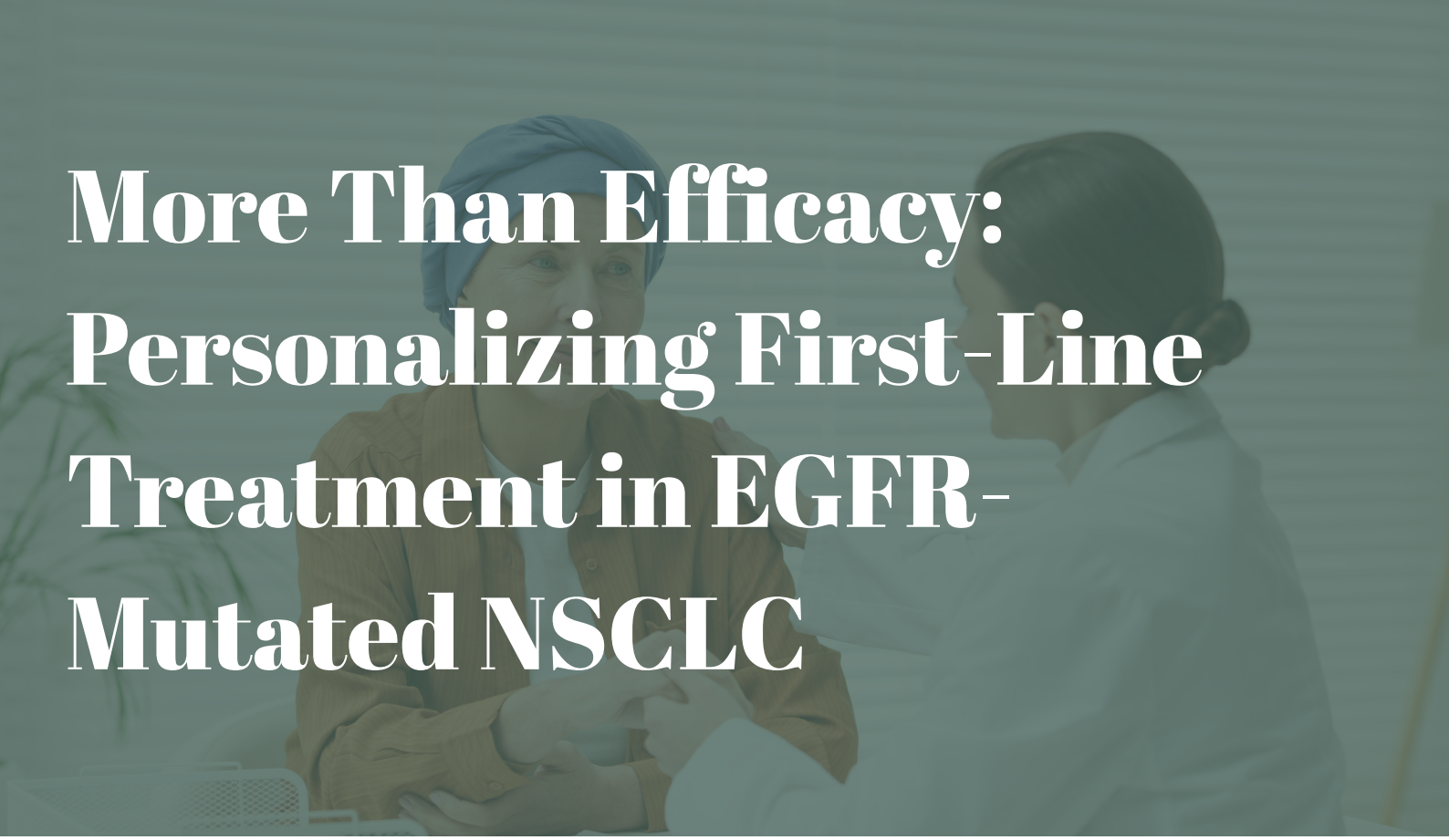

More Than Efficacy: Personalizing First-Line Treatment in EGFR-Mutated NSCLC

Learning Objectives

- Apply shared decision-making (SDM) principles to elicit patient goals and preferences when selecting first-line therapy for patients with metastatic EGFR-mutated NSCLC.
- Integrate clinical evidence with patient goals and values to personalize first-line treatment decisions for patients with metastatic EGFR-mutated NSCLC.

