NET Masterclass 2017

Γρ. Καλτσάς

NET Παγκρέατος, Τι Νεότερο / Νέες Μελέτες

Μελέτη SEQTOR

Arms	Assigned Interventions
Active Comparator: Sequence A, drug: everolimus first Everolimus (10mg/daily, oral) followed by STZ-5FU (injection/infusion; Moertel or Uppsala regime).	Drug: Drug: Everolimus 10mg/daily, oral. Number of Cycles: until progression or unacceptable toxicity develops. Other Name: Afinitor Drug: STZ-5FU 0,5g/m2 STZ on days 1-5 and 400mg/m2 5-FU on days 1-5 every 6 weeks (Moertel) or 0,5g/m2 STZ on days 1-5 and 400mg/m2 5-FU on days 1-3, and then 1 day with 1g/m2 and 1 day 400mg/m2 5-FU every 3 weeks (Uppsala). Number of Cycles: until progression or unacceptable toxicity develops. Other Name: STZ based Chemotherapy
Experimental: Sequence B, drug: STZ - 5FU first STZ-5FU (injection/infusion; Moertel or Uppsala regime) followed by Everolimus (10 mg/ daily, oral)	Drug: Drug: Everolimus 10mg/daily, oral. Number of Cycles: until progression or unacceptable toxicity develops. Other Name: Afinitor Drug: STZ-5FU 0,5g/m2 STZ on days 1-5 and 400mg/m2 5-FU on days 1-5 every 6 weeks (Moertel) or 0,5g/m2 STZ on days 1-5 and 400mg/m2 5-FU on days 1-3, and then 1 day with 1g/m2 and 1 day 400mg/m2 5-FU every 3 weeks (Uppsala). Number of Cycles: until progression or unacceptable toxicity develops. Other Name: STZ based Chemotherapy

Μελέτη Cooperate

A randomized, open-label, phase 2 study of everolimus in combination with pasireotide LAR or everolimus alone in advanced, well-differentiated, progressive pancreatic neuroendocrine tumors: COOPERATE-2 trial.

