Karen L. Reckamp, MS, MD:
Hello, and welcome to this educational activity, Advanced/Metastatic NSCLC Treatment: Advancements for Patients Without Targetable Activating Mutations.

I am Dr. Karen Reckamp, Professor of Medicine at the City of Hope Comprehensive Cancer Center, in Duarte, California. I am joined today by Dr. Mark Socinski, Executive Medical Director at the Advent Health Cancer Institute in Orlando, Florida; and Dr. Helena Yu, Assistant Attending Physician at Memorial Sloan Kettering Cancer Center in New York, New York.
Disclosure of Conflicts of Interest

- Karen L. Reckamp, MS, MD, reported a financial interest/relationship or affiliation in the form of Consultant: Boehringer Ingelheim; Exelixis, Inc; Guardant Health, Inc; Loxo Oncology; Precision Health; Seattle Genetics, Inc; and Takeda Oncology. Data and Safety Monitoring Committee: Genentech, Inc; and Tesaro, Inc. Research Grant: AbbVie; ACEA; Adaptimmune LLC; Boehringer Ingelheim; Bristol-Myers Squibb Co; Genentech, Inc; Guardant Health, Inc; Janssen Oncology; Loxo Oncology; Seattle Genetics, Inc; Takeda Oncology; Xcovery; and Zeno Pharmaceuticals, Inc.

- Mark A. Socinski, MD, reported a financial interest/relationship or affiliation in the form of Speakers’ Bureau: Genentech, Inc; AstraZeneca Pharmaceuticals LP; Bristol-Myers Squibb Co; and Celgene Corp. Contracted Research: Genentech, Inc; Spectrum Pharmaceuticals, Inc; and Bristol-Myers Squibb Co.

- Helena Yu, MD, reported a financial interest/relationship or affiliation in the form of Research funding: Novartis Pharmaceuticals Corp; Lilly USA; AstraZeneca Pharmaceuticals LP; and Daiichi-Sankyo, Inc. Advisory board: AstraZeneca Pharmaceuticals LP.
Learning Objectives

Upon completion of this activity, participants should be better able to:

- Identify first-line therapy options for patients with advanced non–small cell lung cancer without targetable activating mutations based on clinical trial data and guideline recommendations, including platinum-based chemotherapy, and single-agent immune checkpoint inhibitor or in combination with chemotherapy.
- Integrate recommended subsequent chemotherapy and immunotherapy options for the treatment of patients with advanced non–small cell lung cancer without targetable activating mutations.
- Analyze recent clinical trial results supporting the use of chemotherapy and immunotherapy combination regimens for patients with advanced NSCLC without targetable activating mutations.
- Discuss how emerging immunotherapies and chemotherapy combination regimens may be incorporated into future clinical practice.

Approved First-Line Therapy: PD-1/PD-L1 Inhibitors

<table>
<thead>
<tr>
<th>PD-1/PD-L1 Inhibitor</th>
<th>Trial</th>
<th>Indication</th>
<th>Appropriate for Patient</th>
<th>Rationale for Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-024</td>
<td>as a single agent for the first-line treatment of patients with PD-L1–expressing (TPS ≥50%) metastatic NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>X</td>
<td>PD-L1, 0%</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-042</td>
<td>as a single agent for the first-line treatment of patients with stage II NSCLC who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations</td>
<td>X</td>
<td>PD-L1, 0%</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-021</td>
<td>KEYNOTE-189</td>
<td>In combination with pembrolizumab and platinum chemotherapy as first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>X</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-407</td>
<td>In combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of patients with metastatic squamous NSCLC</td>
<td>✓</td>
<td>Stage IV squamous cell carcinoma PD-L1, 0%</td>
</tr>
<tr>
<td>Atezolizumab (PD-L1)</td>
<td>IMpower150</td>
<td>In combination with bevacizumab, nab-paclitaxel, and carboplatin for the first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>X</td>
<td>Squamous cell carcinoma</td>
</tr>
</tbody>
</table>

Here are the learning objectives for this activity. Through case examples, we will evaluate the most recent clinical data and provide evidence-based updates and expert insights on first-line treatment of advanced non–small cell lung cancer without targetable activating mutations. We will also discuss how we discern the best treatment approach and use of chemotherapy and immunotherapy for these patients. So let’s discuss our first case.

We have a 60-year-old woman who is diagnosed with stage IV squamous cell carcinoma of the lung, with metastatic disease to the left adrenal gland, and at least 3 hepatic metastases measuring greater than 2 cm. Other findings include a PD-L1 [programmed cell death protein ligand 1] tumor expression of 0% and a tumor mutational burden of 2 mutations per megabyte. Dr. Socinski, how would you treat this patient?

Mark A. Socinski, MD: This is a relatively young patient with lung cancer, so we’re going to assume her performance status is excellent. We have confidence in her histologic diagnosis being squamous cell. Most of us would choose a platinum doublet; and in squamous, my first choice is a platinum plus a taxane. We can debate what the best taxane may be in that setting.
Then, based on the results of the recent KEYNOTE-407 trial, which grafted pembrolizumab onto that backbone and demonstrated a very positive survival advantage in this population—that would be my recommendation. What we’ve done in the past couple years is take all of our platinum-based doublets that we all used as standard therapy in the first-line setting and we would sequence to second-line immunotherapy. All of the original immunotherapy agents were approved after platinum failure.

What we’ve done is take second-line therapy, graft it onto the first-line therapy, and all of these trials have been positive, and some of them wildly positive. So, that’s changed the standard of care—grafting these things together.

