Aggressive multi-modality treatment of Pancreatic Neuroendocrine Tumours (pNETs): Outcomes in patients with Advanced Disease

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Background

Pancreatic Neuroendocrine Tumours (pNET) are increasing in incidence[(1), (2)].

They carry a relatively poor prognosis compared to other NETs, particularly when hepatic metastasis are present.

We have a proactive management strategy that is agreed in a weekly NET MDT.

We have studied our outcomes and determined survival at 1, 3 & 5 years and compared our outcomes to previously published data.

The data is on our whole cohort not on selected treatments and irrespective of age, fitness, age or co-morbidities.

Methods

Data was analysed from a single centre, prospective collected database.

All NET patients from 01/01/2000 to 31/12/2013 discussed at our NET MDT were analysed.

407 NET patients were identified.

95 were diagnosed as pNETs.

3 patients had incomplete records and were excluded from analysis.

Patients who received no active treatment were included.

Patients were staged according to AJCC 2010[(3)]

Multimodality treatment was analysed by number of treatment modalities & number of treatment episodes.

Kaplan Meier Survival curves used to compare outcomes of patients with pNET.

Results 1

92 patients were identified with a median follow up 39 months.
M:F (1:1), Mean age M:F 60:63
35 patients had stage 1-3 disease (median follow up 42 months), 2 deaths.
57 patients had stage 4 (metastatic) disease: liver only n=42, liver & other distant mets n=13, distant mets only n=2.

• 53 of these patients had unimodal or multimodal treatment as shown below:

Table 1: Modalities used in patients with stage 4 pNET

Surgery (n= 35):	Primary resection +/- Liver or Liver resection alone		
Oncology (n=44):	PRRT	Chemotherapy	Radiotherapy
Radiology (n=21):	Ablation (Cryo/Microwave)	Embolisation	SIRTEX
Medical (n=34):	Octreotide		Lanreotide

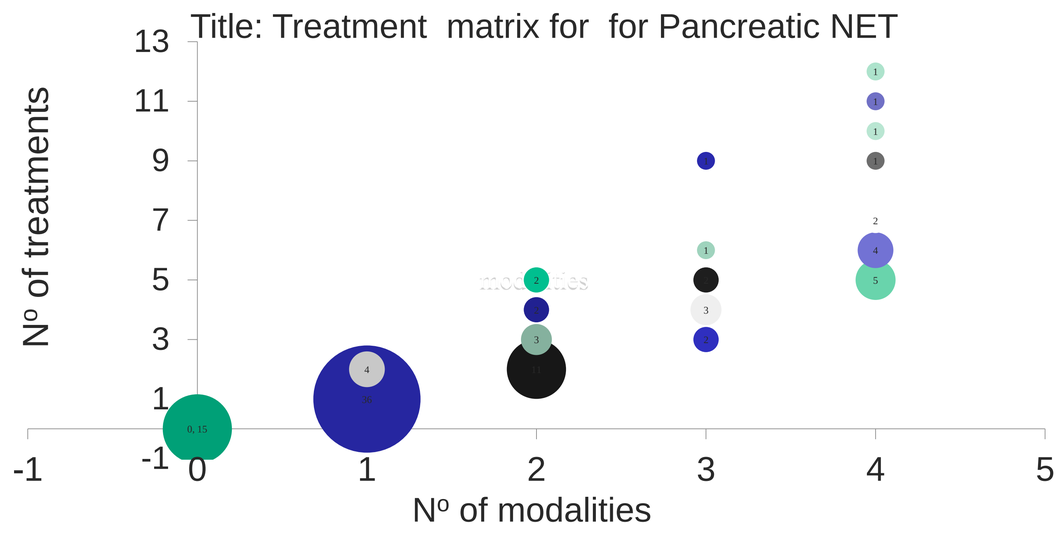

Fig 1: Treatment matrix- bubble size corresponds to Nº of patients

Treatments

Category	Description	Patients (n)	Treatment Episodes (n)
Surgery	Liver Resection	12	12
	Pancreatic resection	15	22
	Synchronous Liver and Pancreatic resection	18	23
IR	TACE/bland embolisation	33	65
	Ablation RFA/MWA/cryo	6	13
Systemic Therapy	Radiotherapy	2	2
	Chemotherapy	24	32
	PRRT	4	6
	Long acting Octreotide/ Lanreotide	33	Multiple doses

