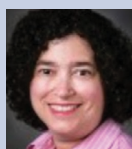


Thoracic Cancer: 2021 ASCO Annual Meeting Highlights for the Advanced Practitioner



Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC, of MD Anderson Cancer Center, reviews important research in thoracic cancers presented at the 2021 ASCO Annual Meeting, including atezolizumab in early-stage lung cancer, the addition of doublet chemotherapy to doublet immunotherapy in advanced-stage NSCLC, the first-in-class *KRAS* G12C inhibitor sotorasib, and the combination of amivantamab and lazertinib. Coverage provided by *The ASCO Post*.

Abstract 8500

Atezolizumab Reduces Risk of Disease Progression in Patients With PD-L1-Expressing Early-Stage NSCLC

By Alice Goodman

Visit <https://meetinglibrary.asco.org/record/195950/abstract> to read the full abstract and view author disclosures.

Atezolizumab given after chemotherapy to patients with resected stage II to IIIA non-small cell lung cancer (NSCLC) significantly improved disease-free survival compared with best supportive care alone in patients whose tumors expressed

PD-L1.¹ These results of the global phase III IMpower010 trial suggest that the addition of atezolizumab to adjuvant chemotherapy has the potential to become a standard of care earlier in the course of disease for this selected group of patients.

“The advances in treating NSCLC have primarily been in the setting of advanced disease. This is the first phase III study to demonstrate that [atezolizumab] after surgery and chemotherapy can significantly delay recurrence in patients with early-stage lung cancer,” stated lead author Heather A. Wakelee, MD, FASCO, Chief of the Division of Oncology, Stanford University Medical Center, at a press briefing held prior to the 2021 ASCO Annual Meeting.

The standard of care for many patients with stage IB to IIIA NSCLC has not changed in many years, although treatments have improved for stage IV NSCLC. “The recent ADAURA trial found that adjuvant treatment with osimertinib improved outcomes for resected *EGFR*-mutated NSCLC,² but for the vast majority of these patients, the standard of care has not changed in over 15 years and remains four cycles of platinum-based chemotherapy,” Dr. Wakelee told listeners.

With adjuvant chemotherapy in patients with completely resected NSCLC, the risk of death and recurrence is reduced by 16%,³ and disease recurrence is still common. The IMpower010 trial was designed to see whether the immune checkpoint inhibitor atezolizumab added to chemotherapy for patients with completely resected stage IB to IIIA NSCLC would improve outcomes.

J Adv Pract Oncol 2021;12(6):586-593
<https://doi.org/10.6004/jadpro.2021.12.6.4> • © 2021 Harborside™

Study Details

The phase III IMpower010 trial enrolled 1,280 patients, who were all treated with adjuvant cisplatin-based chemotherapy after undergoing complete surgical resection for stage IB to IIIA NSCLC. Those patients still meeting eligibility criteria after completion of chemotherapy were randomly assigned 1:1 to receive atezolizumab at 1,200 mg every 21 days vs best supportive care.

The primary endpoint of disease-free survival was analyzed in three subgroups: patients with stage II to IIIA tumors and PD-L1 tumor composite score $\geq 1\%$; all randomly assigned patients with stage II to IIIA NSCLC; and an intention-to-treat analysis of patients with stage IB to IIIA NSCLC. In this analysis, about half of all patients diagnosed with early-stage NSCLC have tumors that express PD-L1.

Major Findings

At a median follow-up of 32.8 months, in patients with stage II to IIIA resected NSCLC and PD-L1 tumor composite score $\geq 1\%$, atezolizumab, given after adjuvant chemotherapy, reduced the risk of disease progression or death by 34% vs best supportive care ($P = .004$). Median disease-free survival was not reached in the atezolizumab-treated group vs 35.3 months for those given best supportive care.

For all patients with stage II to IIIA NSCLC, the addition of atezolizumab reduced the risk of disease progression by 21% vs best supportive care. Median disease-free survival was 42.3 months for the atezolizumab-treated group and 35.3 months for those given best supportive care. In the intention-to-treat analysis of all patients, which included all patients with stage IB to IIIA NSCLC, the significance boundaries have not been crossed for disease-free survival at this interim analysis.