In a patient like this, that would be my go-to recommendation, assuming there are no obvious contraindications to immunotherapy.

Reckamp: Can you talk a little bit about the rationale for combining chemotherapy and immunotherapy?

Socinski: Much of it remains a mystery. One of the lessons that we learned from KEYNOTE-024 is that there might be something magical about giving immunotherapy up-front.

If you look at KEYNOTE-024, which gave patients with greater than 50% PD-L1 expression pembrolizumab versus chemotherapy, I probably would’ve bet that if those patients on chemotherapy transitioned to pembrolizumab in second line, that their survival time would’ve increased if they got pembrolizumab, but it didn’t.
patients could cross over during combination therapy or monotherapy. To be eligible for crossover, PD must have been verified by BICR and all safety criteria had to be met. 

Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay.

PD-L1, programmed cell death protein ligand 1; TPS, tumor proportion score.

Paz-Ares et al. PD-L1, programmed cell death protein ligand 1; Q3W, every 3 weeks; TPS, tumor proportion score.

BICR, blinded independent central radiologic review; ECOG PS, Eastern Cooperative Oncology performance status; NSCLC, non–small cell lung cancer; Taxane choice up to treating physician.


Pembrolizumab – No pneumonitis • No symptomatic brain metastases • Provision of a sample for PD-L1 assessment • ECOG PS 0 or 1 • Untreated stage IV NSCLC with no EGFR or ALK genomic tumor aberrations

Eligibility

• Geographic region (east Asia vs rest of world)

KEYNOTE-407: Carboplatin/Taxane +/- Pembrolizumab

<table>
<thead>
<tr>
<th>Eligibility</th>
<th>N = 559</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geographic region (east Asia vs rest of world)</td>
<td>1:1</td>
</tr>
</tbody>
</table>

KEYNOTE-024 as a single agent for the first-line treatment of patients with PD-L1–expressing (TPS ≥80%) metastatic NSCLC with no EGFR or ALK genomic tumor aberrations

KEYNOTE-042 as a single agent for the first-line treatment of patients with stage I–III NSCLC, who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations

KEYNOTE-021 & KEYNOTE-189 In combination with pemtrexed and platinum chemotherapy as first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations

KEYNOTE-407 In combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of patients with metastatic squamous NSCLC

Atezolizumab (PD-L1) + Paclitaxel 200 mg/m² Q3W + Carboplatin AUC 6 Q3W for up to 31 cycles

Pembrolizumab 200 mg Q3W + Carboplatin AUC 6 Q3W + Paclitaxel 100 mg/m² Q3W or nab-paclitaxel 100 mg/m² Q3W for 4 cycles (each 3 wk) n = 278

Pembrolizumab 200 mg Q3W for up to 35 cycles

Optional Crossover Pembrolizumab 200 mg Q3W for up to 35 cycles

Co-primary Endpoints

- OR (RECIST v1.1, BICR)
- DOR

Secondary Endpoints

- OS
- PFS (RECIST v1.1, BICR)

Stratification Factors

- PD-L1 expression (TPS <1% vs ≥1%)
- ECOG PS 0 or 1
- Geographic region (east Asia vs rest of world)

KEYNOTE-407 was a randomized phase 3 trial. Patients had to have untreated stage IV disease with squamous histology, good performance status, and a sample for PD-L1 assessment. No symptomatic brain metastases were allowed, and there were the usual contraindications for immunotherapy; specifically, no pneumonitis that required systemic steroids.

The randomization, the control arm, was a standard carboplatin, physician’s choice of either solvent-based paclitaxel or nab-paclitaxel. It was a 60-40 split; 60% with solvent-based and 40% with nab-paclitaxel. It got 4 cycles. The investigational arm simply grafted pembrolizumab onto that at standard doses and schedule. There was a maintenance phase for those who didn’t have disease progression, either placebo or pembrolizumab.

Advanced/Metastatic NSCLC Treatment: Advancements for Patients Without Targetable Activating Mutations – 5

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So is there something magical about early on in the course of the disease, is the immune system more on? And when you’re using it with chemotherapy, is there an advantage if you see cytotoxic cell death and other immunologic mechanisms that may enhance the effect of immunotherapy in that setting?

Those were all theoretical sorts of reasons. The clinical data are incontrovertible. I mean, all of these trials, particularly KEYNOTE-407, was a striking benefit in the combination arms.

Reckamp: Can you tell us a little bit about the KEYNOTE-407 trial?

Socinski: Yes. KEYNOTE-407 was a randomized phase 3 trial. Patients had to have untreated stage IV disease with squamous histology, good performance status, and a sample for PD-L1 assessment. No symptomatic brain metastases were allowed, and there were the usual contraindications for immunotherapy; specifically, no pneumonitis that required systemic steroids.

The randomization, the control arm, was a standard carboplatin, physician’s choice of either solvent-based paclitaxel or nab-paclitaxel. It was a 60-40 split; 60% with solvent-based and 40% with nab-paclitaxel. It got 4 cycles. The investigational arm simply grafted pembrolizumab onto that at standard doses and schedule. There was a maintenance phase for those who didn’t have disease progression, either placebo or pembrolizumab.
KEYNOTE-407: Overall Survival at IA2, ITT

- Patients on the control arm were allowed to cross over at the time of disease progression. Primary endpoints were both progression-free survival as well as overall survival. And stratification factors were PD-L1 expression status, choice of the taxane, as well as geographic region.

