health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Essential Medicines List
Tertiary and Quaternary
Medication Review Summary

Indications: Adjuvant chemotherapy of potentially curable fully resected pancreatic cancer.

Medication Names: Capecitabine plus Gemcitabine

Background/Contextualisation:

Pancreatic cancer: Most recent data from National Cancer Registry (2013) reported newly diagnosed pancreatic cancer in 328 patients (176 males and 152 females), which probably represents under-reporting due to lack of histological diagnoses in many patients. The only potential for long-term survival is surgical resection with negative margins (R0) or microscopic residual disease (R1) although the long term outlook remains poor, with 5-year survival rates of less than 10%, making the need for effective adjuvant therapy essential. Data collected from the major academic centres in South Africa showed about 80 patients undergoing such resections per year.

Gemcitabine: Intravenous cytidine nucleoside analogue, on EML for advanced lung and bladder cancer but not pancreas cancer.

Capecitabine: Oral fluoropyrimidine prodrug of 5FU, which competitively inhibits thymidylate synthase, and thereby DNA synthesis, on EML for advanced gastric and colorectal cancer.

Evidence in adjuvant treatment of fully resected pancreatic cancer:

ESPAC-3 study randomised 1088 patients 1:1 to 5FU 425mg/m2 plus folinic acid 20mg/m2 for 1-5 days every 28 days or gemcitabine 1g/m2 once a week for 3 of every 4 weeks for 6 months. Median OS was 23.0 months (95% CI, 21.1-25.0) for 5FU plus folinic acid and 23.6 months (95% CI, 21.4-26.4) for gemcitabine (HR 0.94 [95% CI, 0.81-1.08]). 5 year survival was 17·5% (14·0–21·2) with gemcitabine and 15·9% (12·7–19·4) with 5FU plus folinic acid. **ESPAC-4 study** randomised 730 patients to gemcitabine alone or gemcitabine plus capecitabine, within 12 weeks of an R0 or R1 resection. Median OS for gemcitabine plus capecitabine was 28·0 months (95% CI 23·5-31·5) and 25·5 months (22·7-27·9) with gemcitabine alone (HR 0·82 [95% CI 0·68-0·98], p=0·032). The estimated 5 year survival was 16·3% (95% CI 10·2–23·7) for gemcitabine, and 28·8% (22·9–35·2) for gemcitabine plus capecitabine. 608 grade 3-4 adverse events were reported in 226 of 359 patients on gemcitabine plus capecitabine compared with 481 grade 3-4 adverse events in 196 of 366 patients on gemcitabine alone.

Summary of clinical efficacy:

Adjuvant gemcitabine plus capecitabine in R0 or R1 resected adenocarcinoma of the pancreas increases the median OS to 28 months from 25·5 months with gemcitabine alone (HR 0·82 [95% CI 0·68-0·98], p=0·032) as well as increasing the 5 year survival rate from 16.3% to 28.8% representing an absolute 5 year survival benefit of 12.5% and a NNT of 8.

Safety concerns:	Gemcitabine:	Capecitabine:
	Myelosuppression, mild emesis.	HFS, mucositis, diarrhoea

Budget impact at South African Academic Hospitals: *Estimated number of actual patients based on resection data*

No. of patients/year	Budget impact with gemcitabine plus originator capecitabine
81	**R1,861,685.31**

Recommendation:
Gemcitabine (weekly for 3 of 4 weeks) plus capecitabine x 21 days (for 6 cycles) is recommended for inclusion of the TQEML for the adjuvant treatment of fully resected adenocarcinoma of the pancreas only.

Review indicator: New adjuvant chemotherapy data in patients with R0 or R1 resected adenocarcinoma of the pancreas.

Date: August 2018