“We haven’t analyzed the data separately yet for the patients with stage IB disease, but overall in stage II to IIIA patients, we are not seeing a benefit for atezolizumab in those without PD-L1 expression. Only 12% of patients on the trial had stage IB disease, and this group tends to do better overall with lower rates of recurrence, so we are not surprised that we will have to wait a bit longer to see the outcomes in those patients,” Dr. Wakelee explained. The study is ongoing, and survival data are still immature.

Safety data were consistent with the known safety profile of atezolizumab, and no new safety signals emerged over the course of the trial. More patients who received atezolizumab after chemotherapy and surgery had any-grade adverse events: 92.7% vs 70.7% for best supportive care. Grade 3 to 4 adverse events were reported in 21.8% and 11.5% of patients, respectively, with or without atezolizumab. Grade 5 treatment-related adverse events occurred in 0.8% of the atezolizumab group and were not applicable in the control arm. Adverse events leading to treatment withdrawal were reported in 18.2% of the atezolizumab arm and were not applicable in the control arm.

Study Implications

“Given the significantly improved disease-free survival with adjuvant atezolizumab in patients with tumors expressing PD-L1, it is more important than ever to screen high-risk people for lung cancer to improve detection of NSCLC at early stages, and if NSCLC is detected, to do biomarker testing for *EGFR* mutations and now for PD-L1 expression. “In the IMpower010 trial, the vast majority of the benefit appeared to be in those patients whose tumors express PD-L1.”

When asked whether adjuvant atezolizumab would become a new standard of care earlier in the course of lung cancer, Dr. Wakelee said: “Obviously, we need FDA approval before this is offered as standard of care. The FDA has approved osimertinib in resected early-stage NSCLC with *EGFR* mutations based on a disease-free survival endpoint. The IMpower010 study showed that in patients with stage II to IIIA NSCLC and PD-L1 expression, atezolizumab after chemotherapy improved disease-free survival, and it is a more profound disease-free survival benefit than what was seen with chemotherapy alone in the earlier adjuvant trials.”

References

1. Wakelee H, Altorki N, Zhou C, et al: IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIa non-small cell lung cancer. 2021 ASCO Annual Meeting. Abstract 8500. Presented June 6, 2021.
2. Wu YL, Tsuboi M, He J, et al: Osimertinib in resected EGFR-mutated NSCLC. *N Engl J Med* 383:1711-1723, 2020.
3. Pignon JP, Tribodet H, Scagliotti G, et al: Lung adjuvant cisplatin evaluation. *J Clin Oncol* 26:3552-3559, 2008.

The Advanced Practitioner Perspective

Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC
MD Anderson Cancer Center

The phase III IMpower010 clinical trial evaluates atezolizumab (Tecentriq), a PD-L1 inhibitor, as adjuvant treatment in resected early-stage NSCLC. IMpower010 is similar to the other clinical trials (ADAURA, PACIFIC) in its evaluation of adjuvant treatment—following standard-of-care definitive treatment for early-stage (IB–IIIA) NSCLC (ADAURA) and locally advanced-stage, unresectable NSCLC (PACIFIC trial).

The primary endpoint of IMpower010 was disease-free survival (DFS), and the secondary endpoint was overall survival (OS). Three subgroups of patients were analyzed for DFS: patients with stage II to IIIA tumors with PD-L1 > 1%; all randomly assigned patients with stage II to IIIA NSCLC; and an intention-to-treat analysis of patients with stage IB to IIIA NSCLC. Of note, in this analysis, approximately half of all patients diagnosed with early-stage NSCLC have tumors that express PD-L1.

At the median follow-up of 32.8 months, IMpower010 showed that the addition of atezolizumab following doublet adjuvant chemotherapy for early-stage resected NSCLC reduced the risk of disease progression or death across all subgroups analyzed. Additionally, the median DFS was 42.3 months for the treatment (atezolizumab) arm and 35.3 months for the best supportive care arm.

This study demonstrated benefit of additional treatment, atezolizumab, following adjuvant chemotherapy for early-stage resected NSCLC. Based on the findings from IMpower010 and ADAURA, oncology teams should be testing (if they are not already doing so) for driver mutations and PD-L1 in patients with early-stage NSCLC. IMpower010 demonstrates that patients without driver mutations have an adjuvant option, atezolizumab, that is of benefit to them.

Disclosure: Ms. Waxman has no conflicts of interest to disclose.

Abstract 9000**NSCLC: Nivolumab, Ipilimumab, and Chemotherapy for Advanced Disease**

By The ASCO Post Staff

Visit <https://meetinglibrary.asco.org/record/196799/abstract> to read the full abstract and view author disclosures.

