Post-progression and Safety Outcomes With First-line Amivantamab Plus Lazertinib Versus Osimertinib in Patients With Advanced Non-small Cell Lung Cancer With Common *EGFR* Mutations: Implications for Best Management Practices

Sarah Smith[1], Alexander I Spira[1], Danny Nguyen[2], Seema Sethi[3], Shirish Gadgeel[4]

[1]Virginia Cancer Specialists/US Oncology Research, Fairfax, VA, USA; [2]City of Hope, Long Beach, CA, USA; [3]Janssen Research & Development, LLC, Spring House, PA, USA; [4]Henry Ford Cancer Institute, Detroit, MI, USA.

Key Takeaways

Amivantamab plus lazertinib treatment provided favorable post-progression outcomes, thus representing a viable first-line treatment option for patients with common epidermal growth factor receptor–activating non-small cell lung cancer (*cEGFR* NSCLC)

Nurses and other health care professionals (HCPs) play a vital role in actively managing early adverse events (AEs) associated with EGFR inhibition and informing patients about the potential of disease progression and AEs associated with post-progression treatment intensification

– Through patient support and education, nurses and HCPs can facilitate treatment adherence and persistence to promote optimal disease outcomes, even in the post-progression setting

Conclusions

In the phase 3 MARIPOSA study, patients with *cEGFR* NSCLC receiving amivantamab plus lazertinib remained on treatment longer and exhibited improved post-progression outcomes (ie, time to discontinuation [TTD] and time to subsequent treatment [TTST]) compared with patients receiving osimertinib treatment

Potential reasons for the lower probability of progression observed with amivantamab plus lazertinib may include the ability of this combination to more potently overcome resistance mechanisms, such as mesenchymal epithelial transition (*MET*) amplification and secondary *EGFR* mutations, compared with each treatment alone

The onset of key AEs, such as infusion-related reactions (IRRs), rash, and paronychia, usually occurred within the first 4 months from treatment initiation, with fewer AEs occurring after extended treatment time, highlighting the importance of proactive measures and early intervention

Incorporating nursing and HCP perspectives surrounding optimal AE management and improved patient experience can impact treatment adherence, which is key for ensuring improved outcomes, not only during first-line treatment, but also in the post-progression setting, where intensification-associated AEs can be a challenge for patients

Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing was provided by Holly Clarke, PhD (Lumanity Communications Inc.), and was funded by Janssen Scientific Affairs, LLC. The authors would like to acknowledge Mary Kate Weber and Ashley O'Donnell for contributions for best practices and clinical recommendations.

Disclosures

S Smith: Nothing to declare. **AIS:** Leadership for NEXT Oncology Virginia; stock and other ownership interests from Eli Lilly; honoraria from CytomX Therapeutics, AstraZeneca/MedImmune, Merck, Takeda, Amgen, Janssen Oncology, Novartis, Bristol Myers Squibb, and Bayer; consulting or advisory role for Incyte, Amgen, Novartis, Mirati Therapeutics, Gritstone bio, Jazz Pharmaceuticals, Takeda, Janssen Research & Development, LLC, Mersana, Daiichi Sankyo/AstraZeneca, Regeneron, Eli Lilly, Black Diamond Therapeutics, Sanofi, Array BioPharma, AstraZeneca/MedImmune, Merck, Bristol Myers Squibb, and Blueprint Medicines; and research funding from LAM Therapeutics, Regeneron, AstraZeneca, Boehringer Ingelheim, Astellas Pharma, MedImmune, Novartis, Incyte, AbbVie, Ignyta, Takeda, MacroGenics, CytomX Therapeutics, Astex Pharmaceuticals, Bristol Myers Squibb, Loxo, Arch Therapeutics, Gritstone bio, Plexxikon, Amgen, Daiichi Sankyo, ADCT, Janssen Oncology, Mirati Therapeutics, Rubius, Synthekine, Mersana, Blueprint Medicines, Alkermes, Revolution Medicines, Medikine, Black Diamond Therapeutics, BluPrint Oncology, Nalo Therapeutics, Scorpion Therapeutics, and ArriVent Biopharma. **DN:** Consulting fee or honorarium from Janssen; and provision of writing assistance from Takeda, Novartis, and Seagen. **S Sethi:** Current employment with and stock or stock options from Johnson & Johnson. **SG:** Consulting fee or honorarium from AbbVie, Daiichi Sankyo, AstraZeneca, Blueprint Medicines, Pfizer, Merck, Genentech/Roche, Regeneron, Bayer, Boehringer Ingelheim, Eisai, Mirati Therapeutics, and Takeda; research funding from AbbVie, Daiichi Sankyo, AstraZeneca, Blueprint Medicines, Pfizer, Merck, Genentech/Roche, Regeneron, Bayer, Boehringer Ingelheim, Mirati Therapeutics, Takeda, Amgen, D3 Bio, DeBio, and Genmab; travel support from Merck and Mirati Therapeutics; and advising or review activity fees from AstraZeneca.

