

Capecitabine and streptozocin ± cisplatin for gastroenteropancreatic neuroendocrine tumours: predictors of long-term survival in the NET01 trial

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Background: Cytotoxic chemotherapy for advanced, unresectable pancreatic and gastrointestinal foregut neuroendocrine tumours (GEPNETs) commonly comprises 5-fluorouracil (FU) plus streptozocin (S). The NET01 trial, conducted in the pre-kinase inhibitor era, recruited a broad spectrum of patients (pts) to investigate whether capecitabine (Cap) was an acceptable alternative to FU, with or without adding cisplatin (Cis). At median follow up 3.4 years, objective responses (primary endpoint) were reported as similar in the 2 arms, but CapSCis was more toxic. Final progression-free survival (PFS) and overall survival (OS) (secondary endpoints) as well as outcome predictors are now reported with longer follow up.

Methods: Pts with previously untreated advanced, unresectable NETs of pancreatic, gastrointestinal foregut or unknown primary site were randomised to receive three-weekly Cap 625mg/m² twice daily orally, S 1.0g/m² IV on day 1, ± Cis 70mg/m² IV on day 1. Pts could receive the same treatment beyond 6 cycles if there was evidence of benefit. All pts were followed 12 weekly for a minimum of 5 years.

Results: Of 86 (44 CapS, 42 CapSCis) pts randomised, 16% had poorly differentiated histology. With long-term median follow-up of 8 years, 83 (97%) pts have progressed/ died and 69 (80%) pts have died. The estimated median PFS was 11.1 months for CapS and 9.6 months for CapSCis (HR = 0.82, 95%CI: 0.53, 1.27). Median OS was 27 months for CapS and 26 months for CapSCis (HR = 0.97, 95%CI: 0.60, 1.56). Three and 5-year OS rates were 40% and 29%, with no difference between arms. Statistically significant factors predicting for OS were tumour Ki67 level, WHO grade and pt age. Addition of Cis to CapS did not appear to influence OS for high grade, poorly differentiated tumours, although numbers are small.

Table: 446P

		N	Overall CapS	CapSCis	Median OS (yrs)	Overall CapS	CapSCis
Age (yrs)	<60	46			3.3		
	≥60	40			2.1		
Ki67 (%)	≤ 9	32			3.5		
	10-24	20			4.6		
	≥25	15	7	8	0.4	0.4	0.5
WHO grade	G1	12			2.3		
	G2	43			3.5		
	G3	14	7	7	0.4	0.4	0.4

Conclusions: PFS and OS were similar for the CapS± Cis regimens. High patient age, tumour Ki67 and grade all predicted for poorer outcomes.

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