

## Second-line treatment of NSCLC without actionable oncogenic driver

- Patients clinically or radiologically progressing after first-line therapy with PS 0-2 should be offered second-line therapy irrespective of administration of maintenance treatment [I, A]
- In patients with progression after first-line immunotherapy with pembrolizumab, platinum-based ChT is recommended as second-line treatment option [V, B]
- There is a general trend across each of the phase III studies in second-line (nivolumab, pembrolizumab and atezolizumab versus docetaxel) for enriched efficacy of anti-PD-1/PD-L1 agents in patients with higher PD-L1 expression compared with those with no/less PD-L1 expression. However, unselected patients may still have improved survival and tolerability with anti-PD-1/PD-L1 agents compared with docetaxel [I, A]
- PD-L1 and PD-1 inhibitors (nivolumab, pembrolizumab and atezolizumab) are the treatment of choice for most patients with advanced, previously treated, PD-L1-naive NSCLC, irrespective of PD-L1 expression [I, A]
- Nivolumab is recommended in both squamous [I, A; ESMO-MBCS v1.1 score: 5] and non-squamous NSCLC [I, A; ESMO-MBCS v1.1 score: 5]
- Pembrolizumab is recommended in patients with previously treated NSCLC with PD-L1 expression > 1% [I, A; ESMO-MCBS v1.1 score: 5]
- Atezolizumab is recommended in patients with advanced NSCLC previously treated with one or two prior lines of ChT [I, A; ESMO-MCBS v1.1 score: 5]
- In patients not suitable for immunotherapy, second-line ChT is recommended. Comparable options as second-line therapy consist of pemetrexed, for NSCC only, or docetaxel, with a more favourable tolerability profile for pemetrexed [I, B]
- Treatment may be prolonged if disease is controlled and toxicity acceptable [II, B]
- Nintedanib/docetaxel is a treatment option in patients with adenocarcinoma progressing after previous ChT or immunotherapy [II, B]
- Ramucirumab/docetaxel is a treatment option in patients with NSCLC progressing after first-line ChT or immunotherapy with PS 0-2 [I, B]
- Combination of paclitaxel and bevacizumab is another treatment option [I, C] but it is not EMA-approved
- Erlotinib represents a potential second/third-line treatment option in particular for patients not suitable for immunotherapy or second-line ChT in unknown EGFR status or EGFR WT tumours [II, C]
- In patients with advanced SCC with PS 0-2 unfit for ChT or immunotherapy, afatinib is a potential option with unknown EGFR status or EGFR WT patients [I, C; ESMO-MCBS v1.1 score: 2]