<td>6 (1.2%)</td>
<td></td>
</tr>
<tr>
<td>32 (6.5%)</td>
<td>2 (0.4%)</td>
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<tr>
<td>4 (0.8%)</td>
<td>4 (0.8%)</td>
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</table>

Clinical cutoff: January 21, 2021. ° Data are from the safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). † Includes 2 (0.4%) Grade 5 events. ‡ Includes 1 (0.2%) Grade 5 event.
**IMpower010: Atezolizumab improves DFS in stages II-III A**

**Atezolizumab conveys DFS benefit in:**
- Stage II-III A PDL1 > 1% (HR 0.66)
- Stage II-III A (HR 0.79)

Wakelee et al. ASCO 2021 Abstract 8500; Felip et al. Lancet 398: 1344-1357, Oct 2021

Courtesy of Anne S Tsao, MD, MBA
Neoadjuvant Nivolumab with Chemotherapy Significantly Improves Event-Free Survival for Patients with Resectable NSCLC in the Phase III CheckMate 816 Trial
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...

‘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 non-small cell lung cancer. The combination of nivolumab plus chemotherapy first showed a statistically significant improvement in pathologic complete response rate without impacting surgical outcomes and has now extended the time patients live free of disease progression, recurrence or death,’ said Abderrahim Oukessou, MD, vice president, thoracic cancers development lead. ‘The event-free survival data from CheckMate -816 strengthen the evidence for the potential of nivolumab-based therapies to improve long-term clinical outcomes when used in the earlier stages of non-metastatic cancers.’

Resectable NSCLC: Neoadjuvant CheckMate 816

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

Stratified by Stage (IB-II vs IIIA), PD-L1b (≥ 1% vs < 1%), and sex

N = 358
R 1:1

Primary analysis population

NIVO 360 mg Q3W + chemo^d Q3W (3 cycles)

Chemo^c Q3W (3 cycles)

Radiologic restaging

Surgery (within 6 weeks post-treatment)

Optional adjuvant chemo ± RT^e

Follow-up

Primary endpoints
• pCR by BIPR
• EFS by BICR

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

Exploratory endpoints
• ORR by BICR
• Predictive biomarkers (PD-L1, TMB, ctDNA^f)

pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes
MPR: < 10% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes

Courtesy of Anne S Tsao, MD, MBA
CheckMate 816 Nivolumab + Chemo improves pCR, MPR, ORR

**Objective response rate**

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>NIVO + chemo (n = 179)</th>
<th>Chemo (n = 179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORRa</td>
<td>96 (54)b</td>
<td>67 (37)b</td>
</tr>
<tr>
<td>Best overall response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>1 (1)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Partial response</td>
<td>95 (53)</td>
<td>64 (36)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>70 (39)</td>
<td>88 (49)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>8 (4)</td>
<td>11 (6)</td>
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<tr>
<td>Not evaluable</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Not reported</td>
<td>4 (2)</td>
<td>12 (7)</td>
</tr>
</tbody>
</table>

**Courtesy of Anne S Tsao, MD, MBA**
CheckMate 816

No difference in surgical delays, complications or hospital stay

Median time from last neoadjuvant dose to surgery nivo+chemo 5.3 weeks (4.6-6) vs chemo 5 weeks (4.6-5.9)

<table>
<thead>
<tr>
<th></th>
<th>NIVO + chemo (n = 135)</th>
<th>Chemo (n = 124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of hospital stay, median (IQR), days</td>
<td>10.0 (7.0-14.0)</td>
<td>10.0 (7.0-14.5)</td>
</tr>
<tr>
<td>Length of hospital stay by surgery type, a median (IQR), days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>10.0 (7.0-15.0)</td>
<td>9.0 (6.0-14.0)</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>10.0 (8.0-13.0)</td>
<td>11.0 (9.0-16.0)</td>
</tr>
<tr>
<td>Other b</td>
<td>8.5 (4.0-13.0)</td>
<td>9.0 (7.0-14.0)</td>
</tr>
<tr>
<td>Length of hospital stay per region, c,d median (IQR), days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>4.0 (4.0-7.0)</td>
<td>6.0 (4.0-8.0)</td>
</tr>
<tr>
<td>Europe</td>
<td>9.5 (8.0-14.0)</td>
<td>13.0 (7.0-18.0)</td>
</tr>
<tr>
<td>Asia</td>
<td>11.0 (9.0-16.0)</td>
<td>13.0 (10.0-16.0)</td>
</tr>
</tbody>
</table>

Courtesy of Anne S Tsao, MD, MBA
Local-regional NSCLC: PACIFIC 5-year update shows continued PFS & OS benefit

- 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

Placebo
q2w for up to 12 months
N = 237

- OS HR = 0.72 (95% CI: 0.55–0.89)
- PFS HR = 0.55 (95% CI: 0.45–0.68)

*Stratified HR from the primary analysis (95% CI)
PACIFIC-R (NCT 03798535): An international, observational study

**Patient population**
- Unresectable, Stage III NSCLC, regardless of tumour PD-L1 expression
- No evidence of progression following definitive, platinum-based CRT

