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Modeled Cost of Severe Adverse Events of First Line Amivantamab Plus Lazertinib or Osimertinib Plus Chemotherapy in Patients with Treatment Naïve EGFR-Mutated Advanced NSCLC

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Key Takeaways

In this descriptive cross-trial cost analysis, combined grade ≥3 adverse event (AE) management and prophylaxis costs were lower with first-line subcutaneous (SC) Q4W amivantamab plus lazertinib (A+L) than with osimertinib plus platinum-based chemotherapy (OPC) from both US commercial and Medicare payer perspectives.

Grade ≥3 AE profiles differed between regimens: rash was the most frequent event with SC amivantamab plus lazertinib, whereas hematologic events (anemia, neutropenia, and thrombocytopenia) were most frequent with osimertinib plus platinum-based chemotherapy.

Conclusions

Under the assumptions of this descriptive cross-trial cost analysis, combined grade ≥3 AE management and prophylaxis costs were estimated to be lower with 1L SC Q4W A+L than with OPC from both US Commercial and Medicare Advantage payer perspectives.

Differences in severe AE profiles, associated management costs, and prophylaxis requirements should be considered in shared clinical decision-making by patients and healthcare providers as well as in assessments of overall clinical and economic value by US healthcare decision makers with respect to 1L therapies for EGFR-mutated advanced NSCLC.

Future studies with exposure-adjusted or patient-level comparative methods are warranted to assess relative AE profiles and validate the modeled resource utilization and costs using real-world data, including recurrent AEs, lower-grade AEs, and broader total cost-of-care outcomes.

Base Case Modeled Difference

Combined grade ≥3 AE management and prophylaxis costs were $8,961 lower per patient from the Commercial perspective and $4,179 lower per patient from the Medicare Advantage perspective for subcutaneous Q4W amivantamab + lazertinib versus osimertinib plus platinum-based chemotherapy.

Abbreviations

1L: first-line; A+L: amivantamab + lazertinib; AE: adverse event; ALT: alanine aminotransferase; AST: aspartate aminotransferase; C1D1: cycle 1, day 1; CCSR: Clinical Classification Software Refined; CMS: Centers for Medicare and Medicaid Services; CPT: Current Procedural Terminology; DRG: diagnosis-related group; EGFR: epidermal growth factor receptor; HCUP NIS: Healthcare Cost and Utilization Project National Inpatient Sample; IV: intravenous; NCCN: National Comprehensive Cancer Network; NSCLC: non-small cell lung cancer; OPC: osimertinib + platinum-based chemotherapy; PS: Prospective Payment System; Q4W: every 4 weeks; SC: subcutaneous; US: United States; USD: US dollars; VTE: venous thromboembolism

Disclosures

Alexander Spira reports research/institutional support and consulting relationships with multiple biopharmaceutical companies, including Johnson & Johnson and other oncology drug manufacturers; serves in a leadership role with Virginia Cancer Specialists Research Institute. Robert Musci is an employee of Evidera, Inc., a company that has provided paid services to Johnson & Johnson, which funded the development and conduct of this analysis. At the time this work was conducted, Anjali Donnelly was a student intern at Virginia Cancer Specialists Research Institute and a student at the University of Michigan.

Introduction

- EGFR-targeted therapies have improved clinical outcomes in treatment-naïve EGFR-mutated advanced NSCLC, and first-line (1L) combination regimens including amivantamab + lazertinib (A+L) and osimertinib + platinum-based chemotherapy (OPC) have demonstrated improved efficacy relative to prior standard of care.[1,2]
- Treatment-related toxicities may affect clinical outcomes and healthcare resource use. Severe (grade ≥3) adverse events (AEs) are particularly relevant because of their clinical impact and disproportionate economic burden on healthcare payers.[3]
- Prophylactic regimens use preemptive supportive care to prevent or mitigate treatment-related toxicities and may shift resource use earlier in the treatment course, with the goal of reducing AE risk and severity, preserving treatment continuity, and minimizing downstream healthcare utilization.[3-6]
- Building on a previously published AE-cost framework,[3] this analysis focuses on subcutaneous every four weeks (SC Q4W) A+L from the COPERNICUS trial[7] versus OPC from the FLAURA2 trial[2] with updated 2026 cost inputs, annualized prophylaxis costs, and published prophylaxis cost estimates for OPC.[8]

Objective

- To estimate costs of grade ≥3 AE management and prophylaxis for 1L SC Q4W A+L and OPC from US Commercial and Medicare Advantage perspectives.

