

Therapy for Stage IV Non–Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline, 2026.3.1

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DOI <https://doi.org/10.1200/JCO-26-00842>

ABSTRACT

Living guidelines are developed for selected topic areas with rapidly evolving evidence that drives frequent change in recommended clinical practice. Living guidelines are updated on a regular schedule by a standing expert panel that systematically reviews the health literature on a continuous basis, as described in the [ASCO Guidelines Methodology Manual](#). ASCO Living Guidelines follow the [ASCO Conflict of Interest Policy Implementation for Clinical Practice Guidelines](#). Living Guidelines and updates are not intended to substitute for independent professional judgment of the treating clinician and do not account for individual variation among patients. See appendix for disclaimers and other important information ([Appendix 1](#) and [Appendix 2](#), online only). Updates are published regularly and can be found at <https://ascopubs.org/nsclc-non-da-living-guideline>.

ACCOMPANYING CONTENT

 Article, March 1, 2026 issue on p. **e56**

 Appendix

 Data Supplement

Accepted April 14, 2026

Published May 26, 2026

Evidence Based Medicine

Committee approval:

March 31, 2026

J Clin Oncol 44:e101-e112

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BACKGROUND

In 2022, ASCO launched living clinical practice guidelines for systemic therapy for patients with stage IV non–small cell lung cancer (NSCLC) with and without driver alterations^{1,2} and both have been updated recently.^{3,4} Based on routine literature searches (up to January 21, 2026), this version ([Appendix 3](#)) of the stage IV NSCLC without driver alterations living guideline reviews evidence and provides updated recommendations on new therapeutics. Refer to [Appendix Table A1](#) (online only) for the full list of recommendations, and [Appendix Figure A1](#) for the updated algorithm. The ASCO Guidelines Methodology Manual (available at <https://www.asco.org/practice-patients/guidelines/guideline-methodology>) and Supplement provide additional information.

RESULTS

The guideline Expert Panel ([Appendix Table A2](#)) reviewed new evidence from three studies^{5–7} that met the systematic

review inclusion criteria ([Appendix Table A3](#) and [A4](#)) and reviewed and approved the updated recommendations. Evidence supporting unchanged recommendations is reviewed in previous publications of this guideline.⁴

UPDATED RECOMMENDATIONS

First-Line Treatment Options for Patients With Good Performance Status, Nonsquamous Cell Carcinoma, and Any PD–L1 Expression

Recommendations 1.8, 1.14, and 1.21

Clinicians may offer retifanlimab plus platinum-based chemotherapy (Evidence quality: Moderate; Strength of recommendation: Conditional).

Evidence review. POD1UM-304 was a phase III, double-blind, placebo-controlled trial that enrolled 583 patients with previously untreated stage IV nonsquamous (65%) or squamous (35%) NSCLC without *EGFR*, *ALK*, *BRAF*, or *ROS1* alterations.⁵ All patients received four cycles of platinum–

based chemotherapy (pemetrexed-based for nonsquamous and paclitaxel or nab-paclitaxel-based for squamous) and retifanlimab (PD-1 inhibitor) or placebo administered once every 3 weeks for up to 35 cycles. Median overall survival (OS) was 18.1 months with retifanlimab plus chemotherapy versus 13.4 months with chemotherapy plus placebo (hazard ratio [HR], 0.75 [95% CI, 0.6 to 0.93]; $P = .0042$). Median progression-free survival (PFS) was 7.7 versus 5.5 months, respectively (HR, 0.64 [95% CI, 0.52 to 0.79]; $P < .0001$). The objective response rate was higher with retifanlimab (52% [95% CI, 47 to 57] v 39% [95% CI, 32 to 46]; HR, 0.0012), with a longer median duration of response (12.7 months [95% CI, 9.4 to 15.2] v 6.1 months [95% CI, 4.2 to 8.3]). In the retifanlimab arm, the most common treatment-related adverse events (TRAEs) were anemia (63%), decreased appetite (23%), neutrophil count decrease (22%), nausea (21%), and hyperthyroidism (9%). The most frequent grade ≥ 3 adverse events (AEs) were anemia (19%) and neutrophil count decrease (14%). All-grade toxicities reported to be higher in the investigational arm included anemia (63% v 58%), decreased appetite (23% v 13%), decreased neutrophil count (22% v 17%), and decreased platelet count (19% v 12%). Patients in the investigational arm experienced fewer elevations in alanine aminotransferase (19% v 24%) and aspartate aminotransferase (15% v 20%), as well as less nausea (21% v 24%).