**Index date**
- Start of durvalumab (10mg/kg IV Q2W) through the EAP (Sept 2017 to Dec 2018)

**Data extracted from patients’ medical records — retrospective data collection at different time points**

- **5-year observation to evaluate disease evolution**
  - Dec 2018 to Aug 2020
  - Jul to Oct 2020
  - Estimated Q4 2021 to Q1 2022
  - Estimated Q4 2023

- **Endpoints**
  - **Primary:** investigator-assessed PFS; OS
  - **Key secondary:** demographics; disease characteristics; prior therapy; PFS/OS by subgroups; AEs/Is

**Endpoints**

- **1,399 patients** included in the full analysis set (FAS) from 290 active sites in 11 participating countries
  - France (n=342), Spain (244), Australia (165), Netherlands (155), Belgium (118), Italy (116), Israel (92), Germany (62), UK (54), Norway (36), and Switzerland (15)

- **Median time to initiate durvalumab = 56 days**
- **Median durvalumab infusions = 22**
- **Median durvalumab duration = 335 days**
  - 20.1% > 12 months
  - 4.4% > 14 months

- **PACIFIC-R** Median PFS 21.7 months vs PACIFIC 16.9 months

- **16.7% treatment discontinuation due to AE**
  - 9.5% Pneumonitis permanent discontinuation
  - 5.2% pneumonitis temporary discontinuation
  => 71.3% required corticosteroids

*PACIFIC-R had challenges in data collection: Germany/UK did not collect deaths on 50, RECIST not consistently used, assessments for progression not consistently collected – pandemic led to less visits for assessment.

Girard et al. ESMO 2021 Abstract 1171MO

Courtesy of Anne S Tsao, MD, MBA
COAST (Combination Platform Study in Unresectable Stage III NSCLC; NCT03822351)

Phase 2 study of durvalumab alone or combined with the anti-CD73 mAb oleclumab or anti-NKG2A mAb monalizumab as consolidation therapy

Oleclumab, anti-CD73, Reduces extracellular adenosine production Promotes antitumour immunity

Monalizumab blocks NKG2A to reduce inhibition of NK and CD8+ T cells.

Martinez-Marti et al. ESMO 2021 Abstract LBA42

Courtesy of Anne S Tsao, MD, MBA
COAST: Phase 2

Locally advanced, unresectable, Stage III NSCLC
No progression after prior cCRT
ECOG PS 0 or 1
N=189 randomised

1–42 days post-cCRT

Randomised 1:1:1
Stratification by histology (adenocarcinoma and non-adenocarcinoma)

Study treatment up to 12 months

CONTROL
Durvalumab 1500 mg IV monotherapy Q4W

ARM A
Durvalumab 1500 mg IV Q4W + olecumab 3000 mg IV
Olecumab Q2W for cycles 1 and 2, then Q4W starting cycle 3

ARM B
Durvalumab 1500 mg IV Q4W + monalizumab 750 mg IV Q2W

Primary Endpoint
- ORR by investigator assessment (RECIST v1.1)

Secondary Endpoints
- Safety
- DoR
- DCR
- PFS by investigator assessment (RECIST v1.1)
- OS
- PK
- Immunogenicity

A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumour activities in an early phase setting.

Between Jan 2019 and Jul 2020, 189 patients were randomised of whom 186 received D (n=66), D+O (n=59) or D+M (n=61)
COAST Results favor D+O and D+M for PFS with no significant increase in toxicity

<table>
<thead>
<tr>
<th>Antitumor activity</th>
<th>D (n=67)</th>
<th>D+O (n=60)</th>
<th>D+M (n=62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR</td>
<td>17.9</td>
<td>30</td>
<td>35.5</td>
</tr>
<tr>
<td>DCR 16 weeks</td>
<td>58.2</td>
<td>81.7</td>
<td>77.4</td>
</tr>
<tr>
<td>Median DoR (months)</td>
<td>NR</td>
<td>12.9</td>
<td>NR</td>
</tr>
<tr>
<td>mPFS</td>
<td>6.3</td>
<td>NR</td>
<td>15.1</td>
</tr>
<tr>
<td>HR</td>
<td>-</td>
<td>0.44</td>
<td>0.65</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incidence, n (%)</th>
<th>D (N=66)</th>
<th>D+O (N=59)</th>
<th>D+M (N=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAEs</td>
<td>65 (98.5)</td>
<td>57 (96.6)</td>
<td>61 (100)</td>
</tr>
<tr>
<td>Grade ≥3 TEAEs</td>
<td>26 (39.4)</td>
<td>24 (40.7)</td>
<td>17 (27.9)</td>
</tr>
<tr>
<td>Study drug-related AEs</td>
<td>49 (74.2)</td>
<td>46 (78.0)</td>
<td>50 (82.0)</td>
</tr>
<tr>
<td>Study drug-related SAEs</td>
<td>6 (9.1)</td>
<td>7 (11.9)</td>
<td>5 (8.2)</td>
</tr>
<tr>
<td>AEs leading to discontinuation</td>
<td>11 (16.7)</td>
<td>9 (15.3)</td>
<td>9 (14.8)</td>
</tr>
<tr>
<td>Deaths*</td>
<td>7 (10.6)</td>
<td>4 (6.8)</td>
<td>3 (4.9)</td>
</tr>
</tbody>
</table>