Background

- Patients with advanced *cEGFR* NSCLC have high mortality rates and limited treatment options[1]
- Many patients receiving first-line treatment, such as osimertinib (an EGFR–tyrosine kinase inhibitor [TKI]),[1,2] experience disease progression after 9 to 15 months,[3] possibly due to developing resistance
  - Secondary *EGFR* and *MET* alterations account for 25% to 50% of tumor resistance,[3,4] among other unknown mechanisms[3]
- Amivantamab is an EGFR-MET receptor–directed bispecific antibody approved by the US Food and Drug Administration (FDA) for the treatment of locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations as a first-line treatment in combination with platinum chemotherapy, as a second-line treatment in combination with platinum chemotherapy after progression on osimertinib, or as a monotherapy after chemotherapy progression[5]
- Amivantamab was also recently approved by the FDA in combination with lazertinib, a third-generation, brain penetrant, oral EGFR-TKI,[6] as a first-line treatment for locally advanced or metastatic *cEGFR* NSCLC[5]
- In the phase 3 MARIPOSA study (ClinicalTrials.gov Identifier: NCT04487080), amivantamab plus lazertinib in first-line *cEGFR* NSCLC significantly reduced the risk for disease progression/death and extracranial progression and improved median progression-free survival (PFS) and extracranial PFS by 7.1 and 9.0 months, respectively, compared with osimertinib[7]
- IRRs and dermatologic AEs (eg, rash and paronychia) often occur soon after EGFR inhibition treatment is initiated and can negatively impact the patient experience, resulting in poor adherence and treatment discontinuation[8] and potentially worse outcomes
- Furthermore, some patients' cancer will still progress on amivantamab plus lazertinib and will require treatment intensification, which results in more AEs
- Nurses and other HCPs play a crucial role in the proactive management of early AEs, provide patient education on the possibility of progression and the risk of additional intensification-related AEs, and emphasize the benefits of first-line treatment adherence and persistence

Objectives

- Here, we present additional post-progression efficacy and safety outcomes of amivantamab plus lazertinib versus osimertinib in patients with advanced *cEGFR* NSCLC from the MARIPOSA study
- Furthermore, we provide a clinical perspective on the key roles that nurses play in educating patients on the possibility of disease progression, additional treatment options, mitigation and management of AEs, and optimization of treatment adherence and persistence

