ASCO® Guidelines

Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline				
Clinical Question	**Recommendation**	**Type**	**Evidence Quality**	**Strength**
Updated Recommendations				
What is the most effective first-line therapy for patients with non-SCC and PD-L1 TPS 0-49%, without known EGFR, ALK, or ROS-1 alterations, and PS 0-1?	**2.8.** For patients with non-SCC, PD-L1 TPS 0-49% and PS 0 to 1, clinicians may offer cemiplimab plus chemotherapy.	EB	M	W
	2.9. For patients with non-SCC, PD-L1 TPS 0-49% and PS 0 to 1, clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.	EB	M	W
What is the most effective first-line therapy for patients with SCC and PD-L1 TPS 0-49%, without known EGFR, ALK, or ROS-1 alterations, and PS 0-1?	**4.6.** For patients with SCC, PD-L1 TPS 0-49% and PS 0 to 1, clinicians may offer cemiplimab plus chemotherapy.	EB	M	W
	4.7. For patients with SCC, PD-L1 TPS 0-49% and PS 0 to 1, clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.	EB	M	W
Unchanged Recommendations				
Which patients with stage IV NSCLC should be treated with chemotherapy?	For patients with PS of 0 or 1 receiving chemotherapy a combination of two cytotoxic drugs is recommended. Platinum combinations are recommended over nonplatinum therapy; however, nonplatinum therapy combinations are recommended for patients who have contraindications to platinum therapy. Chemotherapy may also be used to treat selected patients with PS of 2 who desire aggressive treatment after a thorough discussion of the risks and benefits of such treatment.	-	-	-

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	Because there is no cure for patients with stage IV NSCLC, early concomitant palliative care assistance has improved the survival and well-being of patients and is therefore recommended	-	-	-
What is the most effective first-line therapy for patients with non-SCC and high PD-L1 (TPS ≥ 50%) status, and PS 0-1?	For patients with high PD-L1/PD1 expression (TPS ≥ 50%), in the absence of contraindications to immune checkpoint inhibitor therapies, non-SCC PS 0-1:	-	-	-
	1.1. clinicians should offer single-agent pembrolizumab.	EB	H	S
	1.2. clinicians may offer pembrolizumab/carboplatin/pemetrexed.	EB	H	S
	1.3. clinicians may offer atezolizumab/carboplatin/nab-paclitaxel/bevacizumab in the absence of contraindications to bevacizumab	EB	I	M
	1.4. For patients with high PD-L1 expression (TPS ≥ 50%), non-SCC, PS 0-1, clinicians may offer atezolizumab/carboplatin/nab-paclitaxel.	EB	L	W
	1.5. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), non-SCC, and PS 0 to 1, clinicians may offer single-agent atezolizumab.	EB	M	S
	1.6. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), non-SCC, and PS 0 to 1, clinicians may offer single-agent cemiplimab.	EB	M	S
	1.7. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), non-SCC, and PS 0 to 1, clinicians may offer nivolumab and ipilimumab alone or nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.	EB	M	W
	1.8. There are insufficient data to recommend any other checkpoint inhibitors or to recommend combination checkpoint inhibitors or any other combinations of immune checkpoint inhibitors with chemotherapy in the first-line setting.	EB	H	S
What is the most effective first-line therapy for patients with stage IV NSCLC, non-SCC and no	**7.1.** For patients receiving carboplatin plus paclitaxel, the Update Committee recommends the addition of bevacizumab 15 mg/kg once every 3 weeks, except for patients with SCC histologic type, clinically significant hemoptysis, inadequate organ function, ECOG PS > 1, clinically significant cardiovascular disease, or medically uncontrolled hypertension. Bevacizumab may be continued, as tolerated, until disease progression.	-	-	-

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contraindications to bevacizumab?	**7.2.** Bevacizumab should not be added to pemetrexed plus carboplatin or given as maintenance with pemetrexed for patients who do not have contraindications to bevacizumab. Note that first line platinum chemotherapy alone without immunotherapy is not considered standard of care but may be considered in patients ineligible for immunotherapy.	EB	M	W
What is the most effective first-line therapy for patients with stage IV NSCLC with non-SCC, and negative or unknown PD-L1 status (TPS 0-49%), and PS 0-1?	For patients with negative (<1% or unknown) and low positive (TPS 1%-49%) PD-L1 expression, non-squamous cell carcinoma, PS 0-1, AND are eligible for chemotherapy and pembrolizumab,	-	-	-
	2.1. clinicians should offer pembrolizumab/carboplatin/pemetrexed	EB	H	S
	2.2. clinicians may offer atezolizumab/carboplatin/paclitaxel/bevacizumab in the absence of contraindications to bevacizumab.	EB	I	M
	2.3. clinicians may offer atezolizumab/carboplatin/nab-paclitaxel.	EB	I	M
	2.4. (patients who have the above characteristics) AND have contraindications to/declines immunotherapy, clinicians should offer standard chemotherapy with platinum-based two drug combinations as outlined in the 2015 update.	EB	H	S
	2.5. (patients with above characteristics) AND have contraindications to/declines immunotherapy AND not deemed candidates for platinum-based therapy, clinicians should offer nonplatinum based two-drug therapy as outlined in the 2015 update.	EB	L	W
	2.6. For patients with low positive PD-L1 expression (TPS 1%-49%), non-SCC, PS 0-1, AND who are ineligible for or decline combination of doublet platinum ± pembrolizumab, clinicians may offer single-agent pembrolizumab.	EB	L	W
	2.7. In addition to 2020 options, for patients with negative (0%) and low positive PD-L1 expression (TPS 1% to 49%), non-SCC, and PS 0 to 1, clinicians may offer nivolumab and ipilimumab alone or nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.	EB	M	W
What is the most effective first-line therapy for patients with stage IV NSCLC with PS 2, non-SCC?	In the context of shared decision making, combination therapy, single-agent therapy, or palliative therapy alone may be used for patients in this population with PS of 2.	EB chemotherapy EB palliative care	I chemotherapy I palliative care	W chemotherapy S palliative care

