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CORRIGENDUM

Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

D. Planchard, S. Popat, K. Kerr, S. Novello, E. F. Smit, C. Faivre-Finn, T. S. Mok, M. Reck, P. E. Van Schil, M. D. Hellmann & S. Peters, on behalf of the ESMO Guidelines Committee

Ann Oncol 2018; 29: iv192–iv237 (doi:10.1093/annonc/mdy275)

The following corrections are made:

In the section "Management of advanced/metastatic NSCLC, First-line treatment of *EGFR- and ALK*-negative NSCLC disease, regardless of PD-L1 status"

1. In KEYNOTE-189, patients with metastatic non-squamous NSCLC, PS 0-1, without sensitising *EGFR or ALK* mutations, were randomised to receive pemetrexed and a platinum-based ChT plus either 200 mg of pembrolizumab or placebo every 3 weeks for 4 cycles, followed by pembrolizumab or placebo for up to a total of 35 cycles plus pemetrexed maintenance therapy [96].

Is replaced with:
In KEYNOTE-189, patients with metastatic non-squamous NSCLC, PS 0-1, without sensitising *EGFR or ALK* mutations, were randomised to receive pemetrexed and cisplatin or carboplatin plus either 200 mg of pembrolizumab or placebo every 3 weeks for 4 cycles, followed by pembrolizumab or placebo for up to a total of 35 cycles plus pemetrexed maintenance therapy [96].

2. Recently, the combination of carboplatin or cisplatin with pemetrexed and atezolizumab has been shown, in the context of the IMpower132 trial, to be superior to the ChT doublet.

Is replaced with:
Recently, the combination of carboplatin or cisplatin with pemetrexed and atezolizumab followed by maintenance pemetrexed and atezolizumab has been shown, in the context of the IMpower132 trial, to be superior to the ChT doublet followed by maintenance pemetrexed.

3. Atezolizumab was studied in patients with metastatic squamous NSCLC in the IMpower131 study. Patients were randomised to atezolizumab/carboplatin/paclitaxel, atezolizumab/carboplatin/nab-P or carboplatin/nab-P (nab-PC) [100]. Atezolizumab/carboplatin/nab-P had improved PFS compared with nab-PC (HR 0.715, *P*=0.0001), but no improvement in OS was seen at the first interim analysis (mOS 14 versus 13.9 months). More mature data are needed to evaluate long-term benefit of the strategy; with the use of atezolizumab with nab-PC today representing an option in patients with metastatic squamous NSCLC [I, B; not EMA-approved].

Is replaced with:
Atezolizumab was studied in patients with metastatic squamous NSCLC in the IMpower131 study. Patients were randomised to atezolizumab/carboplatin/paclitaxel, atezolizumab/carboplatin/nab-P or carboplatin/nab-P [100]. Atezolizumab/carboplatin/nab-P had improved PFS compared with carboplatin/nab-P (HR 0.715, P=0.0001), but no improvement in OS was seen at the first interim analysis (mOS 14 versus 13.9 months). More mature data are needed to evaluate the long-term benefit of the strategy; with the use of atezolizumab with carboplatin and nab-P today representing an option in patients with metastatic squamous NSCLC [I, B; not EMA-approved].

In the section "First-line treatment of NSCLC without actionable oncogenic driver, with contraindications to use of immunotherapy"

• The nab-PC regimen has been shown in a large phase III trial to have a significantly higher ORR compared with solvent-based paclitaxel/carboplatin (sb-PC), and less neurotoxicity [I, B] [113]. The benefits were observed in both SCC and non-SCC (NSCC), with a larger impact on response in SCC. For this reason, the nab-PC regimen could be considered a chemotherapeutic option in advanced NSCLC patients, particularly in patients with greater risk of neurotoxicity, pre-existing hypersensitivity to paclitaxel or contraindications for standard paclitaxel premedication [I, B].