- As you see on the Kaplan-Meier curve, these curves separate by about 3 months, and the hazard ratio for overall survival is 0.64. Obviously, both statistically significant as well as clinically significant when you look at these curves. The median survival for the control arm was 11.3 months, which is typically what we see with platinum-based doublets. And then, nearly 16 months, 15.9 months for the investigational arm of this trial. So, a pretty impressively positive trial.
KEYNOTE-407: Adverse Events

<table>
<thead>
<tr>
<th>Event (any Grade)</th>
<th>Pembrolizumab Combination (N = 278)</th>
<th>Placebo Combination (N = 280)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any event</td>
<td>273 (98.2%)</td>
<td>274 (97.9%)</td>
</tr>
<tr>
<td>Event leading to discontinuation of all treatment components</td>
<td>37 (13.3%)</td>
<td>18 (6.4%)</td>
</tr>
<tr>
<td>Event leading to discontinuation of any treatment component</td>
<td>65 (23.4%)</td>
<td>33 (11.8%)</td>
</tr>
<tr>
<td>Event leading to death</td>
<td>23 (8.3%)</td>
<td>18 (6.4%)</td>
</tr>
<tr>
<td>Attributed to a trial regimen by an investigator</td>
<td>10 (3.6%)</td>
<td>6 (2.1%)</td>
</tr>
<tr>
<td>Select events occurring in ≥15% of patients in either group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>148 (53.2%)</td>
<td>145 (51.8%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>128 (46.0%)</td>
<td>102 (36.4%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>105 (37.8%)</td>
<td>92 (32.9%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>99 (35.6%)</td>
<td>90 (32.1%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>85 (30.6%)</td>
<td>65 (23.2%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>83 (29.9%)</td>
<td>65 (23.2%)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>68 (24.5%)</td>
<td>82 (29.3%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>64 (23.0%)</td>
<td>61 (21.8%)</td>
</tr>
</tbody>
</table>

Toxicity is shown on the slide here. I commented earlier that we’ve grafted our former second-line standard therapies with the 3 immunotherapies onto our chemotherapy backbones. And the take-home message is that if you give immunotherapy with our standard chemotherapy regimens, it really doesn’t change the toxicity of the chemotherapy. And chemotherapy doesn’t seem to change the toxicity of the immunotherapy.

You have to be prepared to deal with more toxicity because you’re giving a greater number of drugs. But there’s nothing really unusual from the chemotherapy point of view or nothing really unusual from the immunotherapy point of view. You just have to manage them together.

Reckamp:
Thank you, Dr. Socinski. And Dr. Yu, do you agree or have anything else to add to this scenario?

Helena Yu, MD: Mark really comprehensively went over KEYNOTE-407, so I don’t have a whole lot to add. I would just say that in some ways, I do find squamous cell lung cancer a little bit more challenging to treat. There are fewer options, and we’ll go over some of the options for adenocarcinoma so to counterpoint. And just to note that the survival, both the progression-free survival as well as the overall survival, are numerically lower than those with adenocarcinoma. There is less ability to pick out or have predictive markers to figure out who really responds. That’s a challenge.
Approved First-Line Therapy: PD-1/PD-L1 Inhibitors

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<td>KEYNOTE-024</td>
<td>as a single agent for the first-line treatment of patients with PD-L1-expressing (TPS ≥50%) metastatic NSCLC with no EGFR or ALK genomic tumor aberrations • Nonsquamous PFS HR: 0.55</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma PD-L1 50%</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-042</td>
<td>as a single agent for the first-line treatment of patients with stage III NSCLC, who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 (TPS ≥5%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations • Nonsquamous OS HR in TPS ≤5%: 0.86</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-021, KEYNOTE-189</td>
<td>In combination with pemetrexed and platinum chemotherapy as first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>IMpower150</td>
<td>In combination with bevacizumab, pemetrexed, and carboplatin for the first-line treatment of patients with metastatic squamous NSCLC</td>
<td>X</td>
<td>Nonsquamous cell carcinoma</td>
</tr>
</tbody>
</table>

NSCLC, non–small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein ligand 1; TPS, tumor proportion score.

Socinski: What we know about the squamous population, they tend to be a little older, they tend to be much more male dominated. It's a more smoking-related disease than the nonsquamous population. You tend to have more comorbidities, so your observations about the overall survival experience for this group of patients isn’t as good as we see in the nonsquamous population. It could be because of all of those factors.

Yu: In adenocarcinoma, there are some emerging, genomic biomarkers that can help us figure out what the best treatment is. We have yet to find that in squamous cell.

Socinski: We're still waiting.

Reckamp: And is there anything that makes you choose the solvent-based paclitaxel versus nab-paclitaxel in your patients?

Yu: I tend to agree with Mark, where I do end up choosing the nab-paclitaxel more frequently, although not always. In terms of patient tolerability and some of the toxicities, including neuropathy, it’s a little bit easier to tolerate for patients.

Socinski: Now we had at World Lung, last year in Toronto, a retrospective, I believe it was an unplanned analysis, although it was a stratification factor, where they looked at the survival based on what taxane you received, solvent-based versus nab-paclitaxel.

There was a little bit of a trend in favor of nab-paclitaxel for overall survival compared to solvent-based paclitaxel. To your point, most of the people that I talk to think that there’s a toxicity advantage, although there’s also an inconvenience disadvantage because it’s a weekly infusion.
Reckamp: I agree. I mean, these data from the KEYNOTE-407 are pretty straightforward to help you decide whether to use chemotherapy and immunotherapy for squamous cell non–small cell lung cancer. So, we want better therapies. We still have a ways to go with squamous cell and definitely for targeted therapy. But for this case, we all agree.