Martin Reck, MD, PhD, of Lungen-Clinic, discusses a 2-year update of the CheckMate 9LA study, which sought to determine whether nivolumab plus ipilimumab combined with two cycles of chemotherapy is more effective than four cycles of chemotherapy alone as a first-line treatment for patients with stage IV non-small cell lung cancer (NSCLC). A transcript of his interview with *The ASCO Post* follows.

The CheckMate 9LA trial was a randomized trial investigating the combination of two cycles of chemotherapy together, with the combination of nivolumab and ipilimumab, compared with chemotherapy alone in untreated patients with

nononcogenic advanced NSCLC. 719 patients were randomized, and this year's ASCO meeting represented the 2-year update. When we look at the efficacy endpoint, we see a consistent benefit in overall survival favoring the combination compared with chemotherapy alone. We have seen an improvement in overall survival corresponding to a hazard ratio of 0.72, a median overall survival of 15.8 months compared with 11.0 months in the control arm, and a 2-year overall survival rate of 38% compared with 26% in the control arm.

Still, we do have a couple of censored events, so we have to wait for further updates to see mature overall survival data. We have also seen a consistent improvement in progression-free survival and response favoring the combination arm.

Tolerability of the Combination Regimen

When we look at the tolerability data, which is of particular clinical interest, we haven't seen many changes in the additional year of follow-up. We have seen a higher rate of treatment-related adverse events leading to treatment discontinuation in the combination arm compared with the

control arm. However, the duration of treatment was also longer in the combination arm compared with the control arm.

We performed two additional analyses. First, we looked at the time of appearance of treatment-related adverse events, and we saw that the majority of treatment-related adverse events in the combination arm appeared during the first two cycles of treatment, with a fast decline over the maintenance therapy. Second, an analysis looked at patients who had to discontinue treatment due to treatment-related adverse events. We saw that

in these patients who had to discontinue all components of the combination therapy, there was no impact on the efficacy of treatment, in particular, no impact on overall survival.

In summary, we have a consistent signal of efficacy in the Checkmate 9LA trial. We see that the majority of adverse events appear in the first cycle of treatment, and there was no impact on efficacy in those patients who had to discontinue. Furthermore, we see that the signal of efficacy is seen across all patient characteristics and PD-L1 expression levels.

The Advanced Practitioner Perspective

**Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC
MD Anderson Cancer Center**

CheckMate 9LA postulated whether the addition of doublet chemotherapy to doublet immunotherapy (nivolumab [Opdivo] and ipilimumab [Yervoy]) would improve the benefit of doublet immunotherapy for advanced-stage NSCLC. In this study, patients in the experimental arm received nivolumab and ipilimumab plus two courses of platinum-based doublet therapy (carboplatin/paclitaxel for squamous histology; carboplatin or cisplatin/pemetrexed for nonsquamous histology). Patients in the experimental arm remained on treatment with nivolumab and ipilimumab until disease progression. Patients in the control arm received standard-of-care platinum-based doublet therapy (based on histology), with the option of maintenance pemetrexed for patients with nonsquamous histology.

The primary endpoint was overall survival (OS), and the secondary endpoints were pro-

gression-free survival (PFS) and objective response rate (ORR). At the initial prespecified interim analysis, the data showed benefit in the immunotherapy and chemotherapy arm at all endpoints.

This update of CheckMate 9LA again demonstrates continued effectiveness in the experimental arm across all patient demographics and all levels of PD-L1 expression. Of note is that treatment-related toxicities in the experimental arm occurred in the first two cycles of treatment when the patients received all four drugs, and decreased over time when the patients were on doublet immunotherapy. The quadruplet combination of nivolumab and ipilimumab plus doublet chemotherapy is a treatment option for patients with advanced NSCLC. Attention to toxicities with quadruplet therapy and interventions are crucial for patients to be able to continue treatment. More results on OS will come at another update of CheckMate 9LA.

Disclosure: Ms. Waxman has no conflicts of interest to disclose.

Abstract 9003

Sotorasib: Subgroup Analysis of Phase II Trial Shows Activity With Breakthrough *KRAS* Inhibitor in Lung Cancer

By Alice Goodman

Visit <https://meetinglibrary.asco.org/record/196931/abstract> to read the full abstract and view author disclosures.

