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COMMENTARY

Current and Emerging Treatment Options for Patients with Metastatic *EGFR*-Mutated Non-small Cell Lung Cancer After Progression on Osimertinib and Platinum-Based Chemotherapy: A Podcast Discussion

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ABSTRACT

Patients with metastatic epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer (NSCLC) are widely treated with osimertinib, the preferred first-line treatment option. However, disease progression inevitably occurs, driven by *EGFR*-dependent or *EGFR*-independent mechanisms of resistance. Platinum-based chemotherapy is the recommended treatment following progression with osimertinib but responses to platinum-based chemotherapy are transient. Salvage therapies, which are used after progression on platinum-based chemotherapy, have poor clinical outcomes in addition to substantial toxicity. In this podcast, we discuss the current treatment landscape and emerging therapeutic options for patients with metastatic *EGFR*-mutated NSCLC whose disease has progressed following treatment with osimertinib and platinum-based chemotherapy.

Podcast audio available for this article.

Keywords: NSCLC; Non-small cell lung cancer; *EGFR*-activating; *EGFR*-mutated; Biomarker testing; Podcast

Key Summary Points

This podcast features two oncologists discussing current and emerging treatment options for patients with metastatic epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer (NSCLC) after progression on osimertinib and platinum-based chemotherapy (PBC).

The existing treatment landscape for *EGFR*-mutated NSCLC following osimertinib and PBC is highly fragmented, and subsequent treatments provide modest clinical benefit coupled with substantial toxicity.

New effective and safe therapies are needed; emerging therapeutic candidates are being investigated in clinical trials as potential treatment options to overcome resistance to existing treatments and to improve clinical outcomes.

Molecular testing can aid in the monitoring of disease progression, as well as providing insights into the selection of subsequent treatments.

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DIGITAL FEATURES

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PODCAST TRANSCRIPT

Sandip Patel (SP): Hello and welcome to our podcast discussion on the current and emerging treatment strategies for patients with metastatic *EGFR*-mutated non-small cell lung cancer (NSCLC), whose disease has progressed after treatment with osimertinib and platinum-based chemotherapy. This podcast and its transcript will be published in *Advances in Therapy*.

My name is Sandip Patel, and I am a medical oncologist from the University of California, San Diego. My colleague Dr Jyoti Patel joins me in this discussion.

Jyoti D. Patel (JDP): Hi everyone. My name is Jyoti Patel, and I am a medical oncologist from Northwestern University in Chicago. Sandip, I am looking forward to this discussion.

SP: As am I, Jyoti. We know that treatment for patients with metastatic *EGFR*-mutated NSCLC has rapidly evolved over the past decade, driven by advances in biomarker testing [1]. Before delving into our main topic, can you briefly talk about the importance of molecular testing for patients with lung cancer?

JDP: Sure. *EGFR* alterations are pretty common in NSCLC; they account for the mutations that we target in 20% of adenocarcinomas in the Caucasian populations and up to 50% of adenocarcinomas in the Asian populations [2]. ESMO [European Society for Medical Oncology] guidelines recommend genetic testing in patients with lung cancer for *EGFR* mutations, and it is a level I recommendation [3]. It is clear that biomarker testing rates have increased over time. In fact, a real-world study indicated that up to 78% of patients with advanced NSCLC in the USA were appropriately tested for *EGFR* mutations [4]; although one can imagine that these rates would vary widely in other countries [1, 5].

We use both tissue and liquid biopsies together sometimes, or sequentially, for biomarker testing to help the selection of appropriate treatments. More and more of us are using concurrent testing at point of care [1]. We have also shown for over almost 20 years now that multiple drugs can work; three generations of EGFR tyrosine kinase inhibitors (TKIs) have been developed to treat patients with *EGFR*-mutated NSCLC [6].

However, when we say *EGFR*-mutated lung cancer, we know that there is differential sensitivity to EGFR-TKIs [3]. The most common sensitizing mutations are exon 19 deletions and the exon 21 L858R point mutation, which are considered "targetable mutations" [3, 7, 8]. I think it is important to stress that it is no longer adequate to say someone has an *EGFR* mutation. You really want to give some flavor to it, because again, we understand that it is likely [conferring] differential sensitivity. Less common mutations, such as exon 20 insertions, previously were found to be non-targetable, but now there are some newer agents that have been approved in the second-line setting in the USA, such as mobocertinib and amivantamab [2, 9].