Now we’ll discuss case two. This is a 66-year-old man with a newly diagnosed stage IV adenocarcinoma of the lung. Additional findings show PD-L1 is 50%. The patient has no evidence of a targetable actionable mutation. Dr. Yu, which treatment would you select for this patient and why?

<table>
<thead>
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<tbody>
<tr>
<td>PD-1/PD-L1 Inhibitor</td>
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<tr>
<td>-----------------------</td>
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<tr>
<td>Pembrolizumab (PD-1)</td>
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<tr>
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<tr>
<td></td>
</tr>
<tr>
<td>Atezolizumab (PD-L1)</td>
</tr>
</tbody>
</table>


You can probably play it both ways; however, I find myself using the nab approach more often than not.
Yu:
For this patient, there are a few more options we can explore, so there are a few other studies that we could go over. Personally, and most of us would likely agree, I would choose single-agent pembrolizumab for this patient. And that’s really based primarily on this KEYNOTE-024 study.

As you can see on the slide, the study schema, KEYNOTE-024 took patients that had stage IV non-small cell lung cancer, both squamous and nonsquamous histology, specifically EGFR and ALK wild type because they had more appropriate treatments. Then they took patients with PD-L1 expression greater than 50% and randomized them to platinum doublet chemotherapy appropriate to their histology versus pembrolizumab.

You can see that both the progression-free survival and the overall survival results significantly favored the pembrolizumab monotherapy for these patients.
KEYNOTE-042: Pembrolizumab vs Platinum Doublet

Eligibility
- Untreated locally advanced or metastatic NSCLC of any histology
- PD-L1 TPS ≥1%
- No sensitizing EGFR or ALK alterations
- ECOG PS 0 or 1
- No untreated or unstable CNS metastases
- No history of pneumonitis that required systemic corticosteroids

Randomization

Pembrolizumab: 200 mg Q3W for up to 35 cycles
- n = 637

Chemotherapy: Carboplatin/Paclitaxel or Carboplatin/Pemetrexed for up to 6 cycles
- n = 637

Primary Endpoint
- OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%

Secondary Endpoints
- PFS in TPS ≥50%, ≥20%, and ≥1%
- ORR in TPS ≥50%, ≥20%, and ≥1%
- Safety in TPS ≥1%

Stratification Factors
- Region (east Asia vs rest of world)
- ECOG PS (0 vs 1)
- Histology (squamous vs non-squamous)
- PD-L1 TPS (≥50% vs 1–49%)

The toxicity, as Mark mentioned earlier, there are clear toxicities that are attributed to both immunotherapy and chemo, so we really saw no surprises here in terms of toxicity.

That study really most closely mirrors this patient. Since that study came out, there are more data suggesting that we could use single-agent pembrolizumab for more patients. That is based on the KEYNOTE-042 study. So exactly same treatment arms, but this time really looked at patients who had PD-L1 expression greater than or equal to 1% and gave them either pembrolizumab or a platinum-doublet chemotherapy.
Again, it did show in the prespecified greater than 1%, greater or equal to 1%, PD-L1 expression did show an improvement with the pembrolizumab compared to chemotherapy. However, many think that that was primarily driven by the patients with PD-L1 expression greater than 50%. The data were less convincing when they showed us the subset of patients with 1% to 49% PD-L1 expression.

Again, here you see the toxicity. Very similar to that of KEYNOTE-024. The final, or 2 other studies to think about are the chemotherapy/immunotherapy combination studies.
All of us are familiar with KEYNOTE-189, which is the study that specifically took patients—the difference here being nonsquamous adenocarcinoma lung cancer patients—and then randomized them to receive platinum, either carboplatin or cisplatin, with pemetrexed, with or without pembrolizumab.

The primary endpoints of this study were overall survival as well as progression-free survival. As you can see from the study schema, patients received both, in the control arm, received pemetrexed maintenance. And the patients in the study arm received pembrolizumab and pemetrexed maintenance until disease progression or intolerance.

As you can see here from the Kaplan-Meier curves, there was a commanding benefit to the addition of pembrolizumab to the platinum-doublet chemotherapy, with a hazard ratio of 0.49, so quite significant. Again, both statistically and, of course, clinically significant for our patients.
KEYNOTE-189: Summary of Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Pembrolizumab/Pemetrexed/Platinum (N = 405)</th>
<th>Placebo/Pemetrexed/Platinum (N = 202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause</td>
<td>404 (99.8%)</td>
<td>200 (99.0%)</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>272 (67.2%)</td>
<td>133 (65.8%)</td>
</tr>
<tr>
<td>Led to death</td>
<td>27 (6.7%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>Led to discontinuation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All treatment</td>
<td>56 (13.8%)</td>
<td>16 (7.9%)</td>
</tr>
<tr>
<td>Any treatment</td>
<td>112 (27.7%)</td>
<td>30 (14.9%)</td>
</tr>
<tr>
<td>Immune mediated</td>
<td>92 (22.7%)</td>
<td>24 (11.9%)</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>36 (8.9%)</td>
<td>9 (4.5%)</td>
</tr>
<tr>
<td>Led to death</td>
<td>3 (0.7%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Includes patients who discontinued pembrolizumab or placebo, pemetrexed, and carboplatin for an adverse event at any time and patients who discontinued pembrolizumab or placebo and pemetrexed for an adverse event after completing 4 cycles of platinum.

Data cutoff date: Nov 8, 2017.