*All reported deaths within 90 days post-last dose, regardless of relationship to study drug

*In total, 4 deaths were related to study drug, 2 (pneumonitis and radiation pneumonitis) in the D arm, 1 (pneumonitis) in the D+O arm, and 1 (myocardial infarction) in the D+M arm

Martinez-Marti et al. ESMO 2021 Abstract LBA42

Courtesy of Anne S Tsao, MD, MBA
Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma
Module 2: NSCLC — Metastatic Disease

- Follow-up of older first- and second-line trials: PD-1, tumor mutational burden (TMB)
- Cemiplimab
- POSEIDON: Chemotherapy/durvalumab/tremelimumab
- Correlation of immune adverse events and antitumor effect
- Datopotamab deruxtecan (Dato-DXd)
- Plinabulin
- Tiragolumab
First-Line Treatment of Metastatic NSCLC

- Optimal PD-1 assay, choice of agent, TMB
- Long-term survival/cure
- Benefit of immunotherapy: Adenocarcinoma versus squamous
- Monotherapy versus chemotherapy/immunotherapy
- Options for PD-1-negative disease
- Ipilimumab/nivolumab; durvalumab/tremelimumab
- Correlation of immune adverse events with efficacy
- Second-line treatment: Docetaxel with or without ramucirumab; Dato-DXd
**Key Eligibility Criteria**
- Treatment-naïve advanced NSCLC
- PD-L1 ≥50%
- No EGFR, ALK or ROS1 mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases and controlled hepatitis B or C or HIV were allowed

**Stratification Factors:**
- Histology (squamous vs non-squamous)
- Region (Europe, Asia or ROW)

**Arm A**
- Cemiplimab monotherapy IV
- 350 mg Q3W
- Treat until PD or 108 weeks

**Arm B**
- 4–6 cycles of investigator’s choice chemotherapy

**Endpoints:**
- Primary: OS and PFS
- Secondary: ORR (key), DOR, HRQoL and safety

Five interim analyses were prespecified per protocol
Second interim analysis (1 March 2020) presented here

**Optional continuation of cemiplimab + 4 cycles of chemotherapy**

**Optional crossover to cemiplimab monotherapy**

**N=710**

Courtesy of Corey J Langer, MD
EMPOWER-Lung 1: Survival

Overall survival in the PD-L1 ≥50% population

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Median overall survival months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab</td>
<td>283</td>
</tr>
<tr>
<td></td>
<td>Not reached (95% CI 17.9–NE)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>14.2 (95% CI 11.2–17.5)</td>
</tr>
</tbody>
</table>

Progression-free survival in the PD-L1 ≥50% population

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Median progression-free survival months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab</td>
<td>283</td>
</tr>
<tr>
<td></td>
<td>8.2 (95% CI 6.1–8.8)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>5.7 (95% CI 4.5–6.2)</td>
</tr>
</tbody>
</table>

Hazard ratio for death 0.57 (95% CI 0.42–0.77) p=0.0002

Hazard ratio for disease progression or death 0.54 (95% CI 0.43–0.68) p<0.0001

• Overall Survival

**ITT**

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Median OS (95% CI) mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab</td>
<td>356</td>
</tr>
<tr>
<td></td>
<td>22.1 (95% CI, 17.7–NE)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>354</td>
</tr>
<tr>
<td></td>
<td>14.3 (95% CI, 11.7–19.2)</td>
</tr>
</tbody>
</table>

HR, 0.68 (95% CI, 0.53–0.87); P=0.0022

**PD-L1 ≥50% ITT**

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Median OS (95% CI) mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab</td>
<td>283</td>
</tr>
<tr>
<td></td>
<td>Not reached (95% CI, 17.9–NE)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>14.2 (95% CI, 11.2–17.5)</td>
</tr>
</tbody>
</table>

HR, 0.57 (95% CI, 0.42–0.77); P=0.0002

Median duration of follow-up:
- Cemiplimab → 13.1 months (range: 0.1–31.9)
- Chemotherapy → 13.1 months (range: 0.2–32.4)

**PD-L1, programmed cell death-ligand 1.**

Data cut-off date: 1 March 2020 (interim analysis #2)
### Tumour Response and DOR

