Canada's Drug Agency
L'Agence des médicaments du Canada

Trametinib

FMEC Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug Program Implementation Questions	Clinical Expert Response (Clinical experts act as guest specialists for FMEC)	FMEC Response
Considerations for Relevant Comparators		
The GOG 281/LOGS study compared trametinib to standard of care options (paclitaxel, pegylated liposomal doxorubicin, topotecan, letrozole, or tamoxifen).	According to the clinical experts, there are no defined standard of care options in recurrent low-grade serous ovarian cancer, with limited availability of treatment options and of low effectiveness. The clinical experts expressed that the standard of care treatments used in the GOG 281/LOGS trial are indeed those commonly used in clinical practice for patients with low-grade disease, in the absence of more efficacious treatments. The clinical experts outlined that while current treatments for recurrent low-grade serous ovarian cancer mirror that of recurrent high-grade serous ovarian cancer, patients with low-grade disease commonly experience significantly reduced response rates. It would be reasonable to offer treatment with trametinib after experiencing treatment failure with either carboplatin-paclitaxel or hormonal therapy (e.g., letrozole, tamoxifen), according to the clinical experts.	FMEC recommends that the eligibility be the same as the clinical trial, which was failure or recurrence after platinum containing chemotherapy.
Special Implementation Issues		
The GOG 281/LOGS clinical trial requires measurable disease, as defined by RECIST criteria. Is this reasonable, if funded?	The clinical experts indicated that for patients to be eligible for treatment with trametinib, it would be reasonable to include measurable disease, as defined by RECIST criteria per the GOG 281/LOGS trial. The clinical experts noted that in low-grade serous ovarian cancer, tumour markers (e.g., CA125) are often unreliable disease indicators, and that clinicians rely mainly on radiological and clinical assessments to assess treatment effectiveness. The clinical expert remarked that in the scenario where patients undergo optimal secondary cytoreductive surgery such that no gross visible disease remains, it is unclear whether treatment with trametinib would be appropriate due to an absence of evidence from clinical trials to help inform.	FMEC agrees with the clinical experts. Refer to the initiation and discontinuation criteria for details.

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The clinical trial measured efficacy by contrast CT or MRI lesion assessment every 8 weeks for 15 months and then every 3 months thereafter. Access to that frequency may be a concern.	Imaging assessments in the GOG 281/LOGS trial were conducted more frequently than what would be done in clinical practice, according to the clinical experts. Given that disease recurrence occurs at a relatively slow pace in low-grade serous ovarian cancer, the clinical experts felt that it would be reasonable to include CT or MRI assessments every 3 to 6 months (12 to 24 weeks) until stable or resolution of disease. The clinical experts added that subsequent imaging assessment could be alternated with clinical examination approximately every 6 months at the discretion of the prescribing clinician, with earlier or more frequent imaging assessment if patients experienced worsening clinical symptoms.	FMEC agrees with the clinical experts. However, the monitoring should be based on standard local practice. Refer to the initiation and discontinuation criteria for details.

CT = computed tomography; FMEC = Formulary Management Expert Committee; MRI = magnetic resonance imaging; RECIST = Response Evaluation Criteria in Solid Tumors.