

Systemic Therapy for Stage IV NSCLC Algorithms

First-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer without Driver Alterations

Nonsquamous cell carcinoma, High PD-L1
Nonsquamous cell carcinoma, Negative and Low Positive PD-L1
Squamous cell carcinoma, High PD-L1
Squamous cell carcinoma, Negative and Low Positive PD-L1

Second-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer without Driver Alterations

Received first-line platinum doublet chemotherapy, Positive PD-L1
Received first-line platinum doublet chemotherapy, Negative or Unknown PD-L1
Received first-line immunotherapy
Received first-line combination immunotherapy + chemotherapy

Third-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer without Driver Alterations

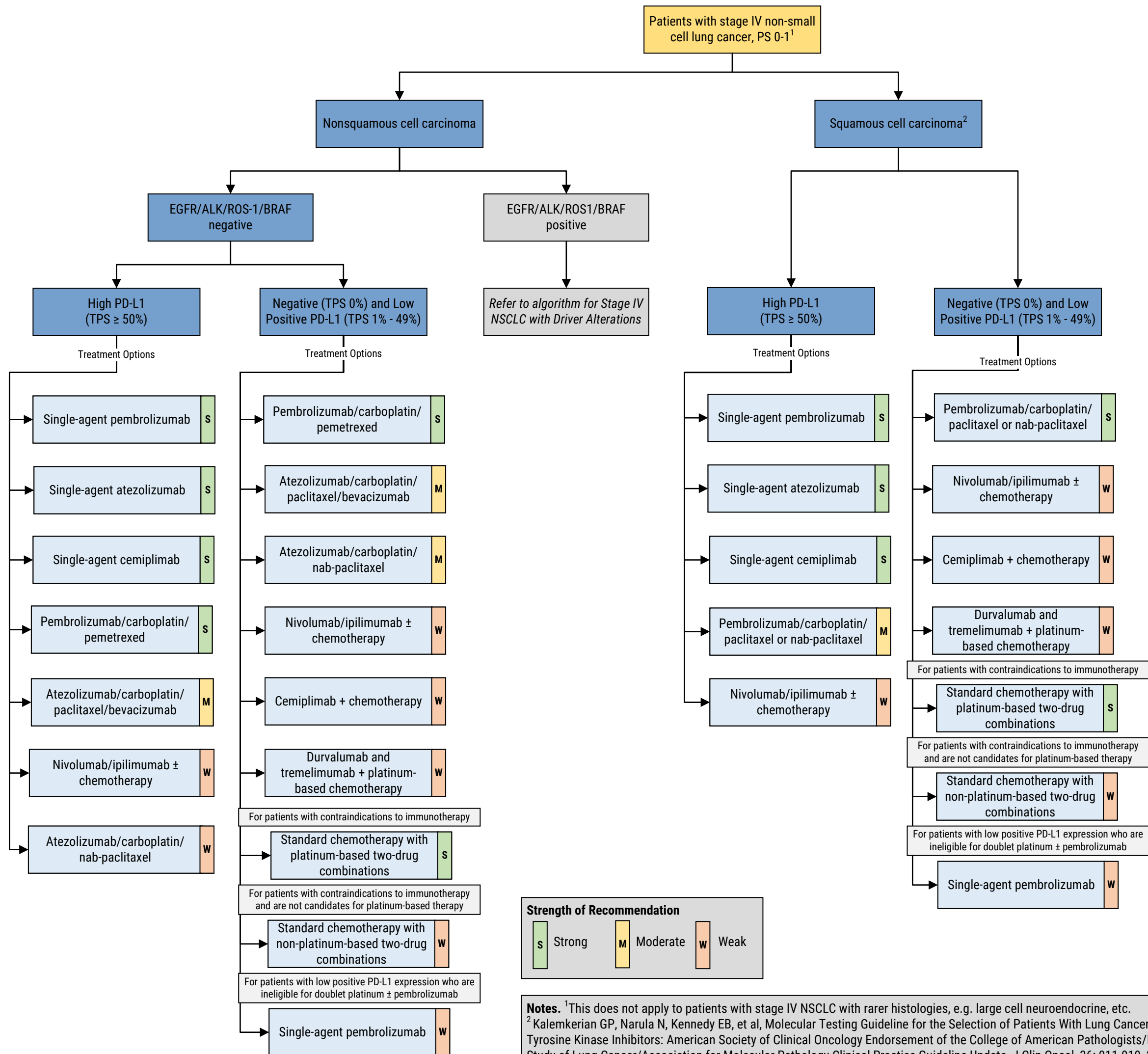
Received chemotherapy ± bevacizumab and immune checkpoint inhibitors