Clinical interpretation. These data indicate retifanlimab plus chemotherapy could represent an additional first-line treatment option, particularly in settings where access and cost of existing agents often influence treatment selection. This study does not fundamentally change current management paradigms. It primarily confirms a class effect of PD-1 inhibitors in this setting, potentially expanding treatment access rather than demonstrating superior efficacy. Given that this was a randomized phase III study and that retifanlimab already has US Food and Drug Administration approval in other oncology indications, we elected to include it in this update.

Additional Studies Reviewed Not Leading to Changes in Recommendations

Ivonescimab Plus Chemotherapy Versus Tislelizumab Plus Chemotherapy (HARMONi-6) Trial

HARMONi-6 (ClinicalTrials.gov identifier: [NCT05840016](#)) is a randomized, double-blind, phase III trial comparing ivonescimab (PD-1/vascular endothelial growth factor [VEGF] bispecific antibody) plus chemotherapy versus tislelizumab (PD-1 inhibitor) plus chemotherapy in 532 Chinese patients with treatment-naïve advanced squamous NSCLC.⁶ The primary end point was PFS. At a median follow-up of 10.3 months, ivonescimab significantly improved PFS compared to tislelizumab (median PFS 11.1 v 6.9 months; HR, 0.60 [95% CI, 0.46 to 0.78]; $P < .0001$). Benefit was observed regardless of PD-L1 status. The benefit was less pronounced

in patients aged 65 years or older (HR, 0.88 [95% CI, 0.61 to 1.27]) compared with younger patients (HR, 0.40 [95% CI, 0.26 to 0.59]). The most common TRAEs were alopecia (65%), anemia (53%), and neutropenia (45%). Grade ≥ 3 TRAEs occurred in 64% of patients receiving treatment with ivonescimab versus 54% with tislelizumab, with grade ≥ 3 hemorrhage rates of 2% and 1%, respectively. OS data remains immature.

Clinical interpretation. Ivonescimab is the first PD-1/VEGF bispecific antibody to demonstrate phase III efficacy across multiple settings, supported by a tetravalent structure designed to enable dual-pathway binding. In HARMONi-2, ivonescimab significantly improved PFS compared with pembrolizumab monotherapy in PD-L1-positive NSCLC (HR, 0.51). HARMONi-6 further demonstrated activity in squamous NSCLC, including in the PD-L1-negative subgroup (PFS HR, 0.55). These findings build on the promising signal observed across the HARMONi program. However, interpretation should remain measured as median follow-up was only 10.3 months. In addition, the control arm had higher rates of brain metastases and a greater proportion of never-smokers. Although HARMONi-6 demonstrated clinically meaningful activity, broader validation in multiregional populations will be important to contextualize the magnitude and generalizability of benefit. Ongoing global studies, including HARMONi-3 (ClinicalTrials.gov identifier: [NCT05899608](#)), which compare ivonescimab plus chemotherapy with pembrolizumab plus chemotherapy, will further clarify its role in the first-line metastatic setting.

Bevacizumab Plus Chemotherapy Versus Chemotherapy in Patients With Brain Metastases (BAP BRAIN) Trial

BAP BRAIN was a phase III, randomized, multicenter study in China that evaluated the intracranial efficacy and safety of bevacizumab added to pemetrexed-platinum chemotherapy in patients with treatment-naïve, nonsquamous NSCLC with brain metastases.⁷ Enrolled patients had to be asymptomatic or have adequately controlled symptoms from brain metastases and have at least three brain lesions; a lower number of brain metastases was permitted only if the patient refused local therapy. One hundred fifty-three participants were randomly assigned to receive platinum doublet with or without bevacizumab at 7.5 mg/kg intravenously on day 1 of each 3-week cycle. The primary end point of the study was intracranial PFS (iPFS). Secondary end points included intracranial response rate (iORR) and OS. The median iPFS was 11.07 months (95% CI, 9.10 to 13.04 months) versus 7.37 months (95% CI, 3.17 to 11.57 months) in the bevacizumab plus pemetrexed-platinum group versus the pemetrexed-platinum group, respectively (HR, 0.494; 95% CI, 0.343 to 0.712, $P < .001$). The addition of bevacizumab also resulted in an increased iORR (69.9% v 32.4%; odds ratio [OR], 4.77 [95% CI, 2.41 to 9.45]; $P < .001$). The median OS was 10 months longer for those receiving bevacizumab plus

chemotherapy (28.07 v 18.53 months; HR, 0.752 [95% CI, 0.505 to 1.122]). The study did not report on change of cognitive function and quality of life due to incomplete data. Participants receiving bevacizumab experienced 10% greater grade ≥ 3 AEs.