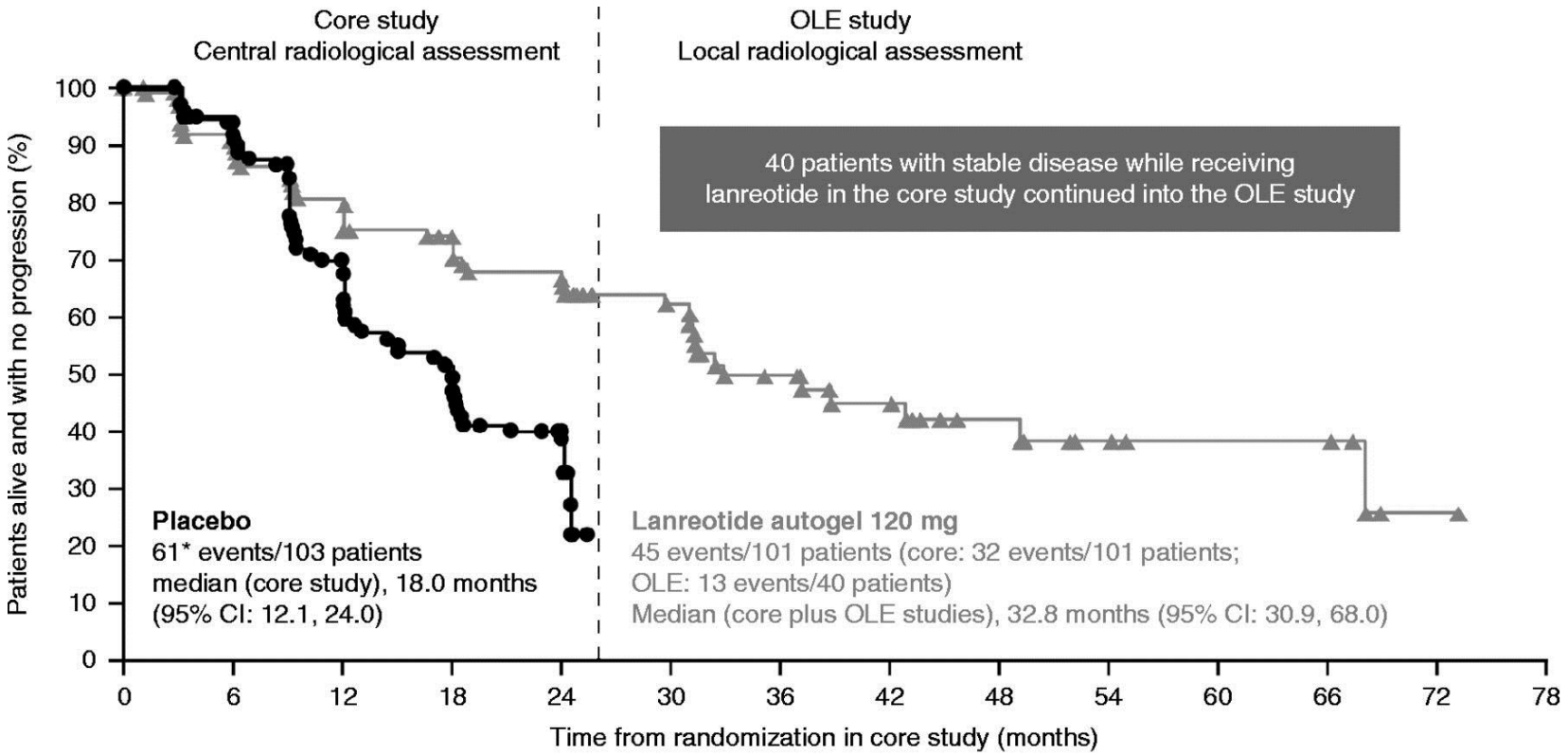
- **PATIENTS AND METHODS:**

Patients were randomized 1 : 1 to receive a combination of everolimus (10 mg/day, orally) and pasireotide long-acting release (60 mg/28 days, intramuscularly) or everolimus alone (10 mg/day, orally); stratified by prior SSA use, and baseline serum chromogranin A and neuron-specific enolase. The primary end point was progression-free survival (PFS).

- **RESULTS:**

No significant difference was observed in PFS: 16.8 months in combination arm versus 16.6 months in everolimus arm (hazard ratio, 0.99; 95% confidence interval, 0.64-1.54). Partial responses were observed in 20.3% versus 6.2% of patients in combination arm versus everolimus arm; however, overall disease control rate was similar (77.2% versus 82.7%, respectively). No significant improvement was observed in median overall survival.

Μελέτη CLARINET / επέκταση



Numbers of patients at risk of death or PD

101	84	71	61	51	36	25	17	11	7	5	5	1	0
103	87	59	43	26	0								

Clarinet Forte

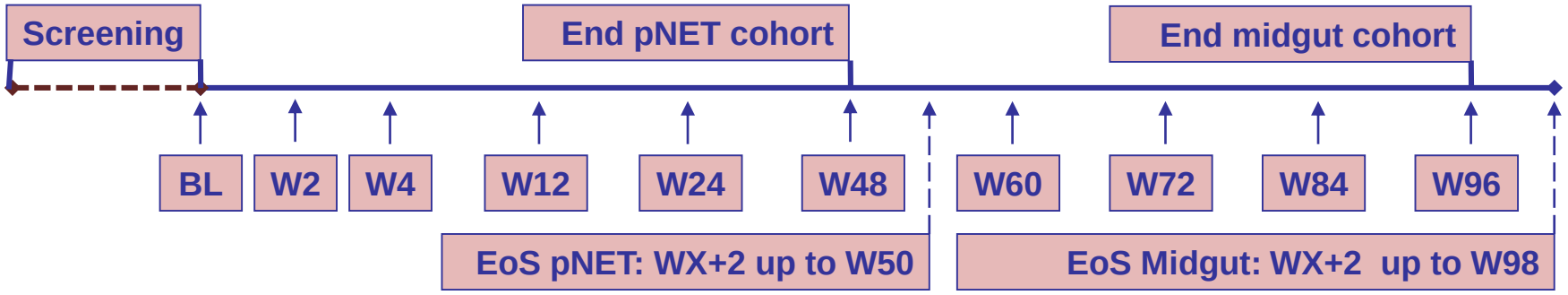
Multicentre, prospective, open label, non-comparative, phase II