First-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer with Driver Alterations

Sensitizing (L858R/exon 19 deletion) *EGFR* mutation
EGFR exon 20 mutation
Activating *EGFR* mutations other than exon 20 insertion mutations, T790M, L858R or Ex19Del
ALK rearrangement
ROS1 rearrangement
BRAF V600 mutation
MET exon 14 skipping mutations
RET rearrangement
NTRK rearrangement
KRAS alterations
HER2 alterations
NRG1 alterations

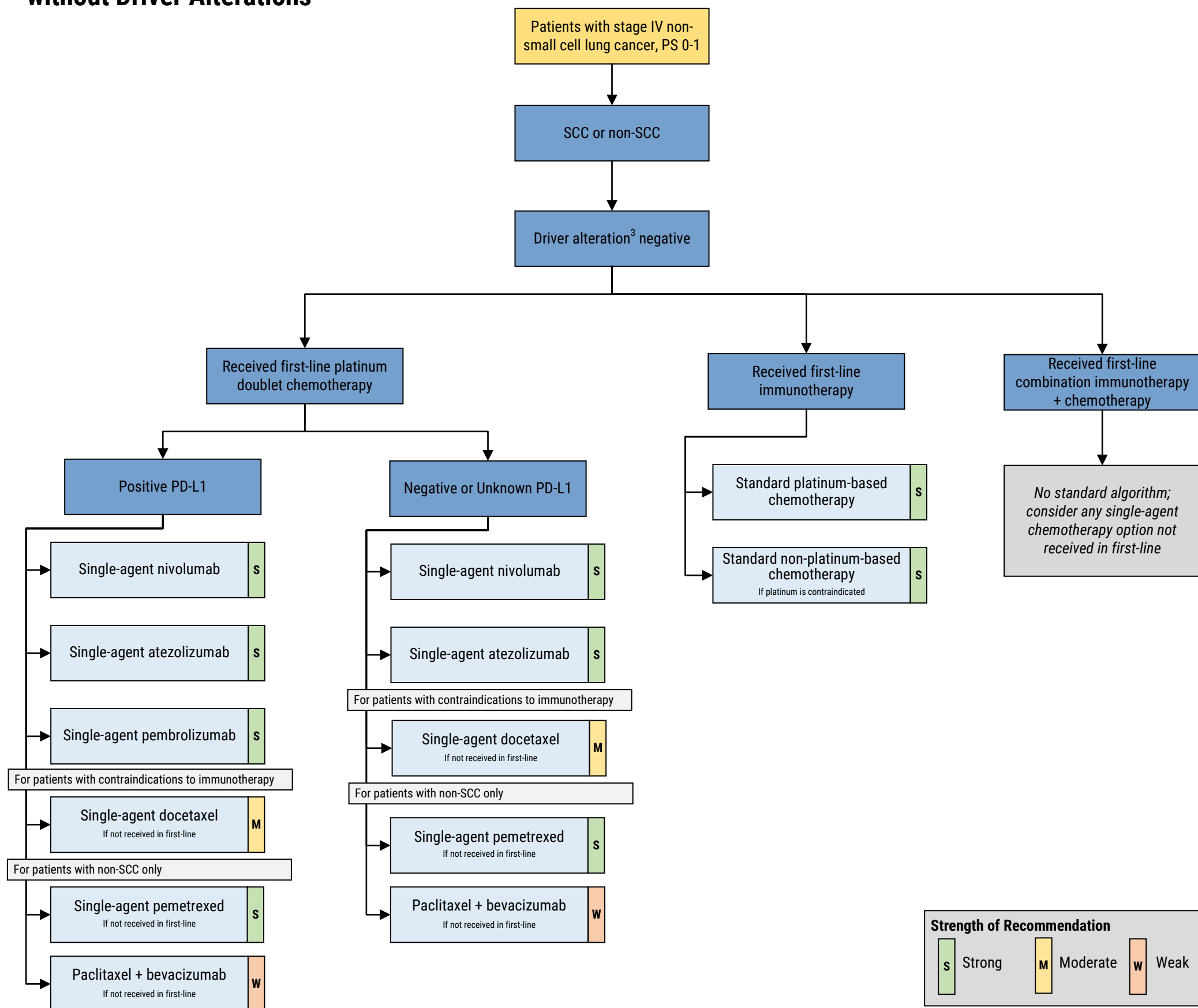
Second- and Third-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer with Driver Alterations

Sensitizing (L858R/exon 19 deletion) *EGFR* mutation
EGFR exon 20 mutation
Activating *EGFR* mutations other than exon 20 insertion mutations, T790M, L858R or Ex19Del
ALK rearrangement
ROS1 rearrangement
BRAF V600 mutation
BRAF mutation other than *BRAF* V600
MET exon 14 skipping mutations
MET abnormalities other than exon 14 skipping mutations or previously treated with *MET*-targeted therapy
RET rearrangement
NTRK rearrangement
KRAS alterations
HER2 alterations
NRG1 alterations



This algorithm is derived from recommendations in Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline. This is a tool based on an ASCO Guideline and is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients. This tool does not purport to suggest any particular course of medical treatment. Use of the guideline and this tool are voluntary.

