Pembrolizumab

Formulary Management Expert Committee Responses to Drug Programs' Questions

Table 1: Response Summary

Drug program implementation questions	Clinical expert response	FMEC response
Considerations for relevant comparators		
Given that the comparator (adjuvant pembrolizumab 200 mg IV given every 3 weeks for a total of 17 to 18 doses) is publicly funded in Canada in patients with stage IIB/C; IIIB/C/D and stage IV melanoma, what should be the number of doses of pembrolizumab (17 or 18) in neoadjuvant-adjuvant settings for adult patients with resectable stage III or stage IV melanoma?	As per the clinical experts, in the neoadjuvant-adjuvant setting for adult patients with resectable stage III or stage IV melanoma, 3 cycles of pembrolizumab are given neoadjuvantly, and 15 cycles of pembrolizumab are given adjuvantly. One clinical expert noted that in one trial (for stage II), only 17 cycles of pembrolizumab were given. The expert also noted that the Ontario public drug plan funds 17 cycles for stage II, and 18 cycles for stage III and resected stage IV.	FMEC defers to the clinical experts' response. FMEC noted, however, that the SWOG S1801 trial used 18 doses in total and that patients with stage II disease were not included in the trial and are not part of the population within the scope of this review.
Considerations for initiating therapy		
Given that the interval between the last neoadjuvant treatment and surgery was expected to be no longer than 5 weeks, in the trial, would patients be eligible for treatment if the time following their last neoadjuvant dose and surgery is > 5 weeks?	As per clinical experts, these patients should be eligible for surgery beyond 5 weeks, as they may have had complications from their therapy or got ill, or there may have been potential issues with scheduling the surgery (i.e., delays in OR times).	FMEC noted that in the SWOG 1801 trial, a delay of up to 84 days (i.e., up to 12 weeks) was permitted.
Given that the current reimbursement policy allows patients to be retreated with PD-(L) 1 inhibitors (pembrolizumab or nivolumab) if 6 months or more have elapsed from the completion of adjuvant immunotherapy; should re-treatment with anti-PD-1 therapy align with this reimbursement policy for adjuvant pembrolizumab?	Clinical experts agree that re-treatment with anti-PD-1 therapy should align with the current reimbursement policy for adjuvant pembrolizumab.	FMEC agrees with the clinical experts that patients should have the same access to standard of care therapy.
Considerations for prescribing therapy		
Given that the dosing regimen in the trials was pembrolizumab 200 mg IV every 3 weeks (a total of 18 doses), can the patient be treated with 400 mg IV every 6 weeks to a maximum of one year (that is, as an extended	As per clinical experts, the extended interval dosing with immunotherapy has been used in some newer clinical trials. The clinical expert considered the extended dosing to be reasonable and noted that it should be left at the	FMEC agrees with the clinical experts that an extended dosing regimen may be considered.

Drug program implementation questions	Clinical expert response	FMEC response
interval) to reduce clinic visits/ chair time?	discretion of the patients and their oncologist.	
The jurisdictions wanted to inform FMEC that they have implemented weight-based dosing with a cap for pembrolizumab at 2 mg/kg to a maximum of 200 mg q3 weeks or 4 mg/kg to a maximum of 400 mg q6 weeks.	—	FMEC is aware that jurisdictions implement weight-based dosing to a cap. However, no data were reviewed regarding this particular issue as part of this project.
Special implementation issues		
Can patients with stable CNS metastasis be eligible for this treatment approach?	As per the clinical experts, patients with stable CNS metastasis are not suitable for this treatment approach, as they are considered metastatic and are better suited for other treatment options.	FMEC agrees with the clinical experts.
Given that CDIAC previously aligned adjuvant therapy to include stage IV pembrolizumab with nivolumab criteria (as oncologists consider them equivalent), would nivolumab possibly be aligned on the same premise in the neoadjuvant-adjuvant setting?	One clinical expert considered pembrolizumab and nivolumab interchangeable drugs in the adjuvant setting, given their similar efficacy and toxicity profile (which is also supported by clinical trials). Therefore, these 2 drugs could be aligned on the same premise. However, the clinical expert noted that there are no specific reasons to use nivolumab (rather than pembrolizumab) in this patient population unless a patient had a severe infusion reaction. Another clinical expert noted that nivolumab cannot be aligned on the same premise as that of pembrolizumab in the neoadjuvant-adjuvant setting, because of the different dosing schedule (i.e., every 2 or 4 weeks)	No data were provided to FMEC for any conclusion to be drawn regarding the alignment of nivolumab to the neoadjuvant-adjuvant pembrolizumab reimbursement criteria.

CNS = central nervous system; CDIAC = Cancer Drug Implementation Advisory Committee, currently CADTH's pan-Canadian Oncology Drug Review Expert Review Committee (pERC); FMEC =. Formulary Management Expert Committee.