#### ITT

- **Cemiplimab**: ORR: 36.5% (95% CI: 31.5–41.8)
  - CR: 3.1%
  - PR: 33.4%

- **Chemotherapy**: ORR: 20.6% (95% CI: 16.5–25.2)
  - CR: 0.8%
  - PR: 19.8%

- **P-value**: P<0.0001

#### PD-L1 ≥50% ITT

- **Cemiplimab**: ORR: 39.2% (95% CI: 33.5–45.2)
  - CR: 2.1%
  - PR: 37.1%

- **Chemotherapy**: ORR: 20.4% (95% CI: 15.8–25.6)
  - CR: 1.1%
  - PR: 19.3%

- **P-value**: P<0.0001

---

<table>
<thead>
<tr>
<th></th>
<th>Cemiplimab</th>
<th>Chemotherapy</th>
<th>Cemiplimab</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong>, unless stated</td>
<td>ITT (n=356)</td>
<td>ITT (n=354)</td>
<td>PD-L1 ≥50% ITT (n=283)</td>
<td>PD-L1 ≥50% ITT (n=280)</td>
</tr>
<tr>
<td><strong>Median DOR, months (95% CI)</strong></td>
<td>21.0 (14.9–NE)</td>
<td>6.0 (4.3–6.4)</td>
<td>16.7 (12.5–22.8)</td>
<td>6.0 (4.3–6.5)</td>
</tr>
<tr>
<td><strong>Median observed time to response, months (range)</strong></td>
<td>2.1 (1.4–10.4)</td>
<td>2.1 (1.4–6.7)</td>
<td>2.1 (1.4–10.4)</td>
<td>2.1 (1.4–6.3)</td>
</tr>
</tbody>
</table>

• CI, confidence interval; CR, complete response; DOR, duration of response; ITT, intention-to-treat; NE, not evaluable; ORR, objective response rate; PD-L1, programmed cell death-ligand 1; PR, partial response.

Data cut-off date: 1 March 2020 (interim analysis #2)

Courtesy of Corey J Langer, MD
Background: Cemiplimab (a high-affinity, fully human anti–PD-1) is approved as first-line monotherapy for advanced NSCLC with PD-L1 ≥50% (EMPOWER-Lung 1 Study)¹

Key eligibility criteria
- Treatment-naive advanced NSCLC (non-squamous and squamous histology; Stage IIIb/c, IV)
- Any PD-L1 expression
- No EGFR, ALK, or ROS1 mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases‡

Stratification factors
- PD-L1 expression: <1% vs 1–49% vs ≥50%
- Histology: non-squamous vs squamous

Endpoints
- Primary: OS
- Key secondary: PFS and ORR
- Additional secondary: DOR, BOR, safety, and PRO

Arm A
Cemiplimab 350 mg Q3W + investigator’s choice platinum-doublet chemo Q3W for 4 cycles§

Arm B
Placebo Q3W + investigator’s choice platinum-doublet chemo Q3W for 4 cycles §

N=466
Two interim analyses were prespecified per protocol
Second interim analysis (14 June 2021) presented here

¹Patient not a candidate for definitive chemoradiation. ‡Patient must have neurologically returned to baseline (except for residual signs or symptoms related to the CNS treatment). §For patients with non-squamous NSCLC, pemetrexed is mandatory as maintenance therapy for those patients initially assigned to receive a pemetrexed-containing regimen. ALK, anaplastic lymphoma kinase gene; BOR, best overall response; chemo, chemotherapy; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor gene; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcomes; Q3W, every 3 weeks; R, randomised; ROS1, c-ros oncogene 1.

Progression-Free Survival

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>No. of events, n (%)</th>
<th>PFS, median (95% CI), months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab + chemo</td>
<td>312</td>
<td>204 (65.4)</td>
<td>8.2 (6.4–9.3)</td>
</tr>
<tr>
<td>Placebo + chemo</td>
<td>154</td>
<td>122 (79.2)</td>
<td>5.0 (4.3–6.2)</td>
</tr>
</tbody>
</table>

HR (95% CI) = 0.56 (0.44–0.70); *P* < 0.0001

Median duration of follow-up (range): 16.4 (8.5–24.0) months

12-month PFS (95% CI), %

- Cemiplimab + chemo: 38.1 (32.4–43.8)
- Placebo + chemo: 16.4 (10.5–23.4)

No. at risk:

<table>
<thead>
<tr>
<th></th>
<th>Cemiplimab + chemo</th>
<th>Placebo + chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month</td>
<td>312 280 248 194 145 113 90 57 27 15 2</td>
<td>154 133 106 64 34 24 16 11 6 1 1 0 0 0</td>
</tr>
</tbody>
</table>

Data cut-off date: 14 June 2021

Courtesy of Corey J Langer, MD
Overall Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>No. of events, n (%)</th>
<th>OS, median (95% CI), months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab + chemo</td>
<td>312</td>
<td>132 (42.3)</td>
<td>21.9 (15.5–NE)</td>
</tr>
<tr>
<td>Placebo + chemo</td>
<td>154</td>
<td>82 (53.2)</td>
<td>13.0 (11.9–16.1)</td>
</tr>
</tbody>
</table>

HR (95% CI) = 0.71 (0.53–0.93); P=0.014

No. at risk:
- Cemiplimab + chemo: 312, 289, 269, 256, 233, 199, 162, 131, 86, 52, 18, 8, 0, 0
- Placebo + chemo: 154, 141, 126, 112, 98, 85, 65, 46, 26, 14, 5, 2, 0, 0

Data cut-off date: 14 June 2021

Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival.