Target Audience

This activity is intended for oncologists, pathologists, nurse practitioners, physician assistants/associates, pharmacists, and other members of the multidisciplinary care team involved in the treatment of patients with metastatic EGFR-mutated NSCLC.

Activity Goal

This activity is designed to equip members of the multidisciplinary care team with practical tools for engaging in shared decision-making conversations with patients, and to illustrate how to personalize first-line treatment selection within the rapidly evolving treatment landscape of metastatic EGFR-mutated NSCLC.

Patient Presentation

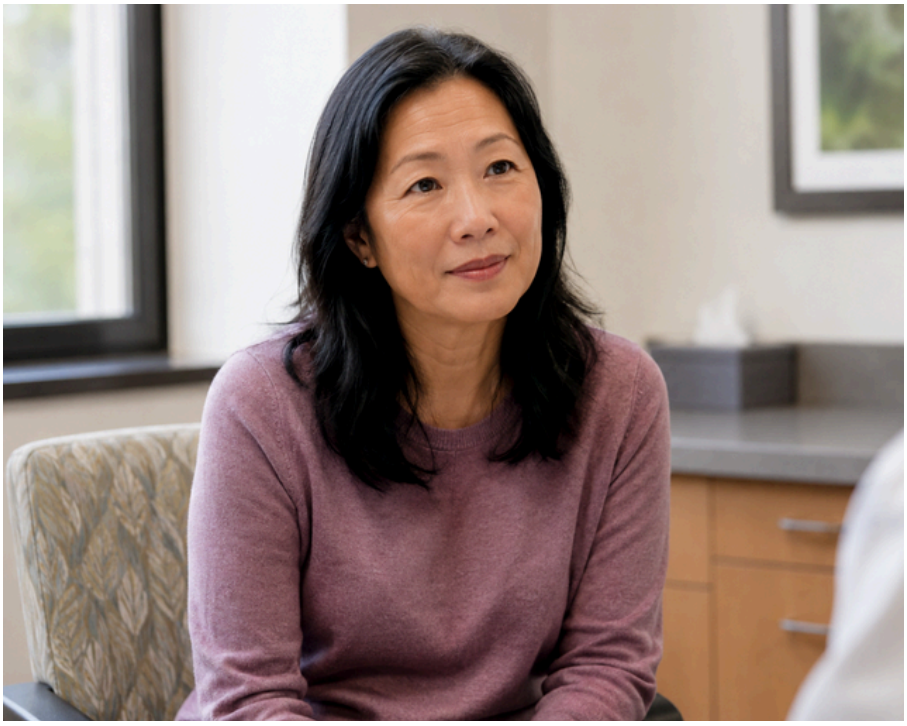

Figure 1. Representative image of Diane in an oncology consultation setting. This image was generated using OpenAI's ChatGPT image generation tool based on an author-developed prompt. The image does not depict a real patient.

Diane is a 60-year-old woman with newly diagnosed metastatic EGFR-mutated non-small cell lung cancer (NSCLC), meeting with her oncology care team for the first time to discuss treatment options.

Past Medical History

- Diagnosis: Metastatic NSCLC, adenocarcinoma histology
- Diagnostic history: Presented to primary care physician with persistent fatigue; chest imaging revealed a lung mass; biopsy confirmed adenocarcinoma; staging imaging confirmed metastatic disease
- Molecular profile: EGFR exon 19 deletion with a co-occurring TP53 mutation
- Smoking history: Never smoker
- ECOG performance status: 1

As you meet with her, Diane shares a little of her story: "*I'm still processing that I have cancer, but I'm here because I want to start treatment as soon as possible.*" She goes on to explain that she helps care for her grandchildren and wants to be there for them for as long as she can. "*I'm hoping we can work together to find the treatment that gives me the best shot at that.*"

Decision Point 1: Starting the Shared Decision-Making Conversation

You are preparing to discuss first-line treatment options with Diane. What is the most appropriate way to begin this conversation?