And finally, the other counterpoint not to omit, especially since my colleague here presented and published these data, is the IMpower150 data. It was a very large study with multiple arms. For our patient, this case really focused on the arms that included the carboplatin/paclitaxel/bevacizumab versus that same trio of chemotherapy and bevacizumab with the addition of atezolizumab so we are looking at cohorts B and C of that study.
**IMpower150: PFS in ITT (Arm B vs. Arm C)**

<table>
<thead>
<tr>
<th></th>
<th>Median PFS, mo</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm B: atezolizumab + bevacizumab + CP</td>
<td>8.3</td>
<td>0.617</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Arm C: bevacizumab + CP</td>
<td>6.8</td>
<td>0.737</td>
<td></td>
</tr>
</tbody>
</table>

There was a clear benefit in all of the different subgroups that were looked at. Not relevant to this case, but unique to IMpower150 is they did include patients who were EGFR and ALK positive and did show both an overall survival and progression-free survival benefit in that subgroup, which is unique, and we might talk about further.

You can see here that there is a clear improvement in progression-free survival with the addition of atezolizumab to that trio of bevacizumab plus a platinum-doublet chemotherapy.
### IMpower150: Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ABCP Group (N = 393)</th>
<th>BCP Group (N = 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-related adverse events*</td>
<td>371 (94.4%)</td>
<td>376 (95.4%)</td>
</tr>
<tr>
<td>Grade 3-4 adverse events</td>
<td>242 (61.6%)</td>
<td>230 (58.4%)</td>
</tr>
<tr>
<td>Treatment-related serious adverse events*</td>
<td>100 (25.4%)</td>
<td>76 (19.3%)</td>
</tr>
<tr>
<td>Immune-related adverse events</td>
<td>77.4%</td>
<td>–</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal from any treatment*</td>
<td>128 (32.6%)</td>
<td>58 (14.7%)</td>
</tr>
<tr>
<td>Treatment-related deaths</td>
<td>11 (2.8%)</td>
<td>9 (2.3%)</td>
</tr>
</tbody>
</table>


### Approved First-Line Therapy: PD-1/PD-L1 Inhibitors

<table>
<thead>
<tr>
<th>PD-1/PD-L1 Inhibitor</th>
<th>Trial</th>
<th>Indication</th>
<th>Appropriate for Patient</th>
<th>Rationale for Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>KEYNOTE-024</td>
<td>as a single agent for the first-line treatment of patients with PD-L1–expressing (TPS ≥50%) metastatic NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma PD-L1 50%</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-042</td>
<td>as a single agent for the first-line treatment of patients with stage II NSCLC, who are not candidates for surgical resection or definitive chemoradation, or metastatic NSCLC, and whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma PD-L1 50%</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-021, KEYNOTE-189</td>
<td>in combination with pemetrexed and platinum chemotherapy as first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>KEYNOTE-407</td>
<td>in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of patients with metastatic squamous NSCLC</td>
<td>X</td>
<td>Non-squamous cell carcinoma</td>
</tr>
<tr>
<td>Atezolizumab (PD-L1)</td>
<td>IMpower150</td>
<td>in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations</td>
<td>✓</td>
<td>Stage IV nonsquamous cell carcinoma</td>
</tr>
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</table>

NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein ligand 1; TPS, tumor proportion score; FDA, US Food and Drug Administration.

And then, giving 4 drugs together compared to 3 drugs, we did see increased toxicity with this combination, which is one of the reasons why for this patient, we wouldn’t choose this regimen.

In conclusion, and I’m interested to hear what my colleagues say, is if we want the best, most effective treatments for our patients, but we also want to consider toxicity. I would need a real reason to escalate treatment or add additional treatments to what I already know is effective. KEYNOTE-024 clearly showed us that pembrolizumab monotherapy would be a good choice for this patient, and I don’t have great confidence that adding the chemotherapy in this particular situation would be additive to the degree that would be worth added toxicity.

**Reckamp:** Dr. Socinski?

**Socinski:** I agree with all the comments that were made. KEYNOTE-024 actually changed the landscape and did allow patients with high expression of PD-L1 to have a very effective treatment that’s very nontoxic.
However, I have several patients with 90% PD-L1 expression and a high volume of disease who are quite symptomatic. If you combine a chemotherapy with pembrolizumab in that setting, you at least improve the response rates. One of the questions we have out there in practice is does adding chemo in that population actually improve outcomes such as progression-free survival as well as overall survival relative to pembrolizumab alone. We don’t have the answer to that question yet.

In terms of KEYNOTE-042, one of the things I would advise the audience to do is to look at the Kaplan-Meier curves. There’s always an early disadvantage in overall survival that you don’t see on the chemotherapy curves. I do not, in my practice, advocate using immuno-monotherapy in patients with less than 50% PD-L1 expression and certainly not the negative populations.

KEYNOTE-189 was, again, a very impressively positive trial. One of the issues in practice is who are the patients that are going to benefit from the IMpower150 regimen. Before we leave KEYNOTE-189, I do want to note that we have a similar trial, IMpower132, that was carbo/pemetrexed plus or minus atezolizumab, which was a negative trial. So you could argue that we have one positive and one negative trial, and we can debate as to why that may be.
Regarding IMpower150, 4 drugs can be demanding on the patient as well as the resources that you may have. I do think it plays a role. This interplay and the reason we did the trial was that VEGF does have an immunosuppressive aspect to multiple levels of the cancer immunity cycle. Targeting VEGF is a valid strategy, in general, and seems to improve outcomes if you use it in combination with anti–PD-1 or anti–PD-L1 agents.