Is replaced with:

• The carboplatin/nab-P regimen has been shown in a large phase III trial to have a significantly higher ORR compared with solvent-based paclitaxel/carboplatin (sb-PC), and less neurotoxicity [I, B] [113]. The benefits were observed in both SCC and non-SCC (NSCC), with a larger impact on response in SCC. For this reason, the carboplatin/nab-P regimen could be considered a chemotherapeutic option in advanced NSCLC patients, particularly in patients with greater risk of neurotoxicity, pre-existing hypersensitivity to paclitaxel or contraindications for standard paclitaxel premedication [I, B].

In "Table 4. Summary of recommendations"

1. • The nab-PC regimen could be considered a chemotherapeutic option in advanced NSCLC patients, particularly in patients with greater risk of neurotoxicity, preexisting hypersensitivity to paclitaxel or contraindications for standard paclitaxel premedication [I, B]

Is replaced with:

• The carboplatin/nab-P regimen could be considered a chemotherapeutic option in advanced NSCLC patients, particularly in patients with greater risk of neurotoxicity, preexisting hypersensitivity to paclitaxel or contraindications for standard paclitaxel premedication [I, B]

2. • The use of atezolizumab with nab-PC today represents an option in patients with metastatic squamous NSCLC [I, B; not EMA-approved]

Is replaced with:

• The use of atezolizumab with carboplatin and nab-P today represents an option in patients with metastatic squamous NSCLC [I, B; not EMA-approved]

A new acronym is defined:
nab-P, albumin-bound paclitaxel.

Figures

In "Figure 1. Treatment algorithm for stage IV SCC"

The following changes apply as shown in the updated version below.

1. PD-L1 < 50%

Is replaced with:
Any expression of PD-L1

2. Pembrolizumab + carboplatin/paclitaxel or nab-PC (4 cycles), followed by pembrolizumab [I, A][c]

Is replaced with:
Pembrolizumab + carboplatin/paclitaxel or carboplatin/nab-P (4 cycles), followed by pembrolizumab [I, A][c]

3. Atezolizumab + nab-PC (4-6 cycles), followed by atezolizumab [II, B][c]

Is replaced with:
Atezolizumab + carboplatin/nab-P (4-6 cycles), followed by atezolizumab [II, B][c]

4. Platinum-based ChT (see first-line treatment for PD-L1 < 50%, PS 0-1)

Is replaced with:
Platinum-based ChT (see first-line treatment without IO)

5. 4-6 cycles Carboplatin-based doublets

Is replaced with:
4-6 cycles Carboplatin-based ChT

New acronyms are defined:
IO, immuno-oncology; nab-P, albumin-bound paclitaxel.

In "Figure 2. Treatment algorithm for stage IV NSCC, molecular tests negative(*ALK/BRAF/EGFR/ROS1*)"
The following changes apply as shown in the updated version below.

1. PD-L1 expression[a] has been added to show the options between "PD-L1 $\geq$ 50%" and "Any expression of PD-L1"

2. Pembrolizumab/pemetrexed and platinum-based ChT (4 cycles), followed by pembrolizumab [I, A; MCBS 4]

Is replaced with:
Pembrolizumab/pemetrexed and platinum-based ChT (4 cycles), followed by pembrolizumab/pemetrexed [I, A; MCBS 4]

3. Atezolizumab/pemetrexed/platinum-based ChT (4-6 cycles), followed by atezolizumab [I, B][b]

Is replaced with:
Atezolizumab/pemetrexed and platinum-based ChT (4-6 cycles), followed by atezolizumab/pemetrexed [I, B][b]

4. 4-6 cycles

Is replaced with:
4-6 cycles Platinum-based ChT

5. nab-PC [I, B]

Is replaced with:
carboplatin/nab-P [I, B]

6. 4-6 cycles Carboplatin-based doublets

Is replaced with:
4-6 cycles Carboplatin-based ChT

7. For the following first-line treatment combinations, links have been added to show the treatment options in case of disease progression: pembrolizumab/pemetrexed and platinum-based ChT (4 cycles), followed by pembrolizumab/pemetrexed; atezolizumab/pemetrexed and platinum-based ChT (4-6 cycles), followed by atezolizumab/pemetrexed; atezolizumab/bevacizumab with carboplatin and paclitaxel (4-6 cycles), followed by atezolizumab/bevacizumab.