Clinical interpretation. This study was conducted before first-line immunotherapy became the standard of care in patients with metastatic NSCLC; therefore, its relevance to the current patient population is limited. Data on efficacy of immunotherapy in this setting is also limited. The single-arm phase II Atezo-Brain trial (ClinicalTrials.gov identifier: [NCT03526900](https://clinicaltrials.gov/ct2/show/study?term=NCT03526900)) evaluated atezolizumab in combination with carboplatin and pemetrexed in 40 patients with advanced nonsquamous NSCLC and untreated, asymptomatic brain metastases, reporting a median iPFS of 6.9 months and iORR

of 42.7%. Systemic PFS was 8.9 months and OS was 11.8 months.⁸ Platinum bevacizumab containing regimens could be considered in patients without oncogenic drivers not eligible for immunotherapy.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

Additional information including supplements, clinical tools, and resources can be found at <https://ascopubs.org/topics/ascoguidelines/thoracic-cancer>. Patient information is available at www.cancer.org.

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EDITOR'S NOTE

This ASCO Living Clinical Practice Guideline provides recommendations, with review and analysis of the relevant literature for each recommendation. Additional information, including links to patient information at www.cancer.org, is available at <https://ascopubs.org/topics/asco-guidelines/thoracic-cancer>.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO-26-00842>.

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ACKNOWLEDGMENT

The authors would like to thank Drs Dwight Owen, Tanyanika Philips, and the ASCO Evidence-Based Medicine Committee for their thoughtful reviews and insightful comments on this guideline update.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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No other potential conflicts of interest were reported.

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APPENDIX 3. VERSIONING AND NUMBERING STATEMENT

To ensure transparency and facilitate the tracking of evidence updates, ASCO has implemented a structured numbering system for living guidelines. This system reflects the status of the recommendations as follows: (1) Major Updates (eg, 2026.2.0): These represent full updates or significant revisions approved by the Expert Panel and the Evidence-Based Medicine Committee. They typically incorporate comprehensive literature reviews and involves resubmission of the entire guideline. (2) Rapid Updates (eg, 2026.2.1): These mini updates serve as timely notifications of revised recommendations or supporting evidence, ensuring that the guideline remains current between full update cycles.

All tables and figures are available in the appendix and online only.

TABLE A1. All Recommendations

Category	Recommendation
<i>General Note.</i> The following recommendations (strong or conditional/weak) and terminology (Data Supplement, online only) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible. For recommendations with multiple treatment options of the same evidence quality and strength of recommendation, the decision of which agent to offer should be tailored based on discussion of efficacy, toxicity, drug access, and cost with each patient. Unless otherwise specified, the recommended number of cycles of platinum-doublet chemotherapy is four.	
What are the most effective first-line treatment options for patients with good performance status and the following biomarkers:	
Biomarker testing	1.0. Biomarker testing with a validated tissue and/or blood-based broad multigene panel and a validated tissue IHC assay for PD-L1, HER2, and MET protein expression should be universally accessible for all patients diagnosed with NSCLC. (Evidence quality: High; Strength of recommendation: Strong) <i>Qualifying Statement for Recommendation 1.0:</i> Combination of blood and tissue testing may maximize chance of detecting molecular alterations. Comprehensive RNA-based NGS testing ideally incorporating RNA-based NGS for detecting genomic alterations is preferred. Tissue testing has the advantage of histologic assessment and should be attempted when feasible, and the false-negative rate of liquid biopsy should be considered. PD-L1 IHC alone should not be used to guide treatment decisions.
Nonsquamous cell carcinoma	
PD-L1 expression, TPS ≥50%	<i>Clinicians should offer any of the following single-agent immune checkpoint inhibitors:</i>
	1.1. Pembrolizumab or cemiplimab or atezolizumab. (Evidence quality: High; Strength of recommendation: Strong)
	<i>Other combination regimens that may be offered in select instances include</i>
	1.2. Pembrolizumab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.3. Cemiplimab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.4. Atezolizumab + carboplatin + (nab)-paclitaxel ± bevacizumab (in the absence of contraindications to bevacizumab). (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.5. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.6. Nivolumab and ipilimumab with two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.7. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.8. Retifanlimab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional) ^a
	<i>Clinicians should offer any of the following combination immune checkpoint inhibitor and chemotherapy regimens:</i>
	1.9. Pembrolizumab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Strong)
	1.10. Cemiplimab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Strong)
	<i>Other combination regimens that may be offered in select instances includes</i>
	1.11. Atezolizumab + carboplatin + (nab)-paclitaxel ± bevacizumab (in the absence of contraindications to bevacizumab). (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.12. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
PD-L1 expression, TPS 1%-49%	1.13. Nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.14. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.15. Retifanlimab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional) ^a
	1.16. Pembrolizumab monotherapy may be offered to patients who are ineligible for or decline combination therapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)