ESMO recommends testing that would cover *EGFR* exons 18 to 21 overall, as well as the resistance mutation T790M in exon 20 in patients who received first- or second-generation EGFR-TKIs [3]. Is there anything you would like to add, Sandip?

SP: No, I think that is a great summary on molecular testing. I like to say, in clinic, as you nicely pointed out, it is not enough to just give the street name. We have to give the full address now for *EGFR*. So, whether it is *EGFR* mutation exon 19 in a typical mutation or an exon 20 insertion, I think your point that we have to be very specific about [*EGFR* mutations] is key. Let us move on to discuss about the treatments that [are] derived from making the proper molecular diagnosis.

Osimertinib is the main EGFR-TKI that is being prescribed in the USA to patients with advanced NSCLC harboring canonical *EGFR*-sensitizing mutations [10]; this is typically

utilized in the frontline space in the USA [11]. Osimertinib is a third-generation EGFR-TKI, it is a pill with activity against the T790M mutation [10], and it has significantly improved clinical outcomes compared with first-generation EGFR-TKIs in patients with previously untreated advanced *EGFR*-mutated NSCLC [12, 13]. This was demonstrated in the phase 3 FLAURA trial, which compared osimertinib with a comparator EGFR-TKI, such as gefitinib or erlotinib, in the frontline setting [12, 13]. To me, one of the things I was impressed about [by] this trial is that this [is not] a comparison to chemotherapy, it is a comparison to state-of-the-art targeted therapies, [which were approved just] a couple of years prior to the initiation of this study. In this study, treatment with osimertinib resulted in a significantly longer median progression-free survival (PFS) of 18.9 months versus 10 months in the comparator group, which here was [a] first-generation EGFR-TKI, such as gefitinib or erlotinib [12]. The median overall survival (OS) was 38.6 months in the osimertinib group versus 31.8 months in the comparator group [13].

Osimertinib is recommended as the preferred frontline EGFR-TKI in the USA and Europe because of its superior survival benefit and favorable safety profile [3, 7]. Oncology societies in Asia also recommend osimertinib as a first-line therapy for these patients in parallel with other first- and second-generation EGFR-TKIs [14, 15]. But for me, I think the efficacy profile, especially the central nervous system (CNS) efficacy, is what really makes me continue to utilize this drug in the frontline space [16, 17], along with its very tolerable toxicity profile [12], which actually makes osimertinib amenable even in that adjuvant setting [18]. Jyoti, can you comment on resistance mechanisms following treatment with osimertinib and what your strategy in these patients is?

JDP: Sure, thanks so much Sandip. [In] patients who are found to have *EGFR* classical mutations [and] receive osimertinib, responses are swift and dramatic, and patients feel much better; but as you point out, we know that the median PFS is just around 19 months [11]. Unfortunately, disease progression on osimertinib inevitably occurs, and this can happen because of *EGFR*-dependent or *EGFR*-independent mechanisms of resistance [6, 8].

The C797X, which is mainly C797S, mutations are probably the most common *EGFR*-dependent mechanisms of resistance to osimertinib, and we see this in about 29% of patients [6, 11]. This is a mutation within the *EGFR* gene, which changes binding to osimertinib [19]. We also know that there are a host of *EGFR*-independent mechanisms that can include histologic transformation, for example, to small cell lung cancer, and these [mechanisms of resistance] can be common [11, 20, 21]. When patients develop small cell transformation, and again, this is something you can only find by doing a biopsy at resistance [11], we generally tend to use platinum-etoposide regimens [22, 23]. Unfortunately, for these patients, although they will have a response, generally [the response] tends to be short, and often we will see progression in the CNS. These two buckets of *EGFR*-dependent mutations and *EGFR*-independent mutations [often] happen. But in over half of the patients who are receiving osimertinib within a first- or second-line setting, we don't understand what the mechanism of resistance is and we call this an unidentified resistance [11, 20].

When patients progress, I think it is important to see the cadence of progression as well as the pattern of progression. Sometimes local treatment can be helpful for patients who have had oligoprogression, and that might be that they are treated with surgery or radiation for limited sites of progressive disease; often [patients] will [also] continue targeted systemic therapy [3, 14]. For some patients who have more systemic progression, the combination of platinum-based chemotherapy plus bevacizumab and atezolizumab is recommended, and the use of this regimen varies by region around the world [3].

