Nab-Paclitaxel With Gemcitabine

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		
How does nab-paclitaxel with gemcitabine compare to currently funded options in this therapeutic space: • modified FOLFIRINOX, which is used as adjuvant therapy for 6 months • gemcitabine plus capecitabine, which is used as adjuvant therapy for less fit patients • gemcitabine alone, for patients with a borderline performance status or a comorbidity profile that precludes multiagent therapy?	As per the clinical experts, nab-paclitaxel with gemcitabine is generally not used in the adjuvant setting due to lack of supportive data and failure to meet primary end points in trials such as APACT. Instead, modified FOLFIRINOX remains the standard for adjuvant therapy when patients can tolerate it. For those who cannot, gemcitabine plus capecitabine is recommended as the standard of care, particularly when multiagent therapy such as FOLFIRINOX is not suitable. Gemcitabine alone is typically reserved for those with borderline performance status or significant comorbidities that preclude more aggressive treatments.	FMEC agrees with the experts (refer to Special Implementation Issues for patients who cannot receive 5-FU–based therapies, such as those with DPD deficiency or *DPYD* polymorphism).
Considerations for initiation of therapy		
Which histologies, stages, and subgroups of pancreatic cancer should be eligible for adjuvant treatment?	As per the clinical experts, patients with resected pancreatic adenocarcinoma are eligible for adjuvant treatment. The experts emphasized that the clinical trials focused exclusively on pancreatic adenocarcinomas, excluding pancreatic neuroendocrine tumours from this review.	FMEC agrees with the experts.
What is an appropriate time frame to initiate adjuvant therapy following resection of pancreatic cancer (e.g., 8 to 12 weeks)?	As per the clinical experts, it is reasonable to initiate adjuvant therapy following resection of pancreatic cancer within 8 to 12 weeks. However, in specific settings, initiating adjuvant therapy beyond 12 weeks may still be considered appropriate.	FMEC agrees with the experts.
Can nab-paclitaxel with gemcitabine be given again to patients who subsequently relapse after completing therapy? If so, what is the appropriate disease-free interval or time frame after completion of adjuvant therapy to use	As per the clinical experts, nab-paclitaxel with gemcitabine can be given again to patients who subsequently relapse after completing therapy. As per the experts, it is appropriate to readminister nab-paclitaxel with gemcitabine if the recurrence occurs 1 year or more after therapy; however, they acknowledge that the	FMEC agrees with the experts and suggests allowing re-treatment if the recurrence occurs after 6 months as per standard oncology procedures.

Drug program implementation questions	Clinical expert response	FMEC response
nab-paclitaxel with gemcitabine in the advanced or metastatic setting?	aggressive nature of pancreatic cancer may necessitate a shorter interval.	
Should patients with a DPD deficiency or a *DPYD* polymorphism, and it is identified that exposure to fluoropyrimidine-based therapy is contraindicated due to concerns about toxicity, be eligible for adjuvant treatment with nab-paclitaxel with gemcitabine?	As per the clinical experts, patients with complete DPD deficiency or *DPYD* polymorphism would be eligible for adjuvant treatment with nab-paclitaxel with gemcitabine.	FMEC agrees with the experts: treatment may be considered with nab-paclitaxel with gemcitabine or gemcitabine monotherapy.
Should patients with borderline resectable or potentially resectable pancreatic cancer be eligible for neoadjuvant or "conversion" therapy prior to surgery?	As per the clinical experts, patients with borderline resectable or potentially resectable pancreatic cancer are suitable candidates for neoadjuvant or conversion therapy before surgery. The experts suggest monitoring patients with CT scans at 3 months and 6 months into treatment to assess eligibility for surgical conversion. If a patient is deemed suitable for surgery at 3 months, they will proceed with the surgery followed by 3 months of adjuvant chemotherapy. Conversely, if a patient becomes suitable after 6 months of neoadjuvant therapy, no further adjuvant treatment is administered. The goal is to complete 6 months of total treatment. As per the experts, such incidents comprise approximately 10% of patients in practice.	FMEC cannot make recommendations for this clinical scenario as it is out of scope for this review.
For patients who received neoadjuvant therapy, should adjuvant systemic therapy with nab-paclitaxel with gemcitabine (if recommended) be administered to complete a total of 6 months of systemic chemotherapy?	As per the clinical experts, patients who undergo neoadjuvant therapy with nab-paclitaxel with gemcitabine should receive a total of 6 months of systemic chemotherapy, including periods of radiologic re-evaluation and potential surgical resection. If a patient completes 6 months of neoadjuvant therapy, typically, no additional treatment is recommended.	FMEC cannot make recommendations for this clinical scenario as it is out of scope for this review.
Special implementation issues		
What downstream treatment options are available in the advanced or metastatic setting for patients who experience disease progression while receiving nab-paclitaxel with gemcitabine in the adjuvant setting?	As per the clinical experts, FOLFIRINOX- or 5-FU–based therapies are primary options for these patients. Additionally, targeted therapies based on tumour NGS sequencing and participation in clinical trials are recommended for suitable patients.	FMEC agrees with the experts, except for patients with DPD deficiency or *DPYD* polymorphism, who would not use 5-FU–based therapy.

5-FU = 5-fluorouracil; FMEC = Formulary Management Expert Committee; FOLFIRINOX = leucovorin calcium (folinic acid)–fluorouracil–irinotecan hydrochloride–oxaliplatin; NGS = next-generation sequencing.