The breakthrough *KRAS*-specific inhibitor sotorasib achieved responses in patients with *KRAS* G12C-mutated non-small lung cancer (NSCLC) who had experienced disease progression on platinum-based chemotherapy, immunotherapy, or both treatments. The objective response rate was 37.1%, and responses extended to all subgroups, according to an analysis of the phase II CodeBreaK 100 trial study presented at the 2021 ASCO Annual Meeting by lead study author Ferdinandos Skoulidis, MD, PhD, Assistant Professor of Thoracic Medical Oncology, at The University of Texas MD Anderson Cancer Center, Houston.¹ A confirmatory phase III CodeBreaK 200 trial is designed to compare sotorasib vs docetaxel.

The first report from the study suggested that patients with co-mutations in *STK11*, a driver of poor outcomes with standard care, derived benefit from sotorasib.² The extended subgroup analysis presented at the ASCO meeting showed a numerically higher response rate and longer progression-free and overall survival in patients with *STK11* co-mutated but *KEAP1* wild-type disease. Due to the small number of patients, further study is needed to determine which subgroups—if any—have more robust responses to sotorasib.

“Extensive efforts are underway to understand the molecular determinants of response to sotorasib and to characterize the full spectrum of possible mechanisms of resistance,” Dr. Skoulidis said. “The CodeBreaK100 results represent a pivotal step in our progress against *KRAS*-mutant tumors and will likely be a stepping stone for even more effective and tailored combination regimens. The future looks promising.”

For the moment, the news is focused on the success of the first drug to target *KRAS*—formerly

considered a nondruggable mutation in NSCLC. The study was published in *The New England Journal of Medicine*³ to coincide with the presentation at the ASCO meeting.

Senior author of the study, Vamsidhar Velcheti, MD, Director of Thoracic Medical Oncology, NYU Langone Health, Perlmutter Cancer Center, New York, was most enthusiastic about the promise of sotorasib. “The phase II CodeBreaK 100 study is an important landmark study. Sotorasib is the first *KRAS* tumor-selective drug to be approved for any tumor type. Patients with *KRAS* G12C-positive lung adenocarcinoma have limited systemic treatment options after progressing on standard chemotherapy and immunotherapy. Sotorasib is now a great treatment option for these patients after disease progression on front-line chemotherapy and immunotherapy,” said Dr. Velcheti. [Editor’s Note: On May 28, 2021, the FDA granted accelerated approval to sotorasib for the first treatment of adults with NSCLC containing the *KRAS* G12C mutation and who had at least one prior systemic therapy.]

“Most importantly, sotorasib is very well tolerated with fewer side effects than salvage chemotherapy options like docetaxel for these patients,” he continued.

“Sotorasib is a highly selective oral drug specifically designed to target tumors with a *KRAS* G12C mutation, which accounts for about 13% to 15% of all newly diagnosed patients with lung cancer. This is the most common *KRAS* mutation in lung cancer, although it can be seen in other tumor types as well,” Dr. Velcheti said.

“The data for the subgroup analysis are based on small numbers of patients. The subgroup with *STK11* mutations may benefit more from the drug, but this is preliminary. We need to study subgroups further to try to understand which ones may benefit more from the drug. A small subset of patients with *KEAP1* alterations appear to be less responsive to sotorasib, and there are several efforts ongoing to study combination-based approaches for this population,” he added. “Sotorasib is obviously a significant advance in developing targeted therapy for patients with NSCLC and *KRAS* mutations. There are a lot of ongoing efforts currently to develop innovative combination approaches with sotorasib to overcome primary and acquired resistance to sotorasib.”

Study Details

CodeBreaK 100 assigned 126 patients with locally advanced or metastatic *KRAS* G12C-mutated NSCLC that had progressed on prior standard therapies to receive sotorasib at 960 mg/d until disease progression. Radiographic scans were conducted every 6 weeks up to week 48 and every 12 weeks thereafter. The primary endpoint was objective response rate according to the Response Evaluation Criteria in Solid Tumors by independent central review. Key secondary endpoints were duration of response, disease control rate, time to recurrence, progression-free survival, overall survival, and safety. Evaluation of biomarkers was an exploratory endpoint.

At baseline, the median patient age was 63.5 years; all patients had an Eastern Cooperative Oncology Group performance status of 0 or 1; 92.9% were current or former smokers. Patients had up to three prior lines of therapy; 89.7% had platinum-based chemotherapy; 91.3% had checkpoint inhibitor therapy; and 81% had both.