SP: Absolutely, the point with that regimen [is that] it [contains] a paclitaxel backbone. There are studies looking at pemetrexed and also [studies] if one wanted to go back to osimertinib or continue osimertinib [3]. The fact [is that] there is an immunotherapy—atezolizumab, [which may] predispose [patients] toward pneumonitis [24]. [There] are a

couple of thoughts around why there is variable utilization of that regimen. But it is really a great summary about how we think about how we treat these patients.

Jyoti, what is your agent of choice when patients develop resistance to osimertinib, and no targetable mutations or no evidence of small cell histologic transformation has been identified? Unfortunately, [this is] an all-too-common problem in our clinic.

JDP: Absolutely right. Generally, for these patients in whom I don't find another targetable mutation, I tend to reflex back to platinum-based chemotherapy, and I really think this is the mainstay of treatment following progression on one of the TKIs [3, 25]. Typical combinations include pemetrexed plus carboplatin, with or without bevacizumab [26], as well as what we alluded to a minute ago with carboplatin/paclitaxel plus bevacizumab [27]. Primarily, the paclitaxel [regimen] is used in patients who may have renal insufficiency in whom we want to integrate immunotherapy at some point [28, 29]. We often will continue on osimertinib if a patient has a history of brain metastases. Again, generally, [osimertinib] is better tolerated [in combination] with carboplatin [plus] pemetrexed [30]. I will often add [osimertinib] in maybe the second cycle of [chemo]therapy, and now I am becoming more comfortable with even adding it or continuing it from cycle 1 [of chemotherapy].

Unfortunately, although we all feel comfortable with these regimens, we know that second-line chemotherapy is not as effective as we would like it to be [25, 31]. Again, the clinical benefit from these platinum-based chemotherapies, even with maintenance pemetrexed, tends to be shorter than one would hope [25, 26, 32]. In fact, in a real-world study, platinum-based chemotherapy resulted in a median PFS of 4.7 months in patients with NSCLC whose disease had progressed on EGFR-TKIs [25]. This is really difficult. Patients had started osimertinib with great anticipation and hope. We have been thinking about a PFS that looks like 19 months [12], and then certainly, your next regimen, with a PFS of less than 5 months [25] is certainly disheartening. In this review of real-world data in patients who received pemetrexed, maybe they fared slightly better with a median PFS of 5.1 months [31].

SP: Absolutely. Great points! What is your opinion on immunotherapy, which is actively being evaluated both as monotherapy and in combination with chemotherapy in these patients after osimertinib stops working for them?

JDP: Immune checkpoint inhibitors (ICIs) have lacked considerable impact in patients with *EGFR*-mutated NSCLC [33, 34]. We know that particularly monotherapy lends minimal clinical benefit for these patients [35]. There are several immunotherapy plus chemotherapy combinations that have been explored and reported recently [36–38].

The IMpower150 trial, which we were talking about before, is adding atezolizumab plus bevacizumab to carboplatin and paclitaxel [36]. This was initially recommended as a treatment option for patients with disease progression on EGFR-TKIs in Europe [3], based on a subgroup analysis of IMpower150 [36]. However, there have been a number of recent trials that really make us reconsider and figure out how to move forward. Recent results from phase 3 trials, such as CheckMate-722 and KEYNOTE-789, indicate that combinations of immunotherapies with chemotherapy that is platinum-based don't do as well following EGFR-TKIs [37, 38].

CheckMate-722 compared chemotherapy alone to chemotherapy with nivolumab, and the primary endpoint in this study was not met. In fact, the median PFS was 5.6 months in the nivolumab plus chemotherapy arm versus 5.4 months in the chemotherapy alone arm. [Objective] response rates were 31% and 27%, respectively [37]. Moreover, the nivolumab arm was associated with a higher incidence of grade 3 or 4 treatment-related hematologic effects, with anemia and decreased white blood cell count being the most common [37]. More recently, KEYNOTE-789 also did not meet its dual primary endpoint of PFS and OS [38]. This was looking at pembrolizumab plus carboplatin-based chemotherapy. The PFS in the pembrolizumab arm was 5.6 months versus 5.5 months with chemotherapy alone; the median OS was 15.9 months in the pembrolizumab arm versus 14.7 [months] in the

chemotherapy arm alone. There was a slight trend toward an improved OS with pembrolizumab, but this was not statistically significant [38]. As a community, we felt that this was a negative trial. These two trials were just ICIs in combination with chemotherapy.