It’s not going to get the majority of play in that setting, but I do think in select patients, where you might want to be more aggressive in that they’re optimal candidates for a drug such as bevacizumab, then I would consider the 150 regimen. And you pointed out in the EGFR/ALK space, there may be a niche for it.

The liver space, the liver metastasis story, is in evolution. Both immunotherapy as well as the anti-VEGF therapy, and perhaps maybe the combination, is best for patients with liver metastases. But, that’s still debatable.

Reckamp: So I would agree. You two have both given us a lot to think about with all the trials that are out there, especially for our patients with nonsquamous, non–small cell lung cancer. I would like to just also note, because we’re talking about our patients with EGFR and ALK, as we can move toward treating patients without potentially testing PD-L1, it’s incredibly important to still make sure we have our molecular testing, and that patients are truly wild-type before they go on to receive chemoimmunotherapy or immunotherapy alone.
The toxicity with first-line EGFR TKIs may be significantly higher if you use immunotherapy first. So, making sure that that testing is done, even if there’s a slight delay in starting therapy, because we have so many options for our patients, they still might not be the right options.

Socinski: And I would advocate being more comprehensive in your testing going beyond even what the NCCN may call out at this particular point—things such as RET fusions or MET exon 14 are very important to identify. This is, generally, not a population that we think it’s a big bang out of immunotherapy, there’s nothing distinguishing about chemo and that crowd. But, obviously, to use the growing number of targeted therapies we have, you’ve got to make the molecular diagnosis.

Reckamp: Right.

Yu: Absolutely. The real point to make is even though these studies have really advanced how we treat people without mutations—the response rates, the progression-free survival, the survival we see with our targeted therapies—we have, you’ve got to make the molecular diagnosis.

Socinski: Yes.

Yu: To Karen’s point, not only are we withholding or leaving to later some really valuable treatment, but also that sequence of starting with immuno-therapy and sequencing quickly with one of the targeted therapies can potentially harm patients. So it’s not only not omission, it’s also potential harm. All the more really important.
First-Line Summary and Emerging Treatment

### Change in Treatment Paradigms: Metastatic NSCLC

<table>
<thead>
<tr>
<th>NSCLC Setting</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line, no actionable mutation, nonsquamous, PD-L1 &lt;50%</td>
<td>Platinum, pemetrexed, pembrolizumab</td>
</tr>
<tr>
<td>First-line, no actionable mutation, squamous, PD-L1 &lt;50%</td>
<td>Carboplatin, paclitaxel or nab-paclitaxel, pembrolizumab</td>
</tr>
<tr>
<td>First-line, no actionable mutation, PD-L1 ≥50%</td>
<td>Pembrolizumab</td>
</tr>
</tbody>
</table>

### Interesting Data, Not Time to Change: Metastatic NSCLC

<table>
<thead>
<tr>
<th>NSCLC Setting</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line, no actionable mutation, any PD-L1, high TMB</td>
<td>Ipilimumab and nivolumab</td>
</tr>
<tr>
<td>First-line cytotoxic therapy with EGFR/ALK mutation after TKI</td>
<td>Carboplatin, paclitaxel, atezolizumab, and bevacizumab</td>
</tr>
<tr>
<td>First-line, no actionable mutation, PD-L1 1%-49%</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Most of result driven by PD-L1 ≥50%</td>
</tr>
</tbody>
</table>

NSCLC, non–small cell lung cancer; PD-L1, programmed cell death protein 1; TKI, tyrosine kinase inhibitor; TMB, tumor mutational burden.

Reckamp:

Right. So next I’d like to summarize where we are and where we’re going in the future with first-line treatment for non–small cell lung cancer. As we’ve heard, for patients without actionable mutations, nonsquamous, PD-L1 less than 50%, the combination of platinum/pemetrexed/pembrolizumab is still our first choice for those patients. First-line, no actionable mutation, squamous cell PD-L1 less than 50%, again, the KEYNOTE-407 study; carboplatin, either paclitaxel or nab-paclitaxel with pembrolizumab. And for those without an actionable mutation who have PD-L1 greater than 50%, pembrolizumab alone is a very reasonable choice. There may be sometimes where you might want to use chemotherapy with pembrolizumab; but generally, pembrolizumab regardless of histology.

Some interesting data that are out there that we’re still learning how we might implement these therapies, and things to watch out for. So, I’ll talk about the IMpower150. We had just talked about this. First-line cytotoxic therapy for patients with EGFR and ALK after they’ve received their tyrosine kinase inhibitor; importantly that they’ve already received their therapy. But the IMpower150 study was the first study to allow those patients into the trial and show a benefit to that combination with bevacizumab, atezolizumab, and carboplatin and paclitaxel. And really the only trial we have that included these patients.
## First-Line Summary and Emerging Treatment (cont.)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Trial</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab/ipilimumab</td>
<td>CheckMate-227</td>
<td>Nivolumab-based regimens versus platinum-doublet chemotherapy in patients with first-line advanced nonsquamous and squamous NSCLC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PFS benefit seen in those with TMB &gt; 10 mt/MB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nivolumab/ipilimumab not associated with OS improvement over chemotherapy among patients with high (HR 0.77) or low TMB (HR 0.78)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Part 1a in PD-L1 ≥1%, met co-primary endpoint of OS, demonstrating superior benefit vs chemo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Part 1b exploratory analysis in tumors that do not express PD-L1: survival benefit observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Part 2: did not meet primary endpoint of OS in nonsquamous NSCLC regardless of PD-L1 status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Median OS: 18.83 months vs 16.57 months (HR 0.86)</td>
</tr>
<tr>
<td>Atezolizumab</td>
<td>IMpower131</td>
<td>In combination with carboplatin and nab-paclitaxel as first-line treatment of advanced squamous NSCLC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PFS benefit, but no OS benefit</td>
</tr>
<tr>
<td></td>
<td>IMpower130</td>
<td>FDA accepted sBLA for atezolizumab in combination with nab-paclitaxel and carboplatin for the first-line treatment of people with metastatic nonsquamous NSCLC who do not have EGFR or ALK genomic tumor aberrations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Target date: September 2, 2019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Significant improvements in median PFS and OS in ITT wild-type population in atezolizumab + chemotherapy group vs. chemotherapy group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Median PFS: 7.0 months vs 5.5 months (stratified HR 0.64)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Median OS: 18.6 months vs 13.9 months (stratified HR 0.79)</td>
</tr>
<tr>
<td></td>
<td>IMpower132</td>
<td>In combination with pemetrexed and cisplatin or carboplatin as first-line treatment of nonsquamous NSCLC</td>
</tr>
</tbody>
</table>