Of 29 receiving chemotherapy:
-Everolimus (n=12)
--Sunitinib (n=5),
-Combination therapy (n= 12)

4 Patients had Peptide Receptor Radionucleotide therapy (PRRT)

New treatments including SIRTEX now being carried out but not in patients up to the end of 2013

Results 2

<50% of patients died, thus mean not median survival calculated

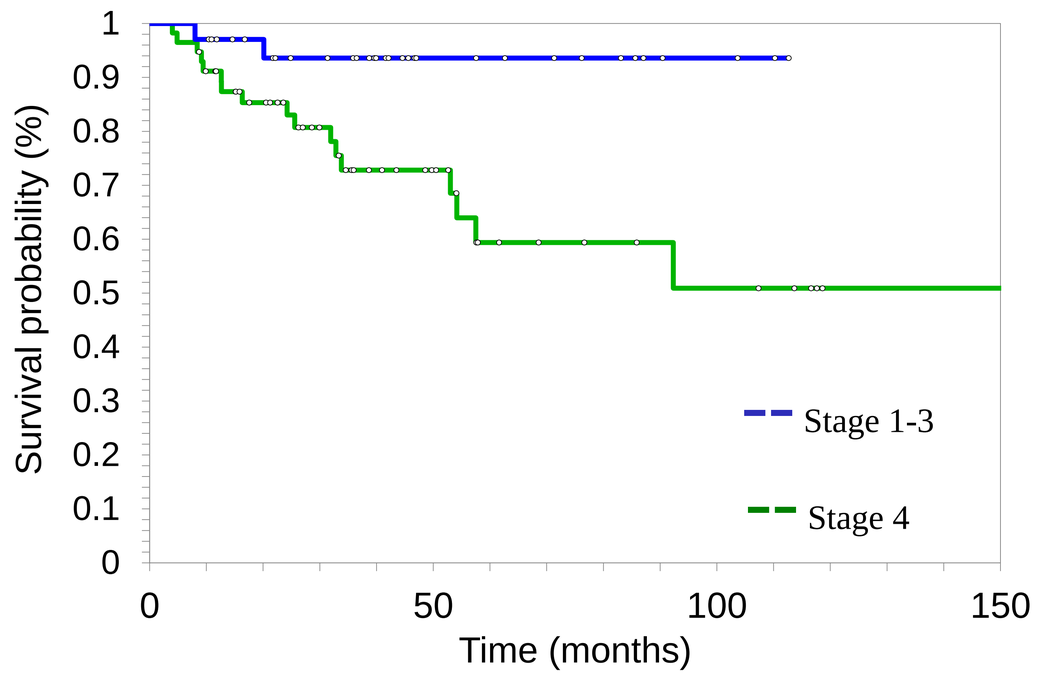

Table 2: Kaplan Meier survival estimates by stage of disease

	1yr	3yrs	5yrs	Mean survival
All pNETs	93%	86%	72%	92 months
Stage 1-3 (n=35)	97%	93%	93%	98 months
Stage 4 (n= 57)	91%	74%	61%	80 months

	p-value
Log-rank	**0.009**
Wilcoxon	**0.027**

Conclusions

- Aggressive multimodal treatment of stage 4 PNETS is likely to confer a survival advantage[(4)]
- Historical studies report 3yr survival at 70%[(5)] and 5 year survival at 13.7-40% in patients with stage 4 disease[(6)] compared to our results showing >60%
- The impact that proactive aggressive management has on quality of life is being studied

References

(1) PNETs: incidence, prognosis and recent trend toward improved survival.
Halfdanarson *et al,* An of Oncology, 19:1727–1733, 2008
(2) A 5 decade analysis of 13715 carcinoid tumours.
Modlin IM et al, CANCER 2003; 97: 934-959
(3) Exocrine and endocrine pancreas.
Springer: AJCC Cancer Staging Manual 7th Ed pp241-9
(4) Neuroendocrine Hepatic Metastases
Does Aggressive Management Improve Survival?
J G Touzios *et al.* Ann Surg. May 2005; 241(5): 776–785
(5) Pancreatic neuroendocrine tumors: presentation, management, and outcomes.
Nissen NN *et al: Am Surg*. *2009 Oct*;*75*(*10*):*1025-9*.(6)
(6) Pancreatic endocrine neoplasms: Epidemiology and prognosis of pancreatic endocrine tumours.
Thorvadur R et al; Endocr relat cancer June 2008; 15(2) 409-427

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