Methods

- A descriptive cost model compared cumulative grade ≥3 AE management costs and prophylaxis costs for SC Q4W A+L and OPC from US Commercial and Medicare Advantage payer perspectives.
- Grade ≥3 AE incidence inputs were obtained from the initial COPERNICUS phase II Cohort 1 report for SC Q4W A+L (N=235)[7] and FLAURA2 phase III for OPC (N=279).[2] AEs occurring in ≥5% of patients in either cohort or considered clinically important based on events of interest for NCCN Category 1-recommended treatment options were included.[9]
- For each AE, expected per-patient management cost was calculated as cumulative incidence interacted with a one-time unit management cost; costs were summed across AEs. Consistent with the underlying framework, events were modeled as independent/nonrecurrent for costing purposes.
- Specialist-visit management was assigned to ALT/AST increases, dermatologic events, fatigue, and hypoalbuminemia based on clinical expert input. Inpatient management was assigned to all remaining AEs captured in the analysis.
- Commercial specialist-visit costs were from the 2026 Physician Fee Reference;[10] inpatient costs used the 2023 HCUP NIS[11] and were inflated to 2026 USD.
- Medicare Advantage specialist-visit and inpatient costs used the CMS 2026 Physician Fee Schedule[12] and 2026 Acute Inpatient PPS,[13] respectively.
- For SC Q4W A+L, prophylaxis costs included dermatologic prophylaxis, venous thromboembolism (VTE) prophylaxis, and administration-/infusion-related premedication. OPC prophylaxis costs were based on a published 2025 cost analysis.[8]
- An expanded-prophylaxis scenario analysis retained dermatologic prophylaxis, allowed 10% SC enoxaparin use for VTE prophylaxis (45% oral apixaban/45% oral rivaroxaban/10% SC enoxaparin), and added subsequent administration-/infusion-related premedication consistent with the amivantamab US prescribing information.[14]
- No statistical or exposure-duration adjustments were applied for differences between cohorts. AE incidence for SC Q4W A+L reflects 4.9 months of available COPERNICUS follow-up,[7] compared with 19.5 months for OPC in FLAURA2;[2] prophylaxis costs were annualized for both regimens.

Results

- Grade ≥3 AE profiles differed between the regimens. Rash was the most frequent AE with SC Q4W A+L (12.3%), whereas anemia (20.0%), neutropenia (13.4%), and thrombocytopenia (6.9%) were the most frequent events with OPC.[2,7]
- Modeled AE management costs alone were $966 for SC Q4W A+L versus $8,934 for OPC under the Commercial perspective and $469 versus $4,247 under Medicare Advantage.
- For OPC, anemia, neutropenia, and thrombocytopenia were the dominant AE cost drivers across payer perspectives. SC Q4W A+L costs were more distributed, with VTE, anemia, diarrhea, and dyspnea among the largest contributors.
- Commercial: combined AE management and prophylaxis costs were $1,633 per patient for SC Q4W A+L versus $10,594 for OPC, a modeled difference of $8,961.
- Medicare Advantage: combined AE management and prophylaxis costs were $1,136 for SC Q4W A+L versus $5,315, yielding a modeled difference of $4,179.
- Across the base case and expanded-prophylaxis scenario, combined costs for SC Q4W A+L ranged from $1,633-$1,896 (Commercial) and $1,136-$1,202 (Medicare Advantage), versus $10,594 and $5,315, respectively, for OPC. Modeled cost differences therefore ranged from $8,698-$8,961 and $4,113-$4,179, respectively. Findings remained directionally consistent with the prior published modelling framework despite updated incidence data and 2026 cost inputs.[3]

Table 1: Incidence and Costs of Grade ≥3 AEs

Event	Costs				Incidence	
	Commercial		Medicare Advantage		SC Q4W A+L	OPC
	CPT/CCSR	Event Cost	CPT/DRG	Event Cost	(N=235)	(N=279)
ALT increased*	CPT 99214	$255	CPT 99214	$136	4.7%	1.0%
Anemia	BLD003	$19,812	811-812	$8,289	1.3%	20.0%
AST increased*	CPT 99214	$255	CPT 99214	$136	3.0%	0.4%
Dermatitis acneiform*	CPT 99214	$255	CPT 99214	$136	3.8%	0.0%
Diarrhea*	SYM006	$11,124	391-392	$6,684	1.7%	3.0%
Dyspnea*	SYM013	$13,382	204	$5,875	0.9%	0.0%
Fatigue*	CPT 99214	$255	CPT 99214	$136	3.8%	3.0%
Hypoalbuminemia*	CPT 99214	$255	CPT 99214	$136	4.3%	0.0%
Neutropenia	BLD007	$22,758	808-810	$12,047	0.0%	13.4%
Paronychia*	CPT 99214	$255	CPT 99214	$136	2.6%	1.0%
Rash	CPT 99214	$255	CPT 99214	$136	12.3%	0.4%
Stomatitis*	CPT 99214	$255	CPT 99214	$136	3.0%	0.4%
Thrombocytopenia	BLD006	$22,793	813	$11,099	0.0%	6.9%
VTE*	CIR013, CIR033	$18,465	175-176; 299-301	$8,748	1.7%	0.0%
Total Management Costs (Commercial)					**$966**	**$8,934**
Total Management Costs (Medicare Advantage)					**$469**	**$4,247**