A. Present the available first-line treatment options along with their supporting clinical evidence.

B. Ask Diane about her treatment goals and what matters more to her as she starts first-line treatment.

C.Hand Diane a decision aid discussing first-line treatments and ask her to choose her preferred one.

Correct answer: B. Beginning the conversation by asking Diane about her goals, priorities, and what matters most to her reflects shared decision making (SDM) in practice: a two-way dialogue in which patients share their values and clinicians share their expertise, together shaping the decision. Putting Diane's goals first ensures the rest of the conversation can be tailored to what matters most to her.

Why A and C fall short: Option A moves directly into clinical data before Diane has had a chance to share her own perspective, which risks positioning her as a passive recipient of information rather than an active participant in the conversation. Option C shifts the full burden of the treatment decision onto Diane alone, which also departs from SDM that should involve both patient and clinician, not one party deciding independently of the other.

Clinical Insights: Shared Decision-Making in First-Line Treatment of EGFR-Mutated NSCLC

The identification of EGFR mutations in NSCLC transformed treatment for this subset of patients, whose disease is associated with poor outcomes with traditional chemotherapy and immunotherapy, thus laying the foundation for a personalized treatment approach.[1] This understanding drove the development of EGFR tyrosine kinase inhibitors (TKIs), which considerably improved outcomes and established targeted therapy as the recommended first-line approach for these patients.[1,2] Within this class, the third-generation TKI osimertinib became the standard of care for first-line metastatic EGFR-mutated NSCLC in 2018, after demonstrating improved overall survival compared with earlier-generation EGFR TKIs.[3] The treatment landscape expanded further in 2024, when the FDA approved two additional first-line regimens: osimertinib plus platinum-pemetrexed chemotherapy and amivantamab plus lazertinib. Both combinations improved outcomes relative to osimertinib monotherapy, though at the cost of increased toxicity.[4,5]

Current guidelines recommend personalizing first-line treatment for patients with metastatic EGFR-mutated NSCLC by weighing each patient's individual risk factors, tolerance for added toxicity, and overall clinical status.[6] Yet these clinical and disease-specific factors represent only half of a truly personalized treatment decision; the other half rests on the patient's own goals and preferences, incorporated through SDM.[1,2]

SDM is a patient-centered process in which clinicians engage patients and caregivers in discussions about diagnosis, prognosis, and treatment options, resulting in decisions that balance patient preferences and values with clinical expertise.[7] Evidence increasingly supports involving patients and caregivers in SDM to align treatment decisions with patient values.[7,8] SDM is especially relevant in settings of clinical equipoise, where multiple options are available, but none has been shown to offer superior outcomes — as is currently the case in metastatic EGFR-mutated NSCLC. In practice, SDM looks like an ongoing dialogue in which health care professionals share clinical information and patients share their goals and values, with both parties collaborating to reach a shared decision that reflects both aspects.[8]

Case Continuation: Patient Goals and Treatment Preferences

You start the conversation by asking Diane about her goals and hopes for treatment, explaining that this will help you work together to reach a shared decision on the treatment that is most appropriate for her.

She tells you:
“I want to live as much as possible. I have young grandchildren, and I want to see them grow up. I also want this fatigue, which I understand is caused by the cancer, to get better, so I can run my daily errands. Some of the doctors I’ve already seen mentioned that the treatments that might help me live longer also come with more side effects. I’d like to talk through that, but if you think it’s something we can manage, I’m open to the trade-off. The one thing that really worries me is that I’m the main caregiver for my grandchildren — they’re with me three days a week after daycare, and I don’t want to leave them hanging if I have to spend full days at the center getting treatment, especially since it’s far from home.”