Courtesy of Corey J Langer, MD
POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study

- Stage IV NSCLC
- No EGFR or ALK alterations
- ECOG PS 0 or 1
- Treatment-naïve for metastatic disease
  
  \[N=1013\text{ (randomized)}\]

Stratified by:
- PD-L1 expression (TC ≥50% vs <50%)
- Disease stage (IVA vs IVB)
- Histology

R \[1:1:1\]

**Primary endpoints**
- PFS by BICR (D+CT vs CT)
- OS (D+CT vs CT)

**Key secondary endpoints**
- PFS by BICR (D+T+CT vs CT)
- OS (D+T+CT vs CT)
- OS in patients with bTMB ≥20 mut/Mb (D+T+CT vs CT)

**Additional secondary endpoints**
- ORR, DoR, and BOR by BICR
- PFS at 12 months
- HRQoL
- Safety and tolerability

**CT options:**
- gemcitabine + carboplatin/cisplatin (squamous), pemetrexed + carboplatin/cisplatin (non-squamous), or nab-paclitaxel + carboplatin (either histology);
- Patients with non-squamous histology who initially received pemetrexed during first-line treatment only (if eligible);
- Patients received an additional dose of tremelimumab post CT (5th dose)

Courtesy of Corey J Langer, MD
Durvalumab + CT vs CT: PFS and OS

**PFS**

<table>
<thead>
<tr>
<th>Events, n/N (%)</th>
<th>253/338 (74.9)</th>
<th>258/337 (76.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, months (95% CI)</td>
<td>5.5 (4.7–6.5)</td>
<td>4.8 (4.6–5.8)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.74 (0.62–0.89)</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.00093</td>
<td></td>
</tr>
</tbody>
</table>

**OS**

<table>
<thead>
<tr>
<th>Events, n/N (%)</th>
<th>264/338 (78.1)</th>
<th>285/337 (84.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mOS, months (95% CI)</td>
<td>13.3 (11.4–14.7)</td>
<td>11.7 (10.5–13.1)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.86 (0.72–1.02)</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.07581</td>
<td></td>
</tr>
</tbody>
</table>

- Median follow-up in censored patients at DCO: 10.3 months (range 0–23.1)
- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Courtesy of Corey J Langer, MD
Durvalumab + Tremelimumab + CT vs CT: PFS and OS

**PFS**

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>D+T+CT</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>338</td>
<td>243</td>
<td>161</td>
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<tr>
<td>219</td>
<td>121</td>
<td>43</td>
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<td>23</td>
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<tr>
<td>5</td>
<td>3</td>
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<tr>
<td>0</td>
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</tbody>
</table>

Events, n/N (%) | 238/338 (70.4) | 258/337 (76.6) |

mPFS, months (95% CI) | 6.2 (5.0–6.5) | 4.8 (4.6–5.8) |

HR (95% CI) | 0.72 (0.60–0.86) |

p-value | 0.00031 |

**OS**

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>D+T+CT</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>338</td>
<td>298</td>
<td>256</td>
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<td>1</td>
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</tbody>
</table>

Events, n/N (%) | 251/338 (74.3) | 285/337 (84.6) |

mOS, months (95% CI) | 14.0 (11.7–16.1) | 11.7 (10.5–13.1) |

HR (95% CI) | 0.77 (0.65–0.92) |

p-value | 0.00304 |

• Median follow-up in censored patients at DCO: 10.3 months (range 0–23.1)

• Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Courtesy of Corey J Langer, MD
Plinabulin: microtubule-targeted agent with distinct MoA

- Direct effect on tumour cells: prevents β-tubulin polymerisation into microtubules
- Vascular disrupting agent: endothelial cells disruption
- Immune functions:
  - Microtubule destabilization in dendritic cells drives DC maturation through the release of GEF-H1 from microtubules
  - Enhances cross-presentation of tumour antigens to CD8 T cells
  - Could promote TAM anti-tumour effector functions

Singh, Blood 2011; Kashyap, Cell Rep 2019; Natoli, Front Oncol 2021

Courtesy of Corey J Langer, MD
**DUBLIN-3 Phase 3 Trial**

**DUBLIN - 3**

- Non-squamous or squamous NSCLC
- Stage IIIb/IV
- ECOG performance status ≤ 2
- Progression during or after treatment with one or two treatment regimens containing platinum
- Must have at least one measurable lung lesion
- Prior checkpoint inhibitor therapy allowed
- Written consent

**Randomized 1:1 21-day cycle (n=599)**

- **Docetaxel + Plinabulin (N=278)**
  - All Cycles:
    - Day 1: Docetaxel 75 mg/m² + Plinabulin 30 mg/m²
    - Day 8: Plinabulin 30 mg/m²

- **Docetaxel + Placebo (N=281)**
  - All Cycles:
    - Day 1: Docetaxel 75 mg/m² + Placebo
    - Day 8: Placebo

**Stratification factors?**

- Only 22% of patients were previously exposed to CPI

**Brain mets allowed?**

- Only 22% of patients were previously exposed to CPI

**Primary endpoint:** Overall Survival (OS)

**Secondary endpoints:** ORR, PFS, Percent of patients with grade 4 neutropenia on C1D8, Month 24 OS rate, Month 36 OS rate, DoR, Q-TWiST, QoL, % patients who received docetaxel >8 cycles, >10 cycles, and >12 cycles

- 87.5% of patients from China
- 59.2% non-squamous NSCLC, EGFR wild-type
- 3.6% PS 2
- 75% one prior treatment line