A new acronym is defined:
nab-P, albumin-bound paclitaxel.

In "Figure 3. Treatment algorithm for stage IV NSCC, molecular tests positive (*ALK/BRAF/EGFR/ROS1*)"

The following changes apply as shown in the updated version below.

Osimertinib [I, A][b]

Is replaced with:
Osimertinib [I, A; MCBS 4].

In "Figure 4. Treatment algorithm for stage IV lung carcinoma with *EGFR*-activating mutation"

The following changes apply as shown in the updated version below.

Carbolatin/paclitaxel/bevacizumab/atezolizumab [III, A][b]

Is replaced with:
Carboplatin/paclitaxel/bevacizumab/atezolizumab [III, A][b]

In "Figure 5. Treatment algorithm for stage IV lung carcinoma with *ALK* translocation"

The following changes apply as shown in the updated version below.

Carbolatin/paclitaxel/bevacizumab/atezolizumab [III, B][a]

Is replaced with:
Carboplatin/paclitaxel/bevacizumab/atezolizumab [III, B][a]

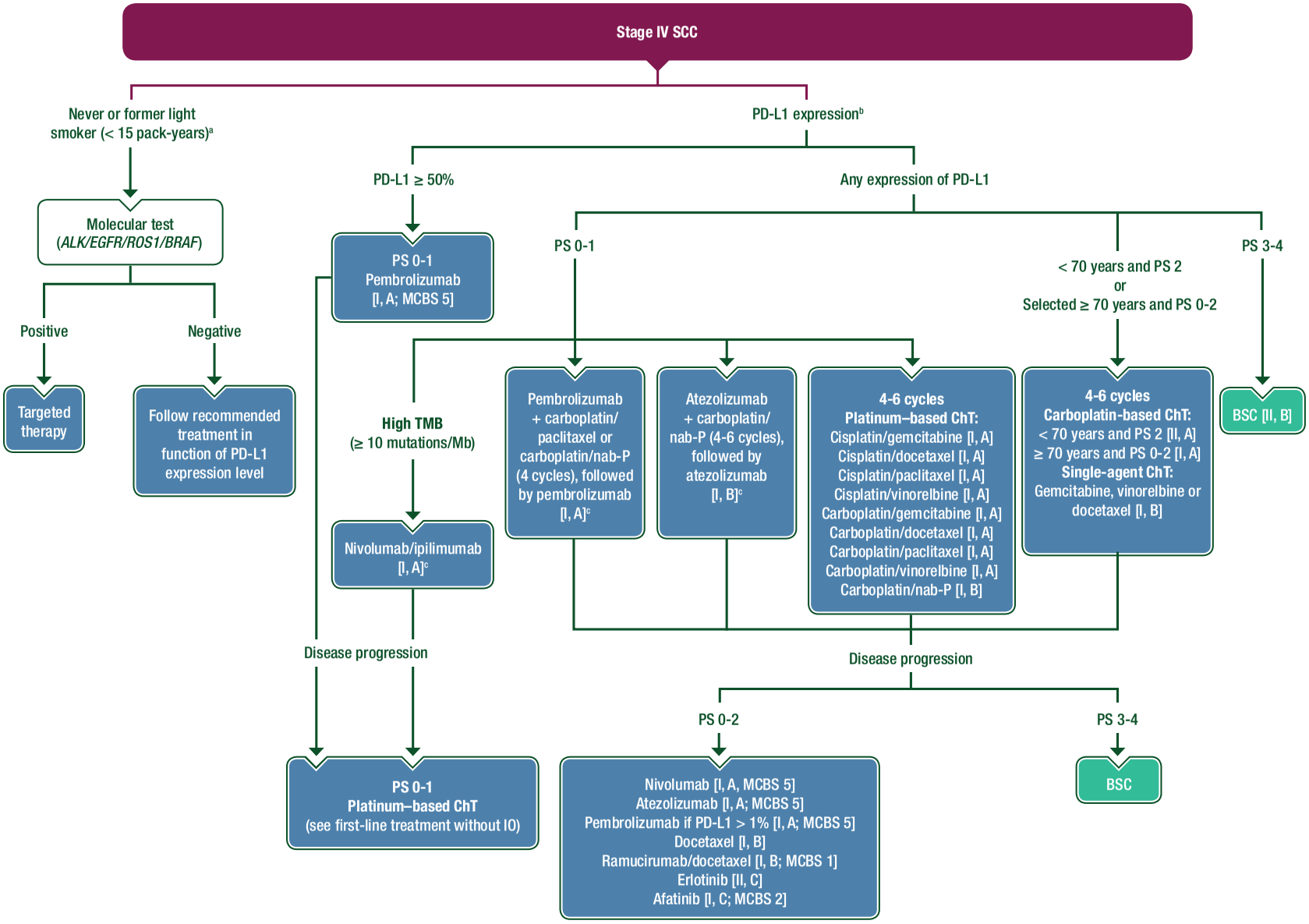

Figure 1. Treatment algorithm for stage IV SCC.

[a]Molecular testing is not recommended in SCC, except in those rare circumstances when SCC is found in a never-, long-time ex- or light-smoker (< 15 pack-years).

[b]In absence of contraindications and conditioned by the registration and accessibility of anti-PD-(L)1 combinations with platinum-based ChT, this strategy will be preferred to platinum-based ChT in patients with PS 0-1 and PD-L1 < 50%. Alternatively, if TMB can accurately be evaluated, and conditioned by the registration and accessibility, nivolumab plus ipilimumab should be preferred to platinum-based standard ChT in patients with NSCLC with a high TMB.

[c]Not EMA-approved.

ALK, anaplastic lymphoma kinase; BSC, best supportive care; ChT, chemotherapy; EGFR, epidermal growth factor receptor; EMA, European Medicines Agency; IO, immuno-oncology; Mb, megabase; MCBS, ESMOMagnitude of Clinical Benefit Scale; nab-P, albumin-bound paclitaxel; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PS, performance status; SCC, squamous cell carcinoma; TMB, tumour mutation burden.