Key Findings

At a median follow-up of 15.3 months, the rate of complete response was 3.2%; the partial response rate was 33.9%; stable disease rate was 43.5%, for a disease control rate of 80.6% in this advanced, pretreated population. The median duration of response was 11.1 months, and the median time to response was 1.35 months.

On the 960-mg dose—the FDA-approved dose—median progression-free survival was 6.8 months, and median overall survival was 12.5 months.

Most treatment-related adverse events were grade 1 and 2 and were generally manageable. No fatal treatment-related adverse events were reported as of data cutoff on March 15, 2021. Treatment-related adverse events led to dose modification in 28 patients (22.2%) and treatment discontinuation in 9 patients (7.1%). Any-grade treatment-related adverse event was reported in 69.8%, and grade 3 events were reported in 19.8%. The most common-

ly occurring adverse events were diarrhea, nausea, and increases in liver enzymes.

In the exploratory biomarker analysis, response to sotorasib was consistently observed among patient subgroups. One standout subgroup included patients treated with prior anti-PD-L1 but no platinum-based chemotherapy; this group had an objective response rate of 69.2% and a median overall survival of 17.7 months.

The efficacy of sotorasib was observed in molecular subgroups associated with suboptimal outcomes with the standard of care, including *TP53*, *STK11*, and *KEAP1*. However, again, it is important to note the small number of patients and the need for further study to determine which subgroups may benefit.

Question of Dose Optimization

Patients enrolled in CodeBreaK100 were treated with sotorasib at 960 mg/d, although evidence from a phase I trial of the drug showed no dose-response relationship. In fact, a small number of patients ($n = 3$) benefited from a daily dose of 180 mg, raising the question of whether lower doses of the drug might be equally efficacious or even more so if given with food. A recent commentary in *The ASCO Post* delved more deeply into optimal doses of anticancer drugs, including sotorasib in NSCLC.⁴

References

1. Skoulidis F, Li BT, Govindan R, et al: Overall survival and exploratory subgroup analyses from the phase 2 CodeBreaK 100 trial evaluating sotorasib in pretreated *KRAS* p.G12C mutated non-small cell lung cancer. 2021 ASCO Annual Meeting. Abstract 9003. Presented June 4, 2021.
2. Li BT, Skoulidis F, Falchook G, et al: CodeBreaK 100: Registrational phase 2 trial of sotorasib in *KRAS* p.G12C mutated non-small cell lung cancer. 2020 World Conference on Lung Cancer. Abstract PS01.07. Presented January 30, 2021.
3. Skoulidis F, Li BT, Dy GK, et al: Sotorasib for lung cancers with *KRAS* p.G12C mutation. *N Engl J Med*. June 4, 2021 (early release online).
4. Raitin MJ, Lichter AS: Empowering the FDA to require dose optimization of all new oncology drugs. *The ASCO Post*. January 25, 2021.

The Advanced Practitioner Perspective

Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC
MD Anderson Cancer Center

The findings from the clinical trial with sotorasib are exciting for patients with Kirsten rat sarcoma (*KRAS*) mutation, which was once felt to be difficult to treat and not sensitive to treatment. *KRAS* mutation is the most prevalent driver mutation in NSCLC and is found in 25% to 30% of nonsquamous NSCLCs (Biernacka et al., 2016; Boch et al., 2013; Riely et al., 2008). Of all the *KRAS* mutations, G12C is the most frequent variant in NSCLC, with a prevalence of 13% in lung adenocarcinomas (Biernacka et al., 2016).

The findings from the clinical trial showed the effectiveness of sotorasib in patients

previously treated with chemotherapy, immunotherapy, or both chemotherapy and immunotherapy. Patients with *STK11* mutations also derived benefit from sotorasib, although further study is needed. Toxicities from sotorasib are similar to those with other oral targeted therapies.

Once again, there is reason for excitement in thoracic oncology, as there is a new, effective targeted therapy—sotorasib—for a mutation once thought to be undruggable. Sotorasib appears to have some efficacy for *STK11* mutations, giving hope to patients who have this mutation, although more studies are needed to validate these findings.

Disclosure: Ms. Waxman has no conflicts of interest to disclose.