Methods

Study design

- The complete study design has been previously reported[7]
- Patients were randomized in a 2:2:1 ratio to receive 28-day cycles of either (1) amivantamab plus lazertinib, (2) osimertinib, or (3) lazertinib alone
  - The third arm (lazertinib alone) was included to assess the contribution of each treatment component; results from this arm are not reported here
- Post-progression outcomes reported here include the following:
  - TTD, defined as the time from randomization to discontinuation of the first treatment for any reason
  - TTST, defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy following study treatment discontinuation or death, whichever occurred first
  - Treatment beyond progression, defined as the duration from the date of disease progression to the date of the last dose of the study drug
    - Patients still deriving clinical benefit, as per the investigator, could continue treatment with amivantamab plus lazertinib or osimertinib
  - Subsequent therapy and subsequent therapy class
  - Safety (first onset of key AEs, such as rash, paronychia, dermatitis acneiform, stomatitis, venous thromboembolism, peripheral edema, pruritus, and fatigue)
- The full analysis population included all randomized patients, and the safety population included all randomized patients who received ≥1 dose of study treatment
- Time-to-event data were analyzed using Kaplan-Meier estimates, with 95% confidence intervals provided

Nursing perspectives

- Nursing implications and best practices for disease progression and AE management were based upon the authors' clinical experience in the trial and beyond, along with qualitative interview responses from 2 clinical oncology nurses

Results

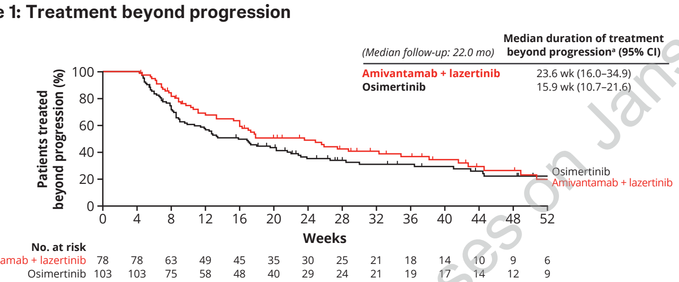
Patients

- Of the 1074 patients enrolled in MARIPOSA, 429 patients each were randomized to the amivantamab plus lazertinib and osimertinib arms
  - 421 and 428 patients were included in the safety analysis set for the amivantamab plus lazertinib and osimertinib arms, respectively
  - Results from patients randomized to the lazertinib alone arm (n = 216) are not analyzed here

Post-progression outcomes

- After a median follow-up of 22.0 months, 147/421 (35%) patients in the amivantamab plus lazertinib arm versus 203/428 (47%) patients in the osimertinib arm had progressive disease
- Among patients with progressive disease, 53% (n = 78) and 51% (n = 103) in the amivantamab plus lazertinib and osimertinib arms, respectively, continued treatment beyond first progression (**Figure 1**)
  - The median duration of treatment beyond progression was 23.6 weeks in the amivantamab plus lazertinib arm versus 15.9 weeks in the osimertinib arm

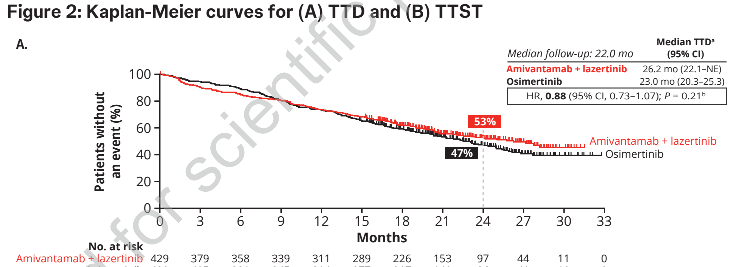
Figure 1: Treatment beyond progression

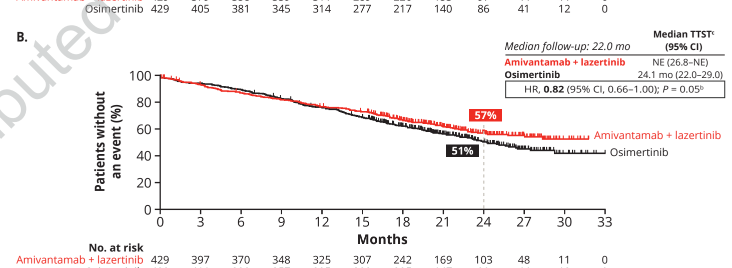


[a]Duration of study treatment beyond disease progression is defined as the duration from the date of disease progression to the date of the last dose of the study drug. Only patients who continued any study treatment for >28 days beyond disease progression are included.
CI, confidence interval.