ORIENT-31 is an ongoing phase 3 trial in China [39]. It evaluated combinations of sintilimab, which is an anti-PD-1 agent, with or without a bevacizumab biosimilar, IBI305, plus platinum-based chemotherapy in patients who had progression following an EGFR-TKI. In the interim analysis, combinations of sintilimab plus chemotherapy [consisting of cisplatin and pemetrexed] with or without IBI305 were associated with statistically significant improvements in PFS compared with chemotherapy alone. In fact, the median PFS was 7.2 months with all four drugs versus 5.5 months in the sintilimab plus chemotherapy group and 4.3 months in the chemotherapy alone group [40]. Incidences of grade 3 or higher treatment-emergent adverse events (TEAEs) ranged from 46% to 60% across different groups.

Sandip, can you comment on treatments available for patients [whose disease has] progressed on both osimertinib and platinum-based chemotherapy?

SP: That is a great question. There is no single established standard of care for these patients [41]. Clinical trials are really an opportunity for us to advance care not only for these patients but for others as well.

Salvage therapies have been used in the third line, including docetaxel combinations, although there have been little improvements in outcomes based on the REVEL study [42], which looked at docetaxel plus ramucirumab, which had a median OS benefit [of] about 10.5 months compared with 9.1 months with docetaxel alone, and a median PFS of 4.5 months with the docetaxel–ramucirumab combination versus docetaxel alone at 3 months. Investigator-assessed objective response rate (ORR) with ramucirumab plus docetaxel was 23% versus 14% with docetaxel. Docetaxel itself has significant toxicities for our patients, and in combination with ramucirumab, there is a higher rate of grade 3 TEAEs, 79% versus 71% for docetaxel alone.

Another combination that is often utilized is bevacizumab plus paclitaxel, which showed improved ORRs compared with docetaxel in a phase 3 trial [43]. However, the median OS was not significantly prolonged with this combination. I think many of our patients in the third-line space start to have decreasing performance status [44], and we often, in the real-world setting, are forced to use weekly versions of docetaxel and paclitaxel regimens to maximize tolerability.

However, clinically meaningful improvements in survival have not yet been seen in patients over these years, and I do think that clinical trials, especially for some of the antibody drug conjugates, are some of the more attractive options for these patients, so is biomarker-directed therapies toward acquired resistance if available.

Jyoti, at AACR 2023, you presented a nice analysis of real-world treatment patterns in patients with *EGFR*-mutated NSCLC after progression on osimertinib and platinum-based chemotherapy in the USA [45]. Can you walk us through your results?

JDP: Sure, thanks so much, Sandip. Real-world analyses present us with an opportunity to generalize our findings [46]. Remember that often in clinical trials, eligibility criteria can be very restrictive; it is definitely a little bit [of a] different population than many of us encounter in the clinic. These kind of analyses, I think, can be sobering for many of us and give us insights that we cannot get from clinical trials.

We used Flatiron Health electronic health record-derived data, and our results showed that treatment patterns were highly variable. Patients received non-platinum-based chemotherapies, immunotherapies, TKI monotherapy, TKI combinations, or platinum-based chemotherapy [45]. As Sandip mentioned, it is in many ways, sort of dealer's choice, and that was very much borne out in the data that we saw. Regardless of these interventions, we can say that OS was poor, with a median PFS of only 3.3 months and a median OS of 8.6 months.

Similar results were seen in another real-world study in patients with NSCLC harboring targetable mutations, including *EGFR* mutations, whose disease had progressed on standard-of-care

regimens [25]. The median OS was 10.3 months and the median PFS was 3.2 months.

Overall, I think these real-world data indicate that we have a lot to do. The treatment landscape after osimertinib and platinum-based chemotherapy is unfortunately highly fragmented and subpar, and, I think, highlights the need for new and more effective treatments for patients with advanced *EGFR*-mutated NSCLC.