Decision Point 2: Selecting an Individualized First-Line Treatment

You are preparing to discuss first-line treatment options with Diane. What is the most appropriate way to begin this conversation?

A. Osimertinib monotherapy

B. Osimertinib plus chemotherapy

C. Subcutaneous amivantamab plus lazertinib

Correct answer: C. Diane's TP53 co-mutation, combined with her expressed wish to pursue the treatment most likely to maximize survival outcomes and her favorable overall performance status, supports upfront treatment intensification rather than osimertinib monotherapy. Based on her clinical characteristics alone, there is no clear basis for preferring osimertinib plus chemotherapy or amivantamab plus lazertinib, since neither has been shown to be superior in a direct comparison. What differentiates them for Diane is her clearly stated preference to minimize time spent at the treatment center: osimertinib plus chemotherapy requires periodic intravenous infusion visits, while amivantamab plus lazertinib is available in a subcutaneous formulation with similar efficacy and substantially shorter administration time.

Why A and B fall short: Option A does not reflect Diane's risk profile or her stated wish to maximize survival even at the cost of added toxicity. Option B matches her risk profile and efficacy goal, but requires periodic intravenous infusion visits, which conflict with her specific concern about spending a long time at the center away from her grandchildren. The recommendation for amivantamab plus lazertinib is not universal; a patient with different priorities might reasonably choose osimertinib plus chemotherapy or osimertinib monotherapy instead. The decision reflects the integration of clinical evidence with this specific patient's circumstances and goals.

Clinical Insights: Evidence for First-Line Treatment Selection

Now that you have selected a treatment approach for Diane, let's review the clinical evidence behind the available first-line options to see how it supports that decision.

The three available first-line options for metastatic EGFR-mutated NSCLC are built on EGFR-targeted therapy, whether delivered as monotherapy (osimertinib) or in combination with other agents (osimertinib plus chemotherapy or amivantamab plus lazertinib). Each regimen demonstrated improved survival outcomes compared with a well-established comparator in a phase 3 trial (Table).[3–5] As a result, NCCN recommends all three as category 1 options, leaving the choice among them to clinical judgment and patient preference.[6]

Osimertinib monotherapy tends to be the preferred choice for patients without high-risk disease features, as well as those who are unable to tolerate or unwilling to accept the additional toxicity associated with combination therapy. In contrast, patients with CNS or visceral metastases, TP53 co-mutation, high overall disease burden, or non-clearing ctDNA are more likely to benefit from upfront treatment intensification with either of the combination regimens.[4,5] However, that added benefit comes at a cost: because both combinations add a second agent to the TKI backbone, they carry a greater toxicity burden than osimertinib monotherapy. The added chemotherapy brings effects such as myelosuppression and gastrointestinal toxicity,[4] while amivantamab brings toxicities such as infusion-related reactions, dermatologic effects, and venous thromboembolism.[5]

Table: Efficacy and patient groups most likely to benefit from each first-line regimen in metastatic EGFR-mutated NSCLC.

Regimen (Trial)	Efficacy	Patient Groups That Benefit Most
Osimertinib monotherapy (FLAURA)3	Improved OS (38.6 vs 31.8 mo) vs standard EGFR-TKI	Not specifically studied by subgroup; broadly appropriate for patients with
Osimertinib + chemotherapy (FLAURA2)4	Improved PFS (25.5 vs 16.7 mo) and OS (47.5 vs 37.6 mo) vs osimertinib alone	Patients with CNS involvement, TP53 co-mutation, or high disease burden
Amivantamab + lazertinib (MARIPOSA)5	Improved OS (3-year OS 60% vs 51%) vs osimertinib alone	Patients with TP53 co-mutation, liver or brain metastases, or non-clearing ctDNA

The three regimens also differ in mode of administration. Osimertinib and lazertinib are both oral medications taken once daily at home.[9,10] The chemotherapy component in the osimertinib + chemotherapy regimen requires patients to present to the clinic for intravenous infusions every 3 weeks.[11] Pemetrexed infuses over about 10 minutes and carboplatin over 15 minutes or longer, with no hydration required; cisplatin, however, requires pre- and post-treatment intravenous hydration, extending the visit further when it is the platinum agent used.[12,13,14]