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TABLE A1. All Recommendations (continued)

Category	Recommendation
Unknown or negative PD-L1 expression, TPS <1%	<i>Clinicians may offer any of the following:</i>
	1.17. Pembrolizumab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.18. Cemiplimab + carboplatin + pemetrexed. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.19. Atezolizumab + carboplatin + (nab)-paclitaxel ± bevacizumab (in the absence of contraindications to bevacizumab). (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.20. Nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.21. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	1.22. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
Squamous cell carcinoma	1.23. Retifanlimab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional) ^a
	<i>Clinicians should offer treatment with single-agent immune checkpoint inhibitors:</i>
	2.1. Clinicians should offer single-agent pembrolizumab or cemiplimab or atezolizumab. (Evidence quality: High; Strength of recommendation: Strong)
	<i>Other combination regimens that may be offered in select instances includes:</i>
	2.2. Pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel) or cemiplimab + carboplatin + paclitaxel. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.3. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.4. Nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
PD-L1 expression, TPS ≥50%	2.5. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	<i>Clinicians should offer any of the following combination immune checkpoint inhibitor and chemotherapy regimens:</i>
	2.6. Pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel). (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.7. Cemiplimab + carboplatin + paclitaxel. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.8. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.9. Nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.10. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
PD-L1 expression, TPS 1%-49%	2.11. Pembrolizumab monotherapy may be offered to patients who are ineligible for or decline combination therapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	<i>Clinicians may offer any of the following:</i>
	2.12. Pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel). (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.13. Cemiplimab + carboplatin + paclitaxel. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.14. Nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.15. Nivolumab and ipilimumab. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.16. Durvalumab and tremelimumab plus platinum-based chemotherapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
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TABLE A1. All Recommendations (continued)

Category	Recommendation
<i>General approaches</i>	
	3.1. Patients with advanced lung cancer should be referred to interdisciplinary palliative care teams (consultation) that provide inpatient and outpatient care early in the course of disease, alongside active treatment of their cancer. (Evidence quality: High; Strength of recommendation: Strong)
	3.2. For patients who are not candidates for immune checkpoint inhibitor therapy, clinicians should offer platinum-doublet combination therapy for patients with preserved PS. (Evidence quality: High; Strength of recommendation: Strong)
	3.3. Clinicians may offer nonplatinum therapy combinations for patients who have contraindications to platinum therapy. (Evidence quality: Moderate; Strength of recommendation: Conditional)
Patients with contraindications to bevacizumab	3.4. Bevacizumab should be avoided for patients with squamous cell carcinoma histologic type, clinically significant hemoptysis, inadequate organ function, ECOG PS > 1, clinically significant cardiovascular disease, or medically uncontrolled hypertension. (Evidence quality: High; Strength of recommendation: Strong)
	3.5. Maintenance bevacizumab given with pemetrexed has no survival advantage and significantly increased toxicity compared to maintenance pemetrexed or bevacizumab alone. (Evidence quality: Moderate; Strength of recommendation: Conditional)
What are the most effective second-line and subsequent treatment options for patients with good performance status:	
Patients previously treated with immune checkpoint therapy without chemotherapy	4.1. Clinicians should offer platinum-doublet chemotherapy. (Evidence quality: Low; Strength of recommendation: Strong)
Patients previously treated with chemotherapy and immune checkpoint therapy	4.2. Clinicians should offer docetaxel with or without ramucirumab if the patient has already received platinum-based chemotherapy. (Evidence quality: Low; Strength of recommendation: Strong)
	4.3. Clinicians may offer pemetrexed, nab-paclitaxel, or gemcitabine if the patient has already received platinum-based chemotherapy. (Evidence quality: Low; Strength of recommendation: Conditional)
	4.4. Clinicians may offer telisotuzumab vedotin (Teliso-V) for patients with c-Met protein-overexpressing NSCLC defined as MET IHC 3+ in ≥50% of tumor cells. (Evidence quality: Low; Strength of recommendation: Conditional)
	4.5. Clinicians may offer trastuzumab deruxtecan for patients with HER2-overexpressing NSCLC defined as HER2 IHC 3+ (by gastric scoring). (Evidence quality: Very Low; Strength of recommendation: Conditional)