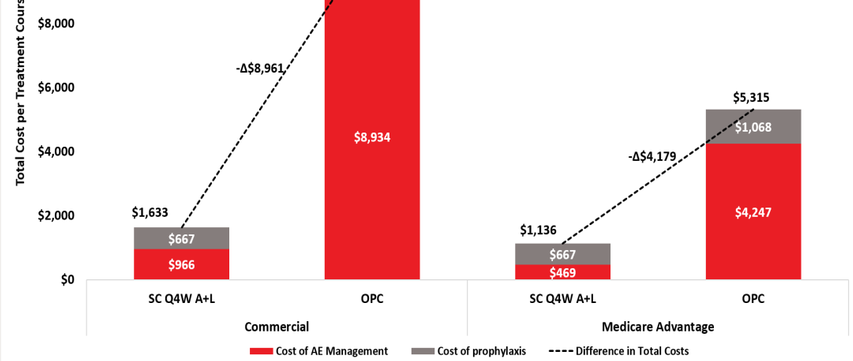
Grade ≥3 AEs with incidence <5% in either treatment arm were included if they met at least one of the following criteria: (1) incidence in ≥5% in any comparator regimen from NCCN Category 1-recommended therapies,[8] or (2) deemed clinically significant (e.g., VTE).
Note: Costs here reflect 2026 USD.

Table 2: SC Q4W A+L prophylaxis costs and assumptions

Prophylaxis component	Base case cost (annualized $)	Expanded scenario cost (annualized $)	Assumptions
Rash	$232	$232	Weeks 1-12 minocycline; week 13+ clindamycin lotion; chlorhexidine solution throughout
VTE	$432	$458 Commercial / $434 Medicare Advantage	Base: oral apixaban / rivaroxaban first 4 months; Scenario: 45% oral apixaban, 45% oral rivaroxaban, 10% SC enoxaparin
Administration-/infusion-related reaction	$3	$241 Commercial / $67 Medicare Advantage	Base: SKIPPirr-aligned[6] oral dexamethasone before C1D1 only; Scenario: USPI-aligned[13] base case + IV dexamethasone for first two doses + oral diphenhydramine / acetaminophen throughout
Total SC Q4W A+L Prophylaxis Costs	**$667**	**$930 Commercial / $733 Medicare Advantage**	**Prophylaxis costs annualized in both scenarios**

Note: Costs here reflect 2026 USD. Acquisition cost data for prophylaxis under the Commercial perspective were informed by publicly available wholesale acquisition cost data while the Medicare Advantage perspective was informed by CMS actual sales price payment limit data (where available). For treatments in which actual sales price payment limit data were unavailable, the wholesale acquisition cost data was applied as a proxy.

Figure 1: Total cost of AE management and prophylaxis among patients receiving SC Q4W A+L and OPC (base case)



Note: dotted lines and delta estimates refer to the difference in total AE management and prophylaxis costs for SC Q4W A+L versus OPC.

Limitations

- This analysis was a descriptive, naïve cross-trial comparison and did not adjust for baseline differences, treatment exposure, or follow-up duration.
- AE incidence for SC Q4W A+L reflects 4.9 months of available COPERNICUS follow-up versus 19.5 months for OPC in FLAURA2; no statistical or exposure-duration adjustment was applied.
- AE management was modeled using simplified one-time site-of-care assumptions that may not capture recurrent events, repeated visits, partial hospitalizations, or heterogeneity in real-world management.
- The analysis included only severe (grade ≥3) AEs and therefore does not capture the broader economic burden of lower-grade toxicities.
- Prophylaxis costs were annualized for both regimens, whereas AE incidence reflected cumulative events over the available trial follow-up. OPC prophylaxis costs were sourced from a separate published cost analysis.[8]

References

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