- **100 Subjects**
  - **50 pNET**
  - **50 midgut NET**
- **Metastatic or locally advanced**
- **G1 and G2 (Ki ≤ 20%)**
- **Symptomatic and non-symptomatic**
- **Progressive disease as per RECIST 1.0 (central review) while on LAN ATG 120 mg q28d**
- **Treated with LAN ATG 120 mg q28d for at least 6 months**

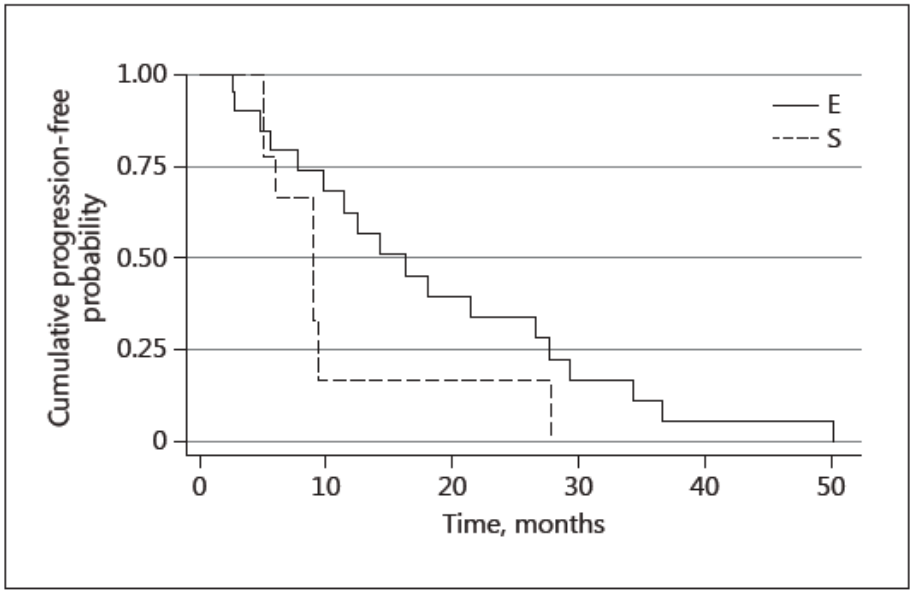
LAN ATG 120 mg q14d

Until tumour progression or death

48 W (pNET) or 96 W (midgut)*