NOTE. The following recommendations (strong or conditional) and terminology (see the guideline in the Data Supplement) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible. The strength of the recommendation is defined as follows, Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional/Weak: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not. Abbreviations: ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; nab, nanoparticle albumin-bound; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PS, performance status; TPS, tumor proportion score.

^aUpdated recommendation.

TABLE A2. Stage IV NSCLC Living Guideline Expert Panel Membership

Name	Affiliation	Role or Area of Expertise
Cochairs		
Lyudmila Bazhenova, MD	University of California, San Diego, San Diego, CA	Medical Oncology
Natasha B. Leighl, MD	Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada	Medical Oncology
Sonam Puri, MD	Moffitt Cancer Center, Tampa, FL	Medical Oncology
Joshua Reuss, MD	Georgetown University, Washington, DC	Medical Oncology
Panel members		
Fawzi Abu Rous, MD	Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI	Medical Oncology
Amith Ahluwalia, MD	Confluence Health Wenatchee Valley Hospital and Clinics, Wenatchee, WA	Medical Oncology
Krishna Alluri, MD	Texas Oncology, San Antonio, TX	Medical Oncology
Ibrahim Hanna Azar, MD	IHA Hematology Oncology Consultants, Ypsilanti, MI	Medical Oncology
Toby Campbell, MD	University of Wisconsin, Madison, WI	Palliative Oncology
Greg Durm, MD	Indiana University Health, Indianapolis, IN	Medical Oncology
Jill Feldman, MA	EGFR Resisters patient advocacy group, Deerfield, IL	Patient Research Advocate
Janet Freeman-Daily, MSc, Engr	The ROS1ders, Seattle, WA	
Naoki Furuya, MD, PhD	St Marianna University School of Medicine, Kawasaki, Japan	Medical Oncology
Shirish Gadgeel, MD	Emory University, Atlanta, GA	Medical Oncology
Balazs Halmos, MD	Montefiore Einstein Comprehensive Center for Cancer Care, Bronx, NY	Medical Oncology
Hidehito Horinouchi, MD	National Cancer Center Hospital, Tokyo, Japan	Medical Oncology
Sara Kuruvilla, MD (Ontario Health representative)	London Health Sciences Center, London, ON, Canada	Medical Oncology
Gary R. MacVicar, MD	Illinois CancerCare, Peoria, IL	Medical Oncology
Narinder Malhotra, MD	Yolanda G. Barco Cancer Institute, Meadville, PA	Medical Oncology
Kristen Ashley Marrone, MD	John Hopkins Medical Center, Baltimore, MD	Medical Oncology
Deebya Raj Mishra, MD	BP Koirala Institute of Health Sciences, Dharan, Nepal	Pulmonology
Michael Mullane, MD	Aurora Cancer Care, Mount Pleasant, WI	Medical Oncology
Bruna Pellini, MD	Miami Cancer Institute, Baptist Health South Florida, Miami, FL	Medical Oncology
Carolyn J. Presley, MD, MHS	Ohio State University, Comprehensive Cancer Center and The James Cancer Hospital/Solove Research Institute, Columbus, OH	Medical Oncology Geriatric Oncology
Angel Qin, MD	University of Michigan Health System, Ann Arbor, MI	Medical Oncology
Logan Roof, MD	Ohio State University, Columbus, OH	Medical Oncology
Erin L. Schenk, MD, PhD	University of Colorado Anschutz Medical Center, Aurora, CO	Medical Oncology
Navneet Singh, MD, DM	Postgraduate Institute of Medical Education and Research, Chandigarh, India	Medical Oncology
Eric K. Singhi, MD	University of Texas MD Anderson Cancer Center, Houston, TX	Medical Oncology
Jennifer Marie Suga, MD	Kaiser Permanente Vallejo Medical Center, Vallejo, CA	Medical Oncology
Ana I. Velazquez, MD, MSc	University of California, San Francisco, CA	Medical Oncology
Yubao Wang, MD, PhD	Lovelace Cancer Care, Albuquerque, NM	Medical Oncology
Paul Wheatley Price, MD, MBChB	The Ottawa Hospital Research Institute/University of Ottawa, Ottawa, ON, Canada	Medical Oncology
Nofisat Ismaila, MD, PhD	ASCO, Alexandria, VA	ASCO Practice Guidelines Staff (Health Research Methods)