**Courtesy of Corey J Langer, MD**
DUBLIN-3 Trial: main efficacy findings

Median OS (95% CI): **10.5** (9.3, 11.9) vs. **9.4** (8.4, 10.7)
HR = **0.82** (0.68, 0.99), p=0.0399
Mean OS (SE): 15.08 vs. 12.77, p=0.0332

Median PFS (95% CI): **3.6** (3.0, 4.4) vs. **3.0** (2.8, 3.7)
HR = **0.76** (0.63, 0.93), p=0.0082
DUBLIN-3 Trial: safety of docetaxel-plinabulin combination

- Clear reduction of grade 4 neutropenia (day 8, all cycles: 5.1% vs 33.6%)
- Reduction of febrile neutropenia incidence?
- Increase of non-haematological toxicities (hypertension, diarrhoea) without apparent impact on QoL

<table>
<thead>
<tr>
<th>Preferred term</th>
<th>All Grade (N=278)</th>
<th>Grade 3/4</th>
<th>All Grade (N=274)</th>
<th>Grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count decreased</td>
<td>183(65.8%)</td>
<td>130(46.8%)</td>
<td>156(56.9%)</td>
<td>75(27.4%)</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>186(66.9%)</td>
<td>144(51.8%)</td>
<td>134(48.9%)</td>
<td>81(29.6%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>63(22.7%)</td>
<td>0</td>
<td>93(33.9%)</td>
<td>3(1.1%)</td>
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<tr>
<td>Diarrhea</td>
<td>47(16.9%)</td>
<td>2(0.7%)</td>
<td>101(36.9%)</td>
<td>23(8.4%)</td>
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<tr>
<td>Hypertension</td>
<td>9(3.2%)</td>
<td>3(1.1%)</td>
<td>85(31.0%)</td>
<td>47(17.2%)</td>
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Quality of life

Courtesy of Corey J Langer, MD
TROPION-PanTumor01: Updated Results From the NSCLC Cohort of the Phase 1 Study of Datopotamab Deruxtecan in Solid Tumors

Garon E et al.
WCLC 2021;Abstract MA03.02.
TROPION-PanTumor01: Study Design

Key Inclusion Criteria
- Relapsed/refractory advanced/metastatic NSCLC
- Unselected for TROP2 expression
- Age ≥18 (US) or ≥20 (Japan) years
- ECOG PS 0-1
- Measurable disease per RECIST version 1.1
- Stable, treated brain metastases allowed

Dose Escalation
- Dato-DXd 0.27 to 10 mg/kg Q3W
- MTD established: 8 mg/kg Q3W

Dose Expansion
- NSCLC cohort
- 50 patients at 4 mg/kg
- 50 patients at 6 mg/kg
- 80 patients at 8 mg/kg

Primary objectives
- Establish MTD; safety, tolerability

Secondary objectives
- Efficacy, PK, ADAs

6-mg/kg dose chosen for further development

Garon E et al. WCLC 2021;Abstract MA03.02.
TROPION-PanTumor01: Best Change in Sum of Diameters (per BICR)

Garon E et al. WCLC 2021;Abstract MA03.02.
TROPIQN-Lung01: Phase III Trial Design

Patient Population (N=590)
- Advanced or metastatic NSCLC
- No EGFR, ALK, or other known actionable genomic alterations
- Previous treatment with platinum-based chemotherapy and anti-PD-1/PD-L1 immunotherapy in combination or sequentially
- Measurable disease (per RECIST version 1.1)
- ECOG PS 0 or 1

Stratified by:
- Histology (squamous vs nonsquamous)
- Immunotherapy in last regimen (yes vs no)
- Region (US/Japan/Western Europe vs rest of the world)

Treatment until:
- Disease progression or death
- Unacceptable toxicity

Yoh K et al. ASCO 2021;Abstract TPS9127.
Novel Anti-TIGIT Tiragolumab Granted FDA Breakthrough Therapy Designation in Combination with Atezolizumab for PD-L1-High NSCLC

Press Release: January 5, 2021

“Today [it was] announced that tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA), in combination with atezolizumab for the first-line treatment of people with metastatic non-small cell lung cancer (NSCLC) whose tumours have high PD-L1 expression with no EGFR or ALK genomic tumour aberrations. Tiragolumab is the first anti-TIGIT molecule to be granted BTD from the FDA, and the designation is based on randomised data from the phase II CITYSCAPE trial. CITYSCAPE provides the first evidence that targeting both immune inhibitory receptors, TIGIT and PD-L1, may enhance anti-tumour activity by potentially amplifying the immune response.