SP: Absolutely, outcomes are indeed limited for this patient population, and another challenge faced by physicians is the treatment of brain metastases, which is unfortunately all too common in patients with NSCLC with *EGFR* mutations [47]. Although osimertinib has shown intracranial efficacy [48], management of brain metastases on progression of osimertinib remains a serious concern, and integration of stereotactic radiotherapy approaches may not be sufficient for all patients [49]. Additional agents with proven intracranial activity are needed as subsequent therapies beyond osimertinib, to help maximize the benefit, not only viscerally outside the brain but most importantly, in addition, in the CNS, where these types of cancers, in particular, have a propensity to grow [47].

JDP: Sandip, I absolutely agree that these patients are in need of agents that can be effective systemically as well as in the CNS, and we know that we need to have therapies that are also well tolerated. We talked a little bit about the role of biopsy for patients at progression, but certainly, I think, this next section highlights why it is so important. When a patient progresses in our clinic, we will do liquid biopsy as well as tissue biopsy when safe and feasible, and the tissue again helps us with histologic transformation. The blood and tissue next generation sequencing (NGS) [can] help us find other avenues to target [3].

One such area in which we have seen efficacy of dual targeting is in *MET* amplifications. We know that *MET* amplifications are the most common *EGFR*-independent mechanism of resistance to osimertinib [6]. In fact, we see this in up to 30% of cases [50]. There is wide discussion about what accounts for being *MET*-positive, what degree of *MET* activation do you know, but we can say very clearly that there are agents that can target MET. Sandip, what are your thoughts on agents targeting MET?

SP: Absolutely. Great point. I think it is an excellent point that we need to be able to do the right test for our right patients to get them on the right treatment. In regards to *MET*, amivantamab is a bispecific MET- and EGFR-directed antibody with particular activity against *EGFR* exon 20 insertions [2]. At this point, we have to name both the street and the address for the mutations.

Amivantamab is also active against exon 19 deletions, the L858R point mutation (which is in exon 21), T790M, and other exon 20 insertions [2]. [Amivantamab] has been assessed in combination with lazertinib, which is a CNS-penetrant, third-generation EGFR-TKI [51, 52], in the CHRYSALIS-2 study [53, 54]. In that study, preliminary ORR by blinded independent central review was 36% in patients with *EGFR*-mutated NSCLC that had progressed on osimertinib and platinum-based chemotherapy. Of particular interest, the combination of amivantamab plus lazertinib showed some evidence of CNS activity in that study. The most common toxicities seen were infusion-related events (which very much relates to the unique nature of amivantamab and its component[s]; infusion schedule [may be adjusted] to mitigate that) and acneiform dermatitis. Soon data will be available from the MARIPOSA-2 study [55], which is a phase 3 study investigating lazertinib in combination with amivantamab, plus platinum-based chemotherapy versus chemotherapy alone, as a second- or third-line treatment in patients with *EGFR*-mutated advanced NSCLC that has progressed on or after osimertinib.

Additional MET inhibitors can be small molecules, [as] amivantamab is a bispecific antibody. An example of a small molecule MET inhibitor [is] savolitinib, which plus osimertinib showed encouraging activity in the phase 1 TATTON study in patients with *MET*-upregulated, *EGFR*-mutated advanced NSCLC after progression on osimertinib [56]. About 42% of those patients had previously received platinum-based chemotherapy as well [57]. In this study of savolitinib plus osimertinib, the ORR was 33% and the median PFS was 5.5 months. The incidence of grade 3 or higher TEAEs was 57% [56].

Another small molecule inhibitor of MET is tepotinib, and preliminary activity was observed with tepotinib plus osimertinib in patients with *EGFR*-mutated NSCLC, harboring *MET* amplifications after progression on frontline osimertinib in the INSIGHT 2 study [50].

JDP: Other than MET inhibitors and other targetable oncogenic drivers, what are we doing with therapies targeting *EGFR*-dependent resistance and how are we really approaching broader coverage for these patients?

SP: That is a great question, Jyoti. [Although]... a substantial proportion of our patients... have developed resistance to osimertinib, many of the mechanisms remain unclear [11]. In addition, many of these patients had mutations in their tumors that are currently not targetable with currently available treatments [6], and clinical trials are investigating novel therapeutic approaches for these patients.