TABLE A3. Characteristics of Studies Identified in the Literature Search Since the Last Update

Author Reference	Interventions and Comparisons	Patients, No.	Patient Characteristic					Disease Characteristic		
			Median Age, Years	Sex, %		Smokers, %	Race or Ethnicity: %	History of Brain Metastasis, %	ECOG PS: %	Other Characteristics: %
				Male	Female					
Phase III RCTs										
Lu et al ⁵ POD1UM-304 phase III, multiregional, placebo-controlled, double-blind RCT	Retifanlimab plus chemotherapy	391	63	81	19	80	White: 66	6	0: 26	PD-L1 expression
	Placebo plus chemotherapy	192	63	78	22	75	Asian: 32	4	1: 74	<1%: 27
		Other: 1					White: 66		0: 27	1%-49%: 40
		Asian: 32					Asian: 32		1: 73	≥50: 33
		Other: 2					Other: 2			<1%: 28
									1%-49%: 40	
									≥50: 33	
Chen et al ⁶ HARMONi-6 Double-blind, phase III study in China	Ivonescimab + chemotherapy	266	64	96	4	Never: 8	Chinese: 100	3	0: 16	<1%: 39
	Tislelizumab + chemotherapy	266	64	89	11	Current or former: 92		6	1: 84	1%-49%: 42
		Never: 14				Never: 14			0: 16	≥50: 18
		Current or former: 86				Current or former: 86			1: 83	<1%: 39
										1%-49%: 37
									≥50: 23	
Li et al ⁷ BAP BRAIN Open-label, randomized, phase III study	Bevacizumab + chemotherapy	79	59	72	28	57	NR	100	0: 14	>1%: 23
	Chemotherapy	74	58	80	20	57			1: 86	Negative: 22
									0: 19	Unknown: 56
									1: 81	>1%: 15
									Negative: 14	
									Unknown: 72	

Abbreviations: ECOG, Eastern Cooperative Oncology Group; No. of Patients, number of patients randomly assigned; NR, not reported; PS, performance status; RCT, randomized controlled trial.

TABLE A4. Lu et al⁵

Population: Patients With Metastatic NSCLC
 Intervention: Retifanlimab Plus Chemotherapy
 Comparator: Placebo Plus Chemotherapy

Outcome	Study Results and Measurements	Absolute Effect Estimates		Quality of Evidence	Summary
		Placebo Plus Chemotherapy	Retifanlimab Plus Chemotherapy		
OS	HR, 0.75 (95% CI, 0.6 to 0.93) Based on data from 583 participants in 1 study Follow-up 13.7 months	693 per 1,000 Difference: 105 fewer per 1,000 (95% CI, 185 fewer to 26 fewer)	588 per 1,000	Moderate Due to serious imprecision ^a	Retifanlimab plus chemotherapy probably improves OS
PFS	HR, 0.64 (95% CI, 0.52 to 0.79) Based on data from 583 participants in 1 study Follow-up 13.7 months	693 per 1,000 Difference: 163 fewer per 1,000 (95% CI, 234 fewer to 86 fewer)	530 per 1,000	Moderate Due to serious imprecision ^a	Retifanlimab plus chemotherapy probably improves PFS
Safety	Based on data from 583 participants in 1 study Follow-up 13.7 months	Overall, higher incidences of TEAEs that were serious (158 [41%] of 389 v 57 [30%] of 190), were grade 3 or worse (238 [61%] v 103 [54%]), or led to retifanlimab or placebo dose delay (169 [43%] v 67 [35%]) or discontinuation (33 [8%] v nine [5%]) were observed in the retifanlimab plus chemotherapy group than in the placebo plus chemotherapy group		Moderate Due to serious imprecision ^a	Retifanlimab had no new safety concerns

Abbreviations: AE, adverse event; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; TEAEs, treatment-emergent adverse events.