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What is the most effective first-line therapy for patients with stage IV NSCLC with SCC, and High PD-L1 status (TPS ≥ 50%), and PS 0-1?	For patients with high PD-L1 expression (TPS ≥ 50%) squamous cell carcinoma, PS 0-1, in the absence of contraindications to immune checkpoint inhibitor therapy:	-	-	-
	3.1. clinicians should offer single-agent pembrolizumab.	EB	H	S
	3.2. clinicians may offer pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel).	EB	I	M
	3.3. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), SCC, and PS 0 to 1, clinicians may offer single-agent atezolizumab.	EB	M	S
	3.4. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), SCC, and PS 0 to 1, clinicians may offer single-agent cemiplimab.	EB	M	S
	3.5. In addition to 2020 options, for patients with high PD-L1 expression (TPS ≥ 50%), SCC, and PS 0 to 1, clinicians may offer nivolumab and ipilimumab alone or nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.	EB	M	W
What is the most effective first-line therapy for patients with stage IV NSCLC with SCC, and negative or unknown PD-L1 status (TPS 0-49%), and PS 0-1?	For patients with negative (TPS 0%, <1%, or unknown) and/or low positive (TPS 1%-49%) PD-L1 expression and squamous cell carcinoma, in the absence of contraindications to immune checkpoint inhibitor therapies:	-	-	-
	4.1. clinicians should offer pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel).	EB	I	S
	4.2. (For patients who have the above characteristics) AND with contraindications to immunotherapy, clinicians should offer standard chemotherapy with platinum-based two-drug combinations as outlined in the 2015 update.	EB	H	S
	4.3. (For patients who have the above characteristics) AND with contraindications to immunotherapy AND not deemed candidates for platinum-based therapy, clinicians should offer standard chemotherapy with non-platinum-based two drug combinations as outlined in the 2015 update.	EB	I	W
	4.4. patients with low positive PD-L1 (TPS 1-49%) AND who are ineligible for or decline combination of doublet platinum/pembrolizumab AND have contraindications to doublet-chemotherapy, clinicians may offer single-agent pembrolizumab, in the absence of contraindications to immune checkpoint therapies.	EB	L	W
	4.5. In addition to 2020 recommendations 4.1-4.4, for patients with negative (TPS 0%) and low positive (TPS 1% to 49%) PD-L1 expression, SCC, and PS 0 to 1, clinicians may offer nivolumab and ipilimumab alone or nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.	EB	M	W

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What is the most effective first-line therapy for patients with stage IV NSCLC, SCC, and PS 2?	In the context of shared decision making, combination chemotherapy, single-agent therapy, or palliative therapy alone may be used for patients with the characteristics described in Clinical Question A3a.	EB chemotherapy	I chemotherapy	W chemotherapy
		EB palliative care	I palliative care	S palliative care
What is the most effective therapy for patients with non-SCC who have received one prior chemotherapy regimen?	**5.1.** In addition to previously recommended regiments, for patients with non-SCC who received an immune checkpoint inhibitor and chemotherapy as first-line therapy, clinicians may offer paclitaxel plus bevacizumab in the second-line setting.	EB	L	W
	The evidence does not support the selection of a specific second-line chemotherapy drug or combination based on age alone. This recommendation has not changed. Age alone is not a contraindication to chemotherapy for NSCLC.	-	-	-
What is the most effective third-line therapy for patients with stage IV NSCLC and PS 0-1?	**6.1.** For the majority of patients with non-SCC, who received chemotherapy with or without bevacizumab and immune checkpoint inhibitor therapy (in either sequence), clinicians should offer the options of single-agent pemetrexed or docetaxel or paclitaxel plus bevacizumab in the third-line setting.	EB	L	W
Is there a role for cytotoxic therapy for patients who have received three prior regimens and good PS?	Data are not sufficient to make a recommendation for or against using cytotoxic drugs as fourth-line therapy; patients should consider experimental treatment, clinical trials, and continued best supportive (palliative) care.	-	-	-

Abbreviations. EB, evidence based; ECOG, Eastern Cooperative Oncology Group; FC, formal consensus; H, high; IC, informal consensus; L, low; M, moderate; N/A, not applicable; NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand 1; PS, performance status; S, strong; SCC, squamous cell carcinoma; TPS, tumor proportion score; W, weak