One example of a novel therapeutic target for these patients includes HER3, which may provide benefit to a broader patient population, because HER3 is often commonly expressed in *EGFR*-mutated NSCLC and has been implicated in therapeutic resistance to EGFR-TKIs [58, 59]. One example of a HER3 antibody drug conjugate is patritumab deruxtecan (HER3-DXd), which in a phase 1 trial was associated with an ORR of 39% and a median PFS of over 8 months in patients with *EGFR*-mutated NSCLC who had previous treatment of EGFR-TKI and platinum-based chemotherapy [58]. Of note, clinical activity was observed across a broad range of HER3 membrane expression levels—meaning HER3 immunohistochemistry (IHC) did not predict which patients benefited from this therapeutic strategy of patritumab deruxtecan—as well as across diverse mechanisms of resistance after progression on EGFR small molecule inhibitor therapy [59]. Grade 3 or higher TEAEs occurred in almost two-thirds of patients, with the most common being thrombocytopenia. HER3-DXd is currently being investigated in the phase 2 HERTHENA-Lung01 trial as a third-line or later option in [patients with] advanced *EGFR*-mutated NSCLC who previously received treatment with one or more EGFR-TKIs and platinum-based chemotherapy [60]. Jyoti, can you comment on some of the other next-generation EGFR-TKIs currently under development?

JDP: Sure, this is certainly an exciting field, because there are a number of next-generation EGFR-TKIs that are in development to overcome this kind of resistance. While there are some candidates demonstrating encouraging antitumor activity, data are primarily preclinical or very early in clinical trials.

BLU-945 is one such drug that is active against T790M as well as C797S resistance mutations. The problem is that there might be less activity against exon 19 deletions [61]. The phase 1/2 trial, called the SYMPHONY trial, showed that BLU-945 showed some antitumor activity in patients who had previously treated lung cancer [and] had received at least one EGFR-TKI [62, 63]. Another such drug, BBT-176, demonstrated preclinical activity against NSCLC that [was] resistant to EGFR-TKIs [64]. Another class of next-generation EGFR-TKIs employs an allosteric binding mechanism to bypass mutations conferring resistance to osimertinib, such as C797S and L718Q [65]. JBJ-09-0632, an allosteric EGFR-TKI, is being investigated as a potential option to overcome acquired resistance to existing EGFR-TKIs.

SP: Thank you, Jyoti. These are indeed promising therapeutic candidates for treatments after osimertinib and platinum-based chemotherapy. To best make informed treatment decisions, molecular testing seems to be of paramount importance to assess tumor evolution over time, as well as a diagnosis to ensure patients get on appropriate therapy to begin with. Therefore, routine NGS is indicated for patients with NSCLC [6, 11]. Tissue [biopsies] may be indicated, in particular, if there are concerns around small cell transformation, and liquid biopsies are generally more available given that they can be done by blood draw as well. These can be complementary in informing the best management of patients with *EGFR*-mutated NSCLC.

One hurdle we often have in the clinic is an insufficient availability of biopsy material, especially on progression [66]. As patients progress through the treatment cycle, they are often less keen to have biopsies due to how they are feeling. However, in the setting of small cell

transformation, as Jyoti has mentioned, it is key to have that information as it affects our ability to optimally treat these patients. Also, agents with broader coverage, as [the previously] discussed HER3-DXd, may be preferred in the setting in which there is unavailable molecular information. However, the ability to use liquid biopsies to try and inform patients, at least for genomic resistance targets, may be an opportunity for some patients.

Finally, treatment tolerability and impact on quality of life are critical, as we are selecting further lines of treatment in the advanced setting.

Jyoti, what are your thoughts on how... we individualize and optimize therapeutic decision-making for our patients?

JDP: Certainly, diverse treatment strategies are necessary for the best chance of success in these patients. We talked a little bit about [the] cadence of progression as well as [the] pattern of progression, systemic versus oligoprogressive disease. Unfortunately, we can say that all patients, despite initial response to EGFR-TKIs, will have disease progression after osimertinib, and that platinum-based chemotherapy, although it improves outcomes, is still substandard. We are all looking for more new and effective and safe treatment options for this disease. I think factors that we have alluded to really include efficacy, as well as CNS activity and tolerability for our patients. Hopefully, we will be seeing some new and effective treatment options for our patients, based on readout from some key phase 2 and 3 trials that we should be seeing in the near future. Hopefully, this will guide us with some insights into future therapies for these patients, really optimizing their treatment journeys.

SP: Absolutely, and thank you, Jyoti! That was a great conversation, and I hope those of you listening have found our podcast useful.

JDP: Thanks so much, Sandip.

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