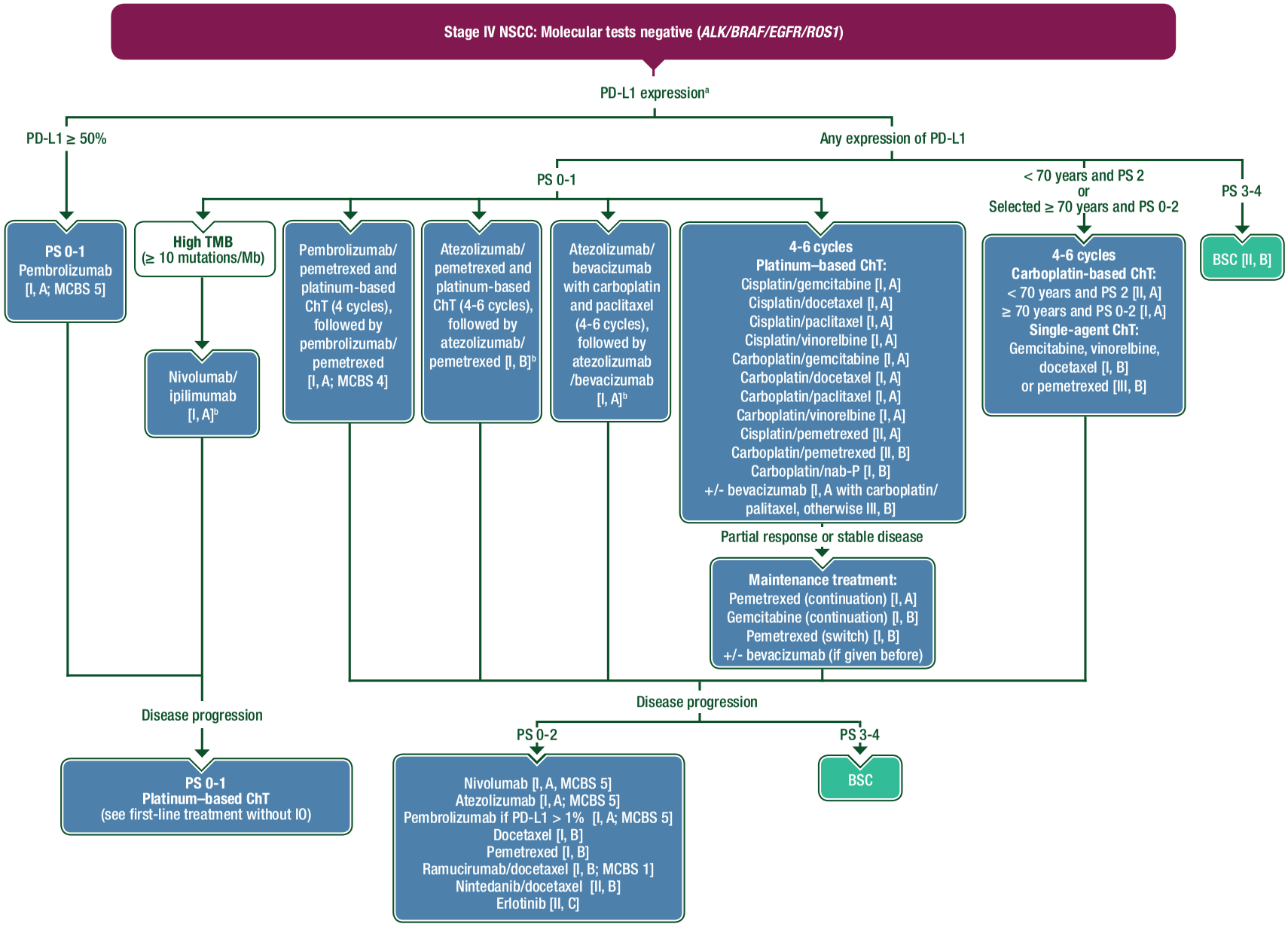

Figure 2. Treatment algorithm for stage IV NSCC, molecular tests negative (*ALK/BRAF/EGFR/ROS1*).

[a]In absence of contraindications and conditioned by the registration and accessibility of anti-PD-(L)1 combinations with platinum-based ChT, this strategy will be preferred to platinum-based ChT in patients with PS 0-1 and PD-L1 < 50%. Alternatively, if TMB can accurately be evaluated, and conditioned by the registration and accessibility, nivolumab plus ipilimumab should be preferred to platinum-based standard ChT in patients with NSCLC with a high TMB.

[b]Not EMA-approved.

ALK, anaplastic lymphoma kinase; BSC, best supportive care; ChT, chemotherapy; EGFR, epidermal growth factor receptor; EMA, European Medicines Agency; IO, immuno-oncology; Mb, megabase; MCBS, ESMO-Magnitude of Clinical Benefit Scale; nab-P, albumin-bound paclitaxel; NSCC, non-squamous cell carcinoma; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PS, performance status; TMB, tumour mutation burden.