Then thinking about patients and other ways of testing for patients. So, in the front-line setting, we’re also looking at other markers where we can test patients and understand benefit of immunotherapy for patients. In the CheckMate 227 study, nivolumab and ipilimumab were investigated versus chemotherapy.

This study looked at PD-L1 as the primary marker but also presented data using high tissue tumor mutational burden and showed that patients with high tumor mutational burden had potentially higher benefit with the combination immunotherapy ipilimumab and nivolumab. Subsequently, there’s been a press release showing that the study was positive in patients with PD-L1 positivity. And we await that data to help us guide how we might treat our patients with combination immunotherapy.

And then back to the data from the KEYNOTE-042 study—the patients without actionable mutation and PD-L1 expression 1% to 49%. We all agree that most patients who benefited were patients with greater than 50% PD-L1 expression. The 1% to 49% subset unplanned analysis does not show significant benefit for these patients. It’s still an area where we would generally give combination chemotherapy with pembrolizumab.
Other emerging areas are looking at blood-based markers, especially blood tumor mutational burden. And this comes from data that was presented this spring at AACR by Dr. Peters. The MYSTIC trial looked at combination immunotherapy with tremelimumab and durvalumab. With that combination, study results were negative overall. When they looked back at blood tumor mutational burden at the highest levels of greater than 16 or greater than 20 mutations per megabase, those patients seemed to have a benefit with combination immunotherapy. These are things to watch out for and things that we may start to look for to help us understand how to treat patients beyond using PD-L1.

There was a European approval for the IMpower130 study looking at first-line metastatic nonsquamous non–small cell lung cancer with carboplatin/nab-paclitaxel. The IMpower131 and 132 were not positive studies with overall survival. And again, as to Dr. Socinski’s comment earlier, not all of these studies are showing the same benefit.
NCCN Guidelines® Subsequent Therapy Options for Advanced/Metastatic NSCLC Without Targetable Activating Mutations

**Systemic immune checkpoint inhibitors (preferred):**
- Nivolumab (category 1)
- Pembrolizumab (category 1)
  - PD-L1 expression levels ≥1%
- Atezolizumab (category 1)

**Other systemic therapy (if not previously given):**
- Docetaxel
- Pemetrexed (nonsquamous)
- Gemcitabine
- Ramucirumab + docetaxel

*If progression on PD-1/PD-L1 inhibitor, switching to another PD-1/PD-L1 inhibitor is not routinely recommended.*

---

**What To Do After First-Line PD-1/PD-L1 Inhibitor?**

- A patient who experiences disease progression after treatment with a PD-1 or PD-L1 inhibitor in the first-line
- For decades, platinum doublet +/- bevacizumab was preferred first-line approach for NSCLC
- Now, nearly all patients will receive immunotherapy first-line

- Key questions:
  - How to treat patients who do not receive immunotherapy in the first-line (eg, began treatment prior to approvals)?
  - How to treat patients who progress on chemoimmunotherapy?
  - Are there patients who may benefit less from immunotherapy?

---

**NCCN Guidelines® Subsequent Therapy Options for Advanced/Metastatic NSCLC Without Targetable Activating Mutations**

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---

**What you would do for a patient who has disease progression after a PD-1 or PD-L1 inhibitor with or without chemotherapy in the first-line setting?**

As Dr. Socinski mentioned earlier, for decades we’ve been using platinum-based doublets with or without bevacizumab. Now we have jumped forward, and we’re giving patients immunotherapy or combination immunotherapy with chemotherapy.

So we’d like to think about how to treat patients who don’t receive immunotherapy in the front-line. Not many of those patients are left, but maybe they began treatment prior to the approvals. How do we treat patients who have disease progression on chemoimmunotherapy? And then, whether there might be patients who will benefit less from immunotherapy that you might think they might not be the right patients to treat with immunotherapy.

Dr. Socinski, we’ll start with you.

---

**Socinski:**

For those patients who have received the regimens we’ve been talking about—chemoimmunotherapy regimens here—we’ve essentially taken our first-line regimens/second-line regimens and combined them. So what we used to do as third line, which was typically docetaxel with or without ramucirumab depending upon if there were any contraindications in this setting, has moved up to historically where docetaxel started, which was second line.