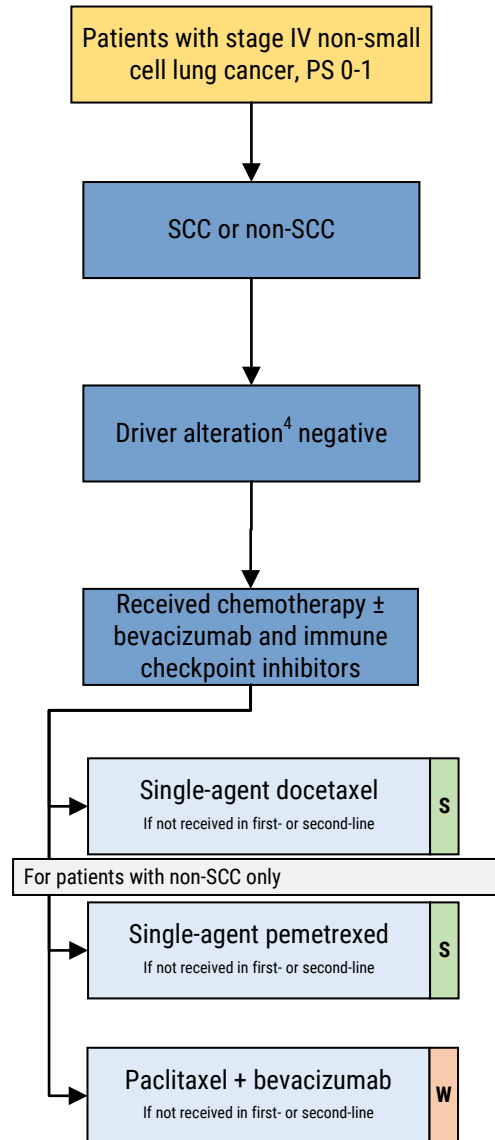
Second-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer without Driver Alterations



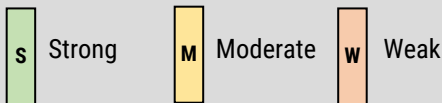
Notes.³ Driver alterations including *EGFR*, *ALK*, *ROS-1*, *BRAF V600E*, *MET* exon 14, *NTRK*, *KRAS*, and *RET*
Abbreviations. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; NSCLC, non-small-cell lung cancer; PD-L1, program death ligand 1; PS, performance status; SCC, squamous cell carcinoma; TPS, tumor proportion score

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Third-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer without Driver Alterations



Strength of Recommendation



Notes. ⁴ Driver alterations including *EGFR*, *ALK*, *ROS-1*, *BRAF* V600E, *MET* exon 14, *NTRK*, *KRAS*, and *RET*