Tiragolumab in combination with atezolizumab has so far shown encouraging efficacy and safety in PD-L1-positive metastatic NSCLC based on data from the phase II CITYSCAPE trial, the first randomised study in the anti-TIGIT field...the combination showed an improvement in the overall response rate (ORR; 37% vs. 21% with atezolizumab alone) and a 42% reduction in the risk of disease worsening or death (progression free survival; PFS) compared with atezolizumab alone. An exploratory analysis in people with high levels of PD-L1 TPS ≥ 50% showed a clinically meaningful ORR vs. atezolizumab alone (66% vs. 24%) and median PFS was not reached (vs. 4.11 months with atezolizumab alone; HR=0.30). The data suggest that tiragolumab plus atezolizumab was generally well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events when combining the two immunotherapies compared with atezolizumab alone (48% vs. 44%).”

https://www.roche.com/media/releases/med-cor-2021-01-05.htm
Abstract LBA2

ESMO IMMUNO-ONCOLOGY

Onsite and Online Congress

Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC

Byoung Chul Cho,¹ Delvys Rodriguez-Abreu,² Maen Hussein,³ Manuel Cobo,⁴ Anjan Patel,⁵ Nevena Secen,⁶ Gregory Gerstner,⁷ Dong-Wan Kim,⁸ Yun-Gyoo Lee,⁹ Wu-Chou Su,¹⁰ Elizabeth Huang,¹¹ Namrata Patil,¹² Meilin Huang,¹² Zoe Zhang,¹² Xiaohui Wen,¹² Diana Mendus,¹² Tien Hoang,¹² Raymond Meng,¹² Melissa Johnson¹³
CITYSCAPE: Background

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers.\textsuperscript{1-3} TIGIT expression correlates with PD-1, especially in tumour-infiltrating T cells.
- Tiragolumab is a fully human IgG1/kappa anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR.
- We hypothesise that anti-TIGIT antibodies, such as tiragolumab, could restore the anti-tumour response and may amplify the activity of anti-PD-L1/PD-1 antibodies.
- CITYSCAPE (NCT03563716) is the first randomised Phase II study of an anti-TIGIT antibody. At the primary analysis, tiragolumab + atezolizumab showed a clinically meaningful improvement in ORR and PFS in the ITT population compared with atezolizumab monotherapy. This was maintained after a further 5 months of follow-up, with a greater magnitude of improvement seen in the PD-L1 TPS ≥50% subgroup\textsuperscript{4}.
- Tiragolumab has been granted Breakthrough Therapy Designation (BTD) by the US FDA, in combination with atezolizumab for first-line treatment of patients with metastatic NSCLC whose tumours have high PD-L1 expression with no EGFR or ALK genomic tumour aberrations.
- Here, we present an updated analysis with ~30 months of follow-up, including OS, updated PFS and safety analyses and patient-reported outcomes (PROs).

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.
CITYSCAPE: Phase II Trial Schema

1L Stage IV NSCLC
- EGFR/ALK wild-type
- Tumour 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

Exploratory endpoints
- Efficacy analysis by PD-L1 status, PROs

Tiragolumab 600 mg IV Q3W + Atezolizumab 1200 mg IV Q3W

Placebo 600 mg IV Q3W + Atezolizumab 1200 mg IV Q3W

No crossover

PD or loss of clinical benefit

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

Exploratory endpoints
- Efficacy analysis by PD-L1 status, PROs

Primary analysis
- Cut-off date of 30 June 2019
- Median follow-up of 5.9 months

Updated analysis
- Follow-up performed to assess safety and efficacy
- Cut-off date of 16 August 2021
- Median follow-up of 30.4 months

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.
CITYSCAPE: Investigator-Assessed PFS – ITT Population

<table>
<thead>
<tr>
<th>Events n (%)</th>
<th>Median PFS, months (95% CI)</th>
<th>PFS HR (95% CI)</th>
<th>ORR, % (95% CI)</th>
<th>Median DOR, months (95% CI)</th>
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<tbody>
<tr>
<td>57 (85.1)</td>
<td>5.6 (4.2–10.4)</td>
<td>0.62*</td>
<td>38.8</td>
<td>17.6 (9.1–26.1)</td>
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<td>64 (94.1)</td>
<td>3.9 (2.7–4.5)</td>
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<td>20.6</td>
<td>10.7 (6.0–18.8)</td>
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12-month rate: 36.2%
12-month rate: 21.1%

Cho BC et al. ESMO Immuno-Oncology 2021; Abstract LBA2.
CITYSCAPE: Investigator-Assessed PFS – PD-L1 Subgroups

**PD-L1 TPS ≥50% (n=58)**

<table>
<thead>
<tr>
<th>Events n (%)</th>
<th>Median PFS, months (95% CI)</th>
<th>PFS HR (95% CI)</th>
<th>ORR, %</th>
<th>Median DOR, months (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Tira + atezo</td>
<td>21 (72.4)</td>
<td>16.6 (5.5–22.3)</td>
<td>0.29*</td>
<td>15.7 (9.1–NE)</td>
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<tr>
<td>Placebo + atezo</td>
<td>28 (96.6)</td>
<td>4.1 (2.1–6.0)</td>
<td>(0.15–0.53)</td>
<td>24.1</td>
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**PD-L1 TPS 1–49% (n=77)**

<table>
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<tr>
<th>Events n (%)</th>
<th>Median PFS, months (95% CI)</th>
<th>PFS HR (95% CI)</th>
<th>ORR, %</th>
<th>Median DOR, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tira + atezo</td>
<td>36 (94.7)</td>
<td>4.0 (1.5–5.6)</td>
<td>1.07*</td>
<td>15.8</td>
</tr>
<tr>
<td>Placebo + atezo</td>
<td>36 (92.3)</td>
<td>3.6 (1.4–5.5)</td>
<td>(0.67–1.71)</td>
<td>17.9</td>
</tr>
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</table>

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.
Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma
Module 3: Small Cell Lung Cancer (SCLC)

- Follow-up of chemotherapy/immunotherapy trials for extensive-stage SCLC
- ATLANTIS: Second-line lurbinectedin with docetaxel
- Trilaciclib
IMpower133 Update continues to show OS benefit
Carbo-etoposide +/- atezolizumab in ES-SCLC

Neither PDL1 IHC status nor blood TMB were predictive of a response to carbo-etoposide-atezolizumab.