Abstract 9006**NSCLC: Amivantamab Plus Lazertinib for Treatment of Relapsed Disease**

By The ASCO Post Staff

Visit <https://meetinglibrary.asco.org/record/196820/abstract> to read the full abstract and view author disclosures.

Byoung Chul Cho, MD, PhD, of the Yonsei Cancer Center, discussed study results that showed treatment with the EGFR-MET bispecific antibody amivantamab plus the EGFR inhibitor lazertinib yielded responses in 36% of chemotherapy-naïve patients with non-small cell lung cancer (NSCLC) whose disease progressed on osimertinib. Genetic biomarkers may be able to identify patients most likely to benefit from the combination regimen. A transcript of his interview with *The ASCO Post* follows.

CHRYSLIS is a phase I study of amivantamab and lazertinib combination. In this phase I study, 45 patients with *EGFR*-mutant NSCLC whose disease had progressed on osimertinib but had not yet received chemotherapy, received combination amivantamab and lazertinib. Of those patients, 36% of patients had a confirmed response with this regimen. Median duration of response was 9.6 months, and duration of response greater than 6 months

was 69%. Median progression-free survival was 4.9 months, and the clinical benefit rate was 64%.

The most exciting part of this presentation was the biomarker studies. Each patient's tumor was characterized through genetic testing of circulating tumor DNA and tumor biopsy to identify mechanisms of resistance to osimertinib. This study identified 17 patients with *EGFR*- and *MET*-based resistance. In these patients, overall response rate was 47%, median duration of response was 10.4 months, and clinical benefit rate was 82%. Median progression-free survival of this subset was 6.7 months. Of the remaining 28 patients without identified *EGFR*- and *MET*-based resistance, 29% of patients experienced confirmed responses.

This study also examined 20 patients who had sufficient tumor tissue to do immunohistochemistry staining for *EGFR* and *MET* expression. Among 10 patients whose tumors stained high for *EGFR* and *MET* expression, 90% of patients had tumor response.

This is really impressive data (although in a small subset of patients) showing a 90% objective response rate in this heavily treated patient population who has already exhausted *EGFR* tyrosine kinase inhibitors, particularly osimertinib. Typically, patients whose disease no longer respond to osimertinib therapy would have little opportunity to seek additional treatment other than cytotoxic chemotherapy. However, in this CHRYSLIS study, we have shown durable response with the

combination of amivantamab and lazertinib. I think this may be a new therapeutic opportunity in patients who have progressed on osimertinib in *EGFR*-mutant NSCLC.

Based on these promising findings and biomarker study results, the CHRYSALIS-2 study

is ongoing. In CHRYSALIS-2, we are evaluating amivantamab and lazertinib combination in the post-osimertinib and platinum chemotherapy patient population, and in cohort D, biomarkers are prospectively validated in the post-osimertinib patient population.

The Advanced Practitioner Perspective

Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC
MD Anderson Cancer Center

CHRYSALIS is a small phase I clinical trial (45 patients) that evaluated combination treatment with amivantamab plus lazertinib for patients with disease progression after first-line treatment with osimertinib. This study evaluated biomarker testing to identify osimertinib resistance. The treatment for patients with disease progression after first-line treatment with osimertinib has been chemotherapy. This study, although small in participant numbers, demonstrated benefit with the combination of amivantamab and lazertinib for patients whose tumors are *EGFR* and *MET* resistant.

Tissue and serum mutation testing were also a large part of this clinical trial. Patients had biopsies for mutation testing to identify osimertinib resistance mechanisms, as well as circulating tumor DNA (serum mutation testing). Seventeen patients were found to have

EGFR and *MET* resistance, and these patients responded to treatment. The duration of response was under 1 year, at 10.4 months, and the median progression-free survival was 6.7 months. The 28 patients without identified *EGFR* and *MET* resistance also responded to treatment. There was another subset of 20 patients whose tumors had immunohistochemistry staining for *EGFR* and *MET* expression (not resistance). Notably, of 10 patients whose tissues had high *EGFR* and *MET* expression, nine had response to treatment.

The combination of amivantamab and lazertinib has similar toxicities to other targeted therapies, including rash and diarrhea. There were infusion-related reactions (amivantamab is an intravenous treatment, lazertinib is oral). The results of this initial trial gives clinicians more options for treating patients who progress on osimertinib.

Disclosure: Ms. Waxman has no conflicts of interest to disclose.