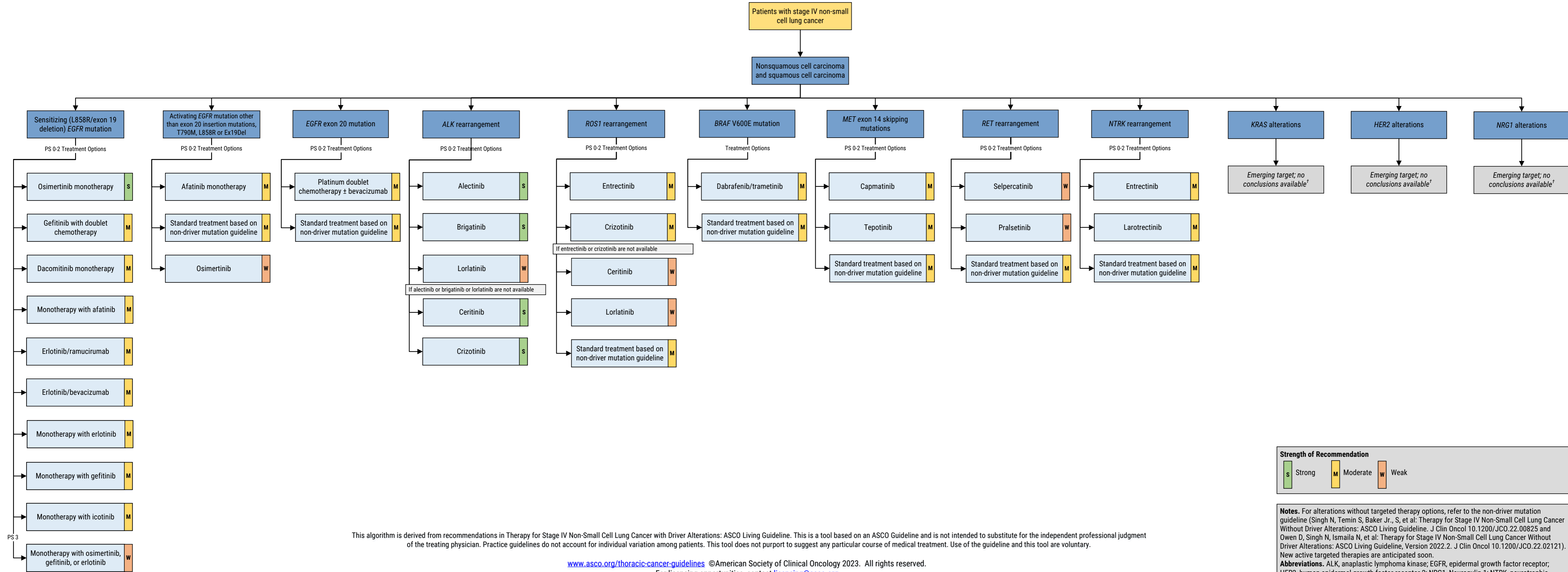
Abbreviations. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; NSCLC, non-small-cell lung cancer; PS, performance status

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First-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer with Driver Alterations



Strength of Recommendation

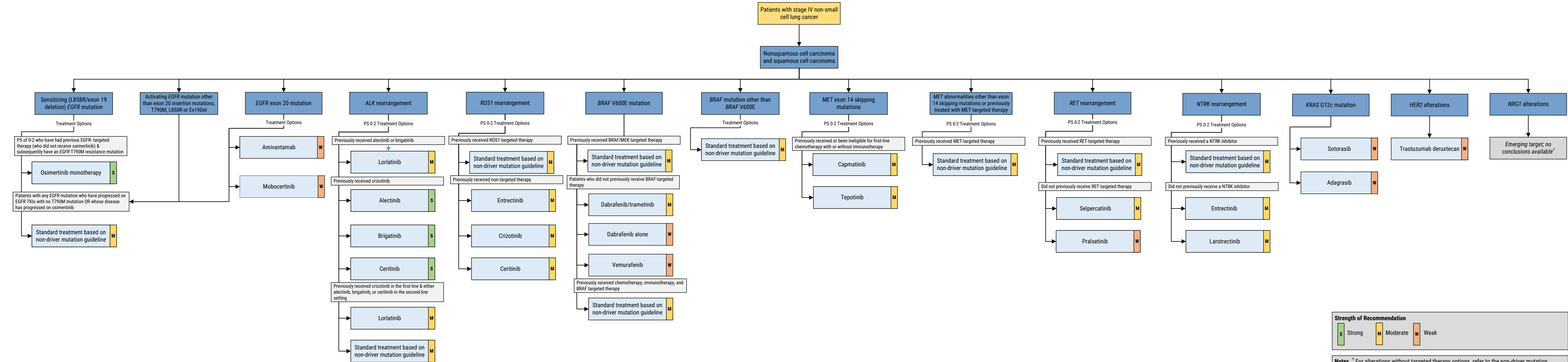
S Strong M Moderate W Weak

Notes. For alterations without targeted therapy options, refer to the non-driver mutation guideline (Singh N, Temin S, Baker Jr., S, et al: Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline. J Clin Oncol 10.1200/JCO.22.00825 and Owen D, Singh N, Ismaila N, et al: Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline, Version 2022.2. J Clin Oncol 10.1200/JCO.22.02121). New active targeted therapies are anticipated soon.

Abbreviations. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; NRG1, Neuregulin 1; NTRK, neurotrophic tropomyosin receptor kinase; PS, performance status

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Second- and Third-Line Treatment Options for Patients with Stage IV Non-Small Cell Lung Cancer with Driver Alterations



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Abbreviations. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; NRG1, Neuregulin 1; NTRK, neurotrophic tropomyosin receptor kinase; PS, performance status; TKI, tyrosine kinase inhibitors