That’s my go-to regimen. In the majority of patients, I tend to use ramucirumab.
REVEL: Docetaxel + Ramucirumab

N = 1,253
1:1

Eligibility
- Stage IV NSCLC
- Progressed after platinum-based chemotherapy
- Prior bevacizumab permitted
- Squamous and non-squamous histology

Ramucirumab 10 mg/kg + Docetaxel 75 mg/m² Q3W n = 628

Placebo + Docetaxel 75 mg/m² Q3W n = 625

Parameter Median OS (95% CI) Censoring Rate
Ramucirumab plus docetaxel 10.5 mo (9.5-11.2) 31.8%
Placebo plus docetaxel 9.1 mo (8.4-10.0) 27.0%
Stratified HR 0.86 (95% CI 0.75-0.98)
P 0.023

Because we know from the REVEL trial that we did see the triple benefit—overall response, progression-free survival, and overall survival—although, you know, not in very modest improvements in the survival outcomes.

Approved Second-Line Therapies

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Approval Date</th>
<th>Trial</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (PD-1)</td>
<td>March 2015</td>
<td>CheckMate-017</td>
<td>Metastatic squamous NSCLC that progresses on or after platinum-based chemotherapy</td>
</tr>
<tr>
<td></td>
<td>October 2015</td>
<td>CheckMate-057</td>
<td>Metastatic nonsquamous NSCLC that progresses on or after platinum-based chemotherapy</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>October 2015 (accelerated)</td>
<td>KEYNOTE-001</td>
<td>Metastatic NSCLC that expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy</td>
</tr>
<tr>
<td></td>
<td>October 2016 (regular)</td>
<td>KEYNOTE-010</td>
<td>Metastatic NSCLC that expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy</td>
</tr>
<tr>
<td>Atezolizumab (PD-L1)</td>
<td>October 2016</td>
<td>OAK POPLAR</td>
<td>Metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy</td>
</tr>
<tr>
<td>Ramucirumab (VEGFR-2 inhibitor)</td>
<td>December 2014</td>
<td>REVEL</td>
<td>In combination with docetaxel for the treatment of metastatic NSCLC with disease progression on or after platinum-based chemotherapy</td>
</tr>
</tbody>
</table>

For those patients who might not have gotten immunotherapy first line—maybe because they were treated a while ago, or someone missed the boat—then immunotherapy is our standard second-line therapy. We had all 3 agents that were compared to docetaxel, all of which clearly beat docetaxel in the second-line setting. So that’s what I would do in that setting. It really comes down to where we find ourselves using more docetaxel. This is an area to try to figure out what further immunologic strategies could be employed for those patients who have run through anti-PD-1/anti-PD-L1 agents. I don’t know that we know that much about resistance mechanisms or what direction to go in in this setting, although that would be very helpful to design subsequent trials.
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FDA, US Food & Drug Administration; NSCLC, non–small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein ligand 1; TPS, tumor proportion score; VEGFR, vascular endothelial growth factor receptor.


Right now, in standard practice, we’re back to docetaxel second line. Usually I give it with ramucirumab; sometimes there’s a contraindication.

Reckamp: Dr. Yu.

Yu: Just to echo what Mark is saying, it’s such a black box as to what to do after this new first-line standard of care; even the REVEL study that was done prior to the era of immunotherapy. So, do those results stand up after first-line immunotherapy?

With targeted therapies, we know acquired resistance, figuring out the mechanism, and then addressing that has been the key to progress. We’re really not there yet with immunotherapy in terms of figuring out why people become resistant, can we re-harness that immune response? We’re trying a lot of different combination immunotherapies a little bit blindly.

Finally, certain people really benefit from immunotherapy, but there is a subset that don’t. There are really intriguing data at ASCO this year about certain genomic subsets that might not respond. So thinking about KEAP1 mutants or a STK11, which comprise 25% of lung adenocarcinomas—they really did not seem to benefit. So there are emerging data to help us pick the best treatments for our patients.

Socinski: I want to ask my colleagues a question that I thought of when you said the REVEL trial was done before the era of immunotherapy. Every once in a while, I hear anecdotal things that maybe chemotherapy works better after you’ve been exposed to immunotherapy. Does that resonate with either one of you?
There are some data on second progression-free survival, and that has some support to show that maybe there's a longer progression-free survival indicating that maybe you are getting better benefit. Again, as you mentioned from the first, the KEYNOTE-024 study, these patients went on to receive other therapies; but getting immunotherapy first was the important thing. So, actually it's hypothetical, but we're changing the milieu of the tumor microenvironment in a way and the immune system in a way that potentially can help other therapies to work better. But that's based more on anecdotes and small subset analyses than primary data at this time.

We've discussed a lot of topics—first-line therapy squamous cell, first-line therapy nonsquamous cell non–small cell lung cancer and the large number of amount of data that has really been presented over the past year/year and a half that have changed how we treat non–small cell lung cancer. And we can see, even in the next 6 to 12 months, we'll probably get more data that may make us think about how we're choosing and treating our patients.

I'd like to thank both Dr. Socinski, Dr. Yu for discussing these cases with me today and for your participation in this activity. Thank you.
REFERENCES


REFERENCES


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The executive leadership of AXIS combines 75 years of experience in adult learning theory, curriculum design/implementation/assessment, continuing education accreditation standards, and medical meeting planning and logistics. Our team has a deep understanding of the governing guidelines overseeing the medical education industry to ensure compliant delivery of all activities. AXIS employs an experienced team of medical and scientific experts, medical writers, project managers, meeting planners, and logistics professionals. This team is dedicated to meeting the unmet educational needs of healthcare professionals, with the goal of improving patient outcomes.

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