- TTD and TTST were numerically longer in patients receiving amivantamab plus lazertinib (26.2 months and not estimable, respectively) versus those receiving osimertinib (23.0 and 24.1 months, respectively; **Figure 2**)

Figure 2: Kaplan-Meier curves for (A) TTD and (B) TTST

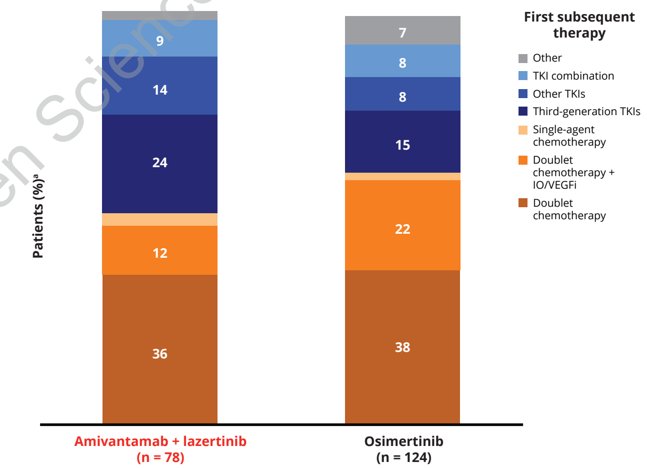




Percentages indicate rates of patients who did not discontinue or did not receive subsequent treatment, respectively, at 24 months.
[a]TTD was defined as the time from randomization to discontinuation of the first treatment for any reason.
[b]Nominal *P* value; endpoint is not part of the defined hierarchical hypothesis testing.
[c]TTST was defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy following study treatment discontinuation or death, whichever occurred first.
CI, confidence interval; HR, hazard ratio; NE, not estimable; TTD, time to treatment discontinuation; TTST, time to subsequent therapy.

- Fewer patients discontinued study treatment when receiving amivantamab plus lazertinib (116/421 [28%]) versus those who received osimertinib (171/428 [40%])
  - 78/116 (67%) and 124/171 (73%) patients, respectively, received first subsequent therapy (**Figure 3**)
  - The most common subsequent therapy in both arms was doublet chemotherapy

Figure 3: Most common first subsequent therapy classes

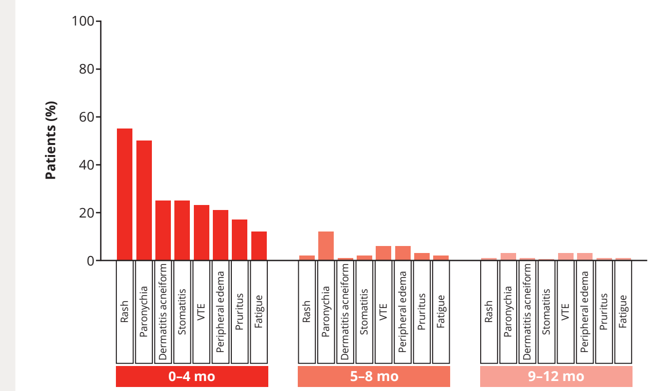


[a]Percentage calculated using the number of patients who discontinued study treatment as the denominator.
IO, immuno-oncology; TKI, tyrosine kinase inhibitor; VEGFi, vascular endothelial growth factor inhibitor.