Liu et al. JCO 39: 619-630, 2021

Courtesy of Anne S Tsao, MD, MBA
CASPIAN: 3-year update shows OS benefit
platinum-etoposide + durvalumab +/- tremelimumab

- Treatment-naive ES-SCLC
- WHO PS 0 or 1
- Asymptomatic or treated and stable brain metastases permitted
- Life expectancy ≥12 weeks
- Measurable disease per RECIST v1.1
- N=805 (randomized)

3-year Overall Survival Update: D+EP vs EP

3-year Overall Survival Update: D+T+EP vs EP

Courtesy of Anne S Tsao, MD, MBA

Paz-Ares et al. ESMO 2021, Abstract LBA61
ATLANTIS: 2\textsuperscript{nd} line SCLC doxorubicin + lurbinectedin vs topotecan or CAV

ATLANTIS did not reach its primary endpoint

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lurbinectedin + Doxorubicin (n=307)</th>
<th>Control (n=306)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS</td>
<td>8.6</td>
<td>7.6</td>
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<tr>
<td></td>
<td>HR 0.967, p=0.7032</td>
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<tr>
<td>Median PFS</td>
<td>4</td>
<td>4</td>
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<tr>
<td></td>
<td>HR 0.831, p=0.0437</td>
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<tr>
<td>PFS 6 month</td>
<td>31.3</td>
<td>24.4</td>
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<td></td>
<td>0.0851</td>
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<tr>
<td>PFS 12 month</td>
<td>10.8</td>
<td>4.4</td>
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<td>0.0129</td>
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</table>
Trilaciclib in ES-SCLC improves outcomes

- Trilaciclib is an intravenous CDK4/6 inhibitor that protects against myelosuppression from chemotherapy.
- Data was pooled from 3 phase II randomized placebo-controlled studies (NCT02499770, NCT03041311, and NCT02514447) and analyzed retrospectively.
Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma
Agenda

Module 4: Mesothelioma

- CheckMate 743: Nivolumab/ipilimumab – Update with histology
- SWOG-1619: Neoadjuvant chemotherapy/atezolizumab
CheckMate 743: Mesothelioma 3-year update shows OS, PFS, DoR benefit

Key eligibility criteria
- Unresectable MPM
- No prior systemic therapy
- ECOG PS 0-1

Stratified by
Histology (epithelioid vs non-epithelioid) and gender

NIVO 3 mg/kg Q2W +
IPI 1 mg/kg Q6W
(for up to 2 years)

ITT Overall Survival

- 3-year OS rate 23% with ipi-nivo vs 15%
- 28% of responders have an ongoing response at 3 years
- TMB does not predict for benefit

Until disease progression, unacceptable toxicity, or for 2 years for immunotherapy

• 3-year OS rate 23% with ipi-nivo vs 15%
• 28% of responders have an ongoing response at 3 years
• TMB does not predict for benefit

Courtesy of Anne S Tsao, MD, MBA

Peters et al. ESMO 2021, AbstractLBA65
CheckMate 743: 3-year update by histology

**Clinical Implications:**
- Greatest magnitude of benefit seen in non-epithelioid histology
- Ipi-nivo would be a frontline choice for non-epithelioid patients unless rapid debulking is needed
- Epithelioid patients can receive either chemo +/- bevacizumab or ipi-nivo as 1st line therapy

**Conclusion CheckMate 743**
- New SOC for mesothelioma
- 3-year update survival results confirm the clinical benefit
- Mesothelioma is an immunogenic disease

**Future Research Directions:**
1) Combination I/O with chemo backbones
2) Sequencing studies on chemo vs I/O
3) Novel targets – T cell CART

Courtesy of Anne S Tsao, MD, MBA
SWOG 1619
Neoadjuvant cisplatin-pemetrexed-atezolizumab

4 cycles of neoadjuvant cisplatin-pemetrexed-atezolizumab successfully delivered in 21 eligible and evaluable patients.

- 18 patients (radiographic SD or PR) proceeded to surgical resection
- 16 patients received maintenance atezolizumab
- Median f/u time 10.3 months, median PFS 18.6 months and median OS has not been reached.
- To date, no delayed treatment related adverse events > grade 3 reported.

S1619 Clinical Implications and Future Research Directions:
- No new safety signals from the CPA regimen nor atezolizumab maintenance therapy.
- Neoadjuvant therapy trials in this patient population are needed.
- Translational studies are pending to identify predictive biomarkers.

Courtesy of Anne S Tsao, MD, MBA
Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty
Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator
Kristen K Ciombor, MD, MSCI
Thank you for joining us!

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