^aImprecision: serious. Only data from one study.

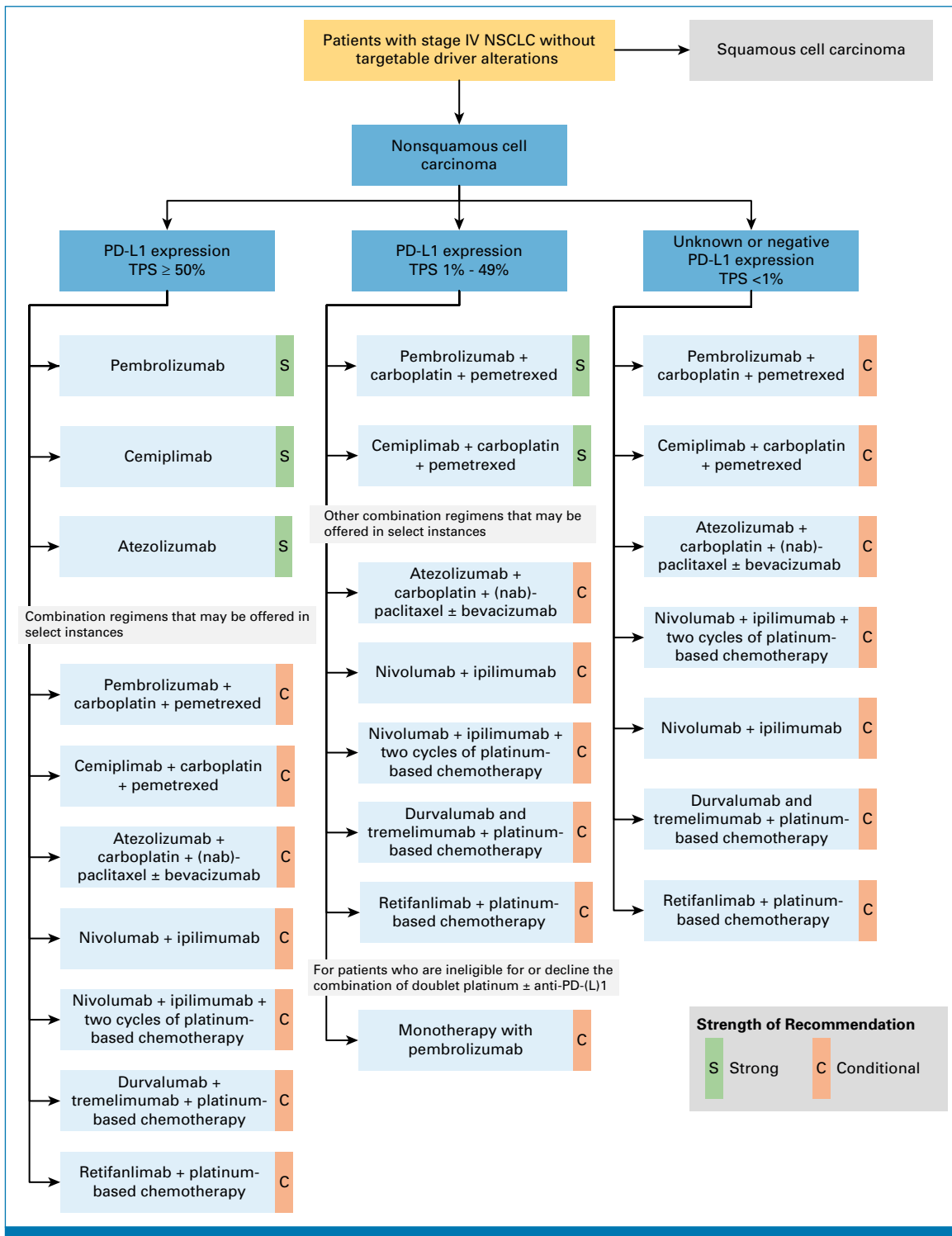


FIG A1. First-line treatment options for patients with stage IV non–small cell lung cancer without driver alterations and nonsquamous cell carcinoma. For recommendations with multiple treatment options of the same evidence quality and strength of recommendation, the decision of which agent to offer should be tailored based on discussion of efficacy, toxicity, drug access, and cost with each patient. Unless otherwise specified, the recommended number of cycles of platinum-doublet chemotherapy is four. nab, nanoparticle albumin-bound; NSCLC, non–small cell lung cancer; TPS, tumor proportion score.