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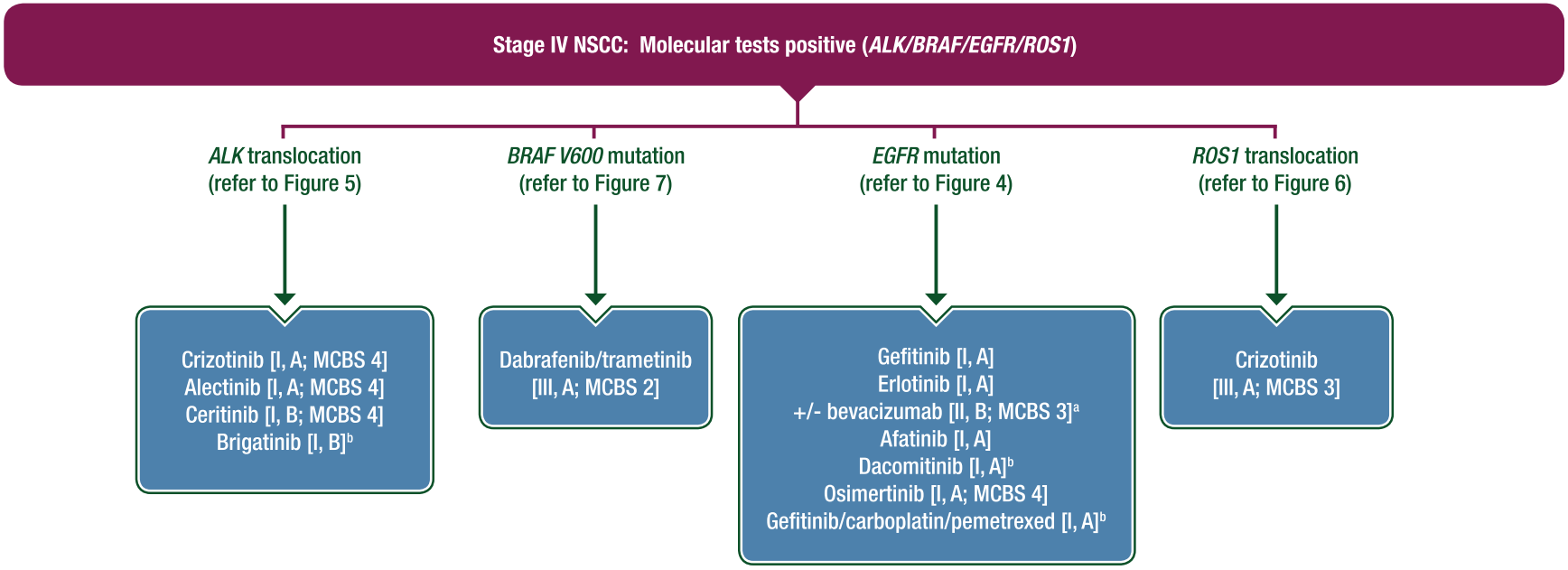

Figure 3. Treatment algorithm for stage IV NSCC, molecular tests positive (*ALK/BRAF/EGFR/ROS1*).
[a]MCBS score for the combination of bevacizumab with gefitinib or erlotinib.
[b]Not EMA-approved.
ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; EMA, European Medicines Agency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; NSCC, non-squamous cell carcinoma.