Amivantamab plus lazertinib was originally approved for first-line use with amivantamab administered intravenously, a regimen requiring multi-hour infusion visits.[15] In December 2025, the FDA approved a subcutaneous formulation of amivantamab for all previously approved indications, including first-line treatment, based on data from the PALOMA-3 trial showing the subcutaneous formulation to be non-inferior to the intravenous formulation in pharmacokinetics and response rate, while reducing administration time to 5 to 7 minutes and lowering the rate of infusion-related reactions from approximately 66% to 13%.[16,17] In February 2026, the FDA approved a further simplified dosing schedule allowing patients to transition to subcutaneous dosing every 4 weeks after an initial 4-week weekly induction period, replacing the prior every-2-week maintenance schedule and further reducing time spent at infusion centers.[18] For a patient like Diane, whose clearly stated priority is minimizing time away from her grandchildren, this shorter and less frequent administration schedule directly supports the treatment goal she identified earlier in the conversation.

Case Resolution

Having elicited Diane's goals and weighed them against the clinical evidence, you and Diane agree to begin treatment with subcutaneous amivantamab plus lazertinib.

You review how treatment will get started, including the initial dosing schedule, and then connect her with other members of the multidisciplinary care team to discuss adverse event management and what to watch for as she begins therapy — including reporting whether her fatigue improves, and staying alert to potential toxicities such as rash or other side effects. Before she leaves, she tells you:

"Thank you for really listening to what matters to me. I feel good about our decision.I hope it'll get me the outcome I want without taking me away from my grandkids. I'm looking forward to starting treatment."

The conversation depicted in this case is only the beginning. Selecting a first-line regimen is one step in the ongoing management of Diane's cancer, and SDM — with her goals and preferences at the center — will continue to guide her care as treatment unfolds and new considerations arise.

This case illustrates how starting a treatment conversation by eliciting a patient's goals and values lays the foundation for SDM. It also shows how integrating clinical evidence with a patient's individual circumstances and preferences can guide selection among multiple evidence-based first-line regimens for metastatic EGFR-mutated NSCLC, resulting in a treatment plan that reflects both what the evidence supports and what matters most to the patient. Individualizing treatment is not a single decision, but an ongoing process — the choice of a first-line regimen is only the first of many decisions patients and clinicians will navigate together over the course of care. As you return to your own practice, consider how you might continue to incorporate your patients' goals and preferences into the conversation, not only when selecting an initial treatment, but throughout their care as new decisions arise.

About this Sample:

This patient case was developed as a practice exercise for the Write CME Summer Portfolio Camp, not as client-commissioned work. I chose the EGFR-mutated NSCLC space to demonstrate how I approach shared decision-making and evidence integration in an interactive case format. It's intentionally scaled down from a full-length patient case to keep the sample focused and reviewable — a complete case would include additional decision points and depth.

AI Disclosure Statement:

Generative AI tools were used during the development of this educational case. During July 2026. the medical writer used Claude Sonnet 4.6/5 (Anthropic) and ChatGPT 5.5 (OpenAI), both accessed via paid platforms. These tools supported activities such as editing bulleted content for narrative flow, formatting and verifying the reference list against primary sources, summarizing guideline and evidence support for shared decision-making, and generating and refining a representative patient image.

All AI-assisted content was reviewed by the medical writer, including verification of AI-identified sources, review of AI-generated statements for accuracy, and iterative editing to ensure appropriate tone and scientific integrity. Only publicly available information and materials developed by the medical writer were used as inputs to any AI tool; no proprietary or third-party client materials were uploaded.

The medical writer assumes full responsibility for the accuracy, scientific balance, and integrity of the final content. This statement is provided in compliance with ACCME recommendations for disclosure of AI usage in accredited continuing education.

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