Safety

- The median duration of exposure was 18.5 months for patients receiving amivantamab plus lazertinib
  - Key AEs occurred within the first 4 months from treatment initiation, and late onset was uncommon (**Figure 4**)
- Few patients in the amivantamab plus lazertinib arm were prescribed antibiotics at study initiation for rash management (21%) or initiated the study on anticoagulation treatment (5%)

Figure 4: Frequency and onset of key AEs in the amivantamab plus lazertinib arm

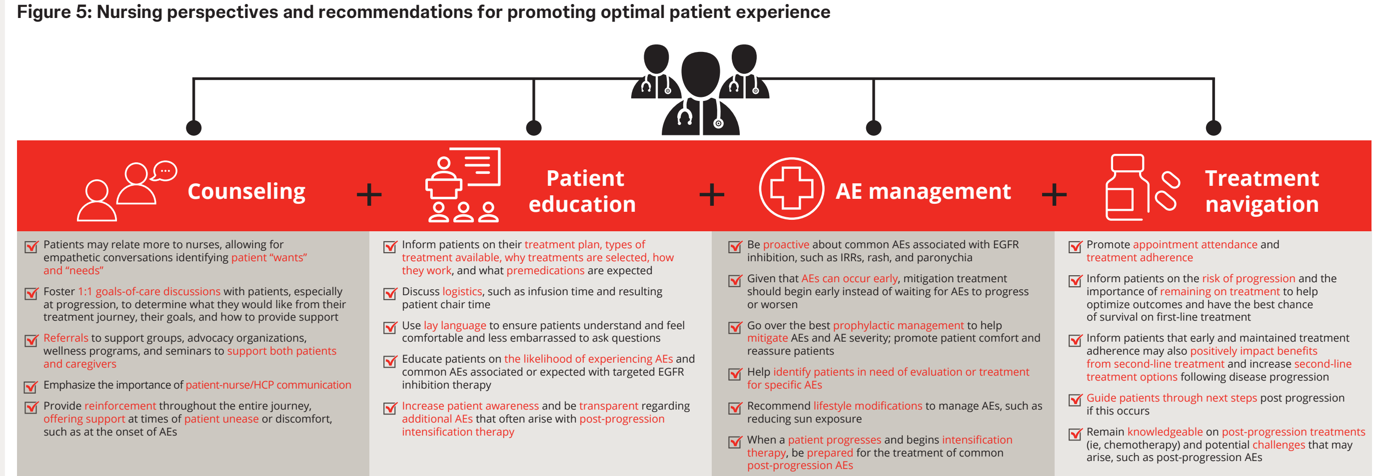


AE, adverse event; VTE, venous thromboembolism.

Nursing perspectives

- Nurses and other HCPs play a crucial role throughout the patient journey and offer comprehensive and multidisciplinary care to optimize the patient experience (**Figure 5**)
- Nurses and other HCPs should discuss and establish treatment goals with their patients, educate them on available treatment options, inform them on AEs and how they will be managed, and highlight the importance of treatment adherence and persistence to promote improved outcomes
- Importantly, all HCPs understand the possibility of progression and can thus prepare patients for that outcome and offer support as they initiate post-progression intensification treatment, especially with regard to managing the highly probable intensification-related AEs

Figure 5: Nursing perspectives and recommendations for promoting optimal patient experience



AE, adverse event; EGFR, epidermal growth factor receptor; HCP, health care professional; IRR, infusion-related reaction.

References

1. Park K, et al. *J Clin Oncol*. 2021;39(30):3391–3402. 2. Fu K, et al. *J Hematol Oncol*. 2022;15(1):173. 3. Leonetti A, et al. *Br J Cancer*. 2019;121(9):725–737. 4. Ramalingam SS, et al. *Ann Oncol*. 2018;29(suppl 8):VIII740. Abstract LBA50. 5. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [prescribing information]. Janssen Biotech, Inc.; 2024. 6. Dhillon S. *Drugs*. 2021;81(9):1107–1113. 7. Cho BC, et al. *N Engl J Med*. 2024; doi: 10.1056/NEJMoa2403614. 8. O'Connell NS, et al. *J Clin Oncol*. 2024;42(3):266–272.

Lung Cancer

Presented at the Academy of Oncology Nurse & Patient Navigators (AONN) Annual Conference; November 5–7, 2024; Las Vegas, NV, USA