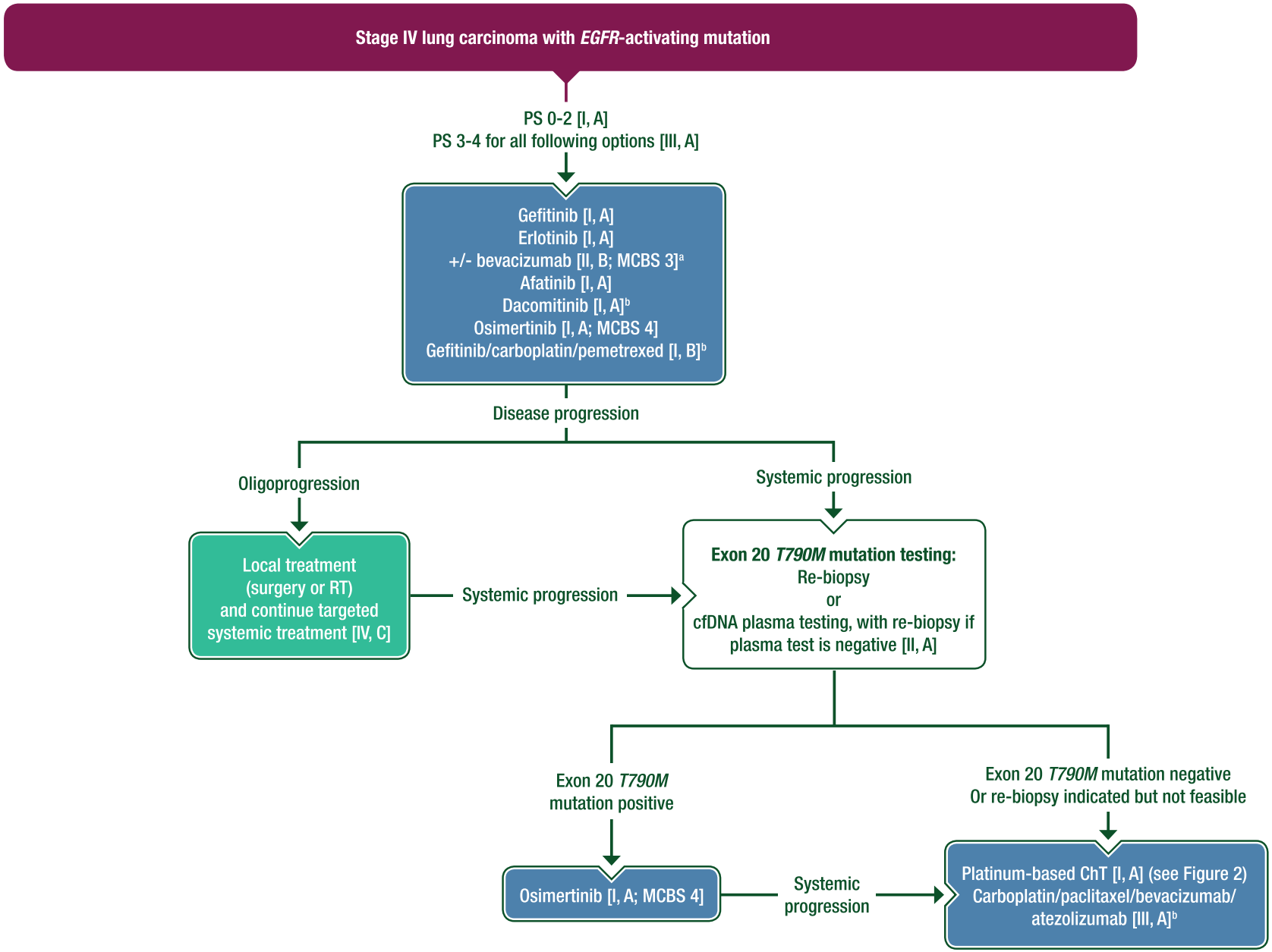

Figure 4. Treatment algorithm for stage IV lung carcinoma with *EGFR*-activating mutation.
[b]Not EMA-approved.
cfDNA, cell-free DNA; ChT, chemotherapy; EGFR, epidermal growth factor receptor; EMA, European Medicines Agency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PS, performance status; RT, radiotherapy.

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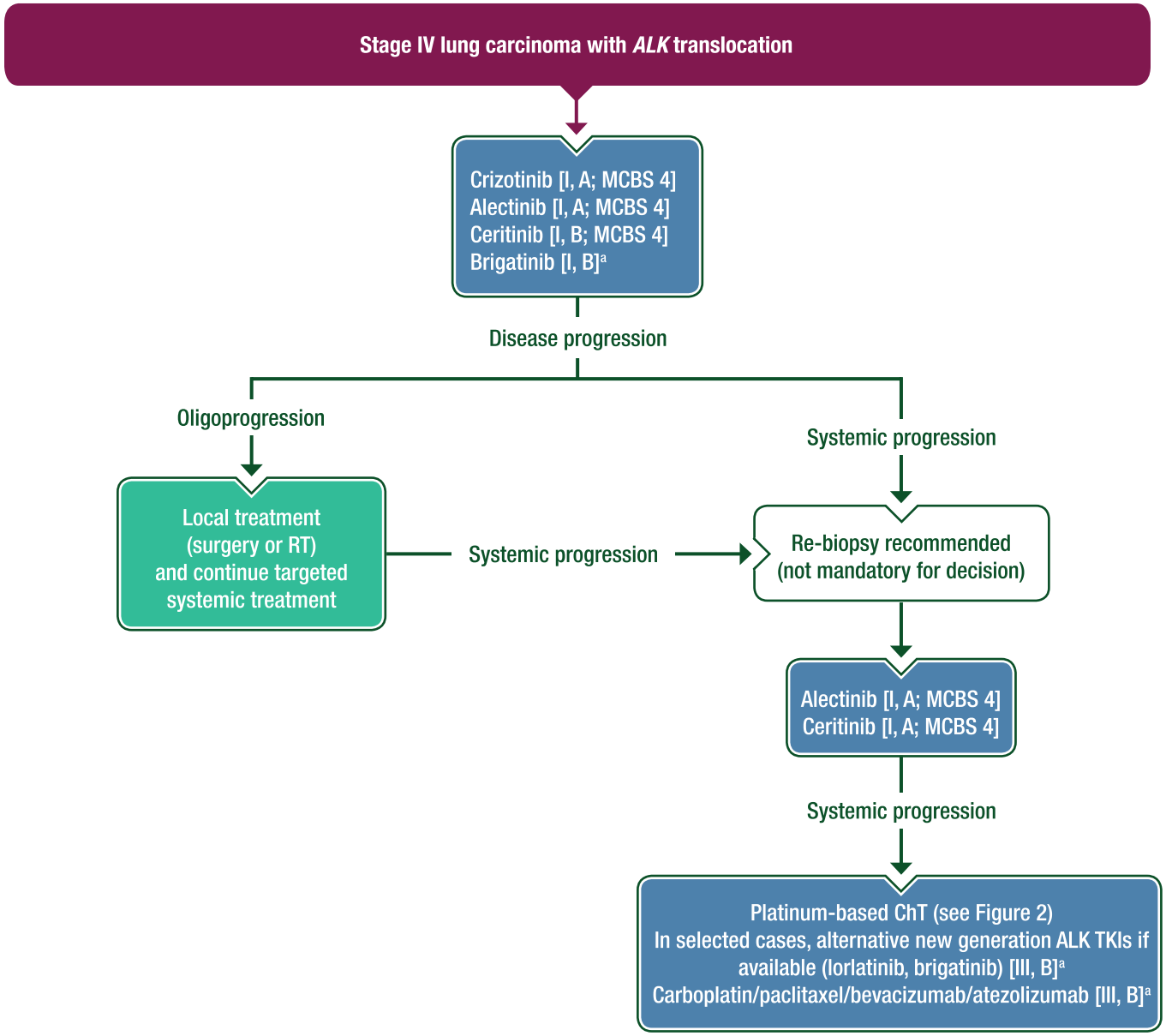

Figure 5. Treatment algorithm for stage IV lung carcinoma with ALK translocation.
[a]Not EMA-approved.
ALK, anaplastic lymphoma kinase; ChT, chemotherapy; EMA, European Medicines Agency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; RT, radiotherapy; TKI, tyrosine kinase inhibitor.