Διαδοχική Θεραπεία με ΜΤΤ



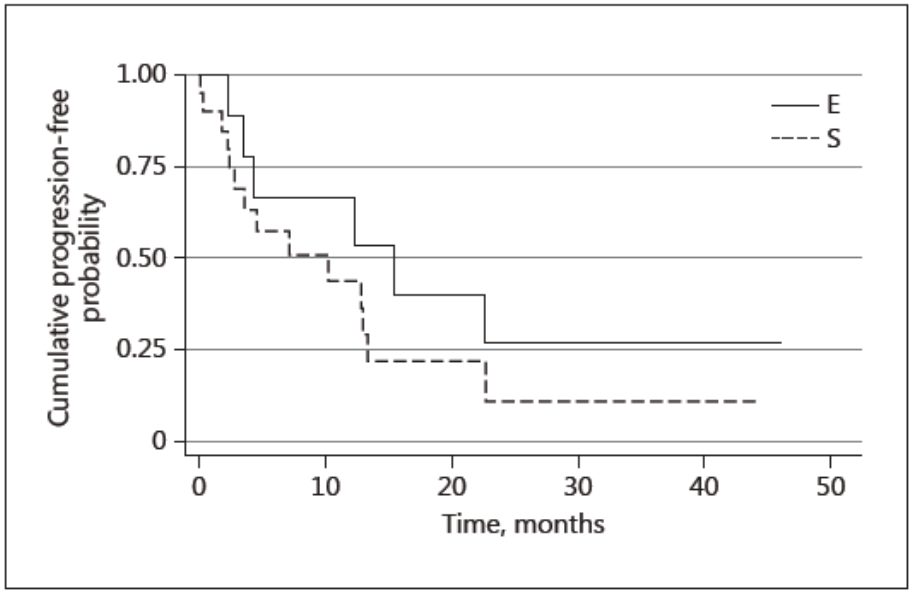
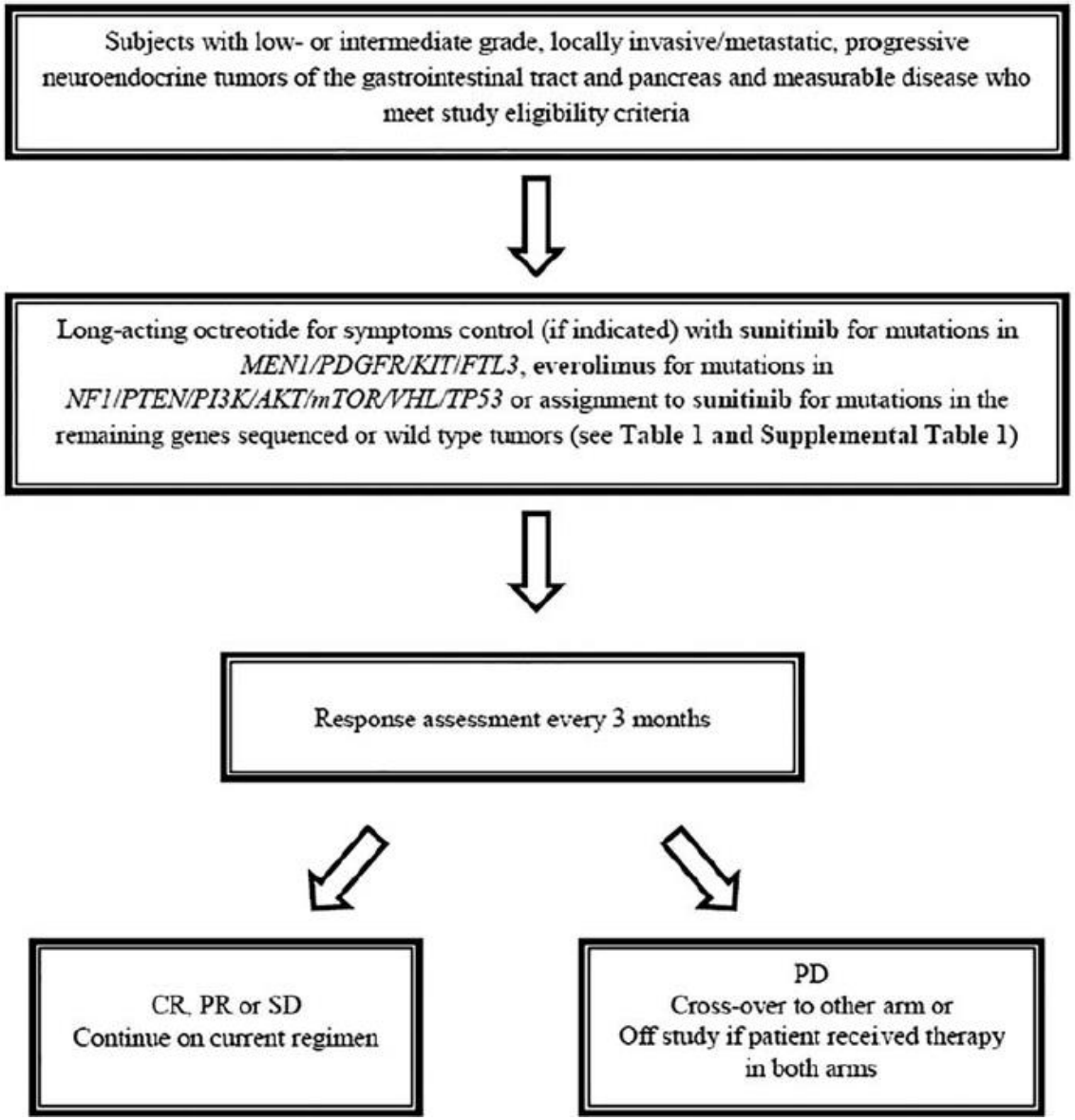


Table 1. Baseline patient characteristics and comparison of the patients in the 2 studied groups (sunitinib to everolimus vs. everolimus to sunitinib)

Characteristics	Whole group	Sunitinib to everolimus group	Everolimus to sunitinib group	*p* value
Patients, *n*	31	11	20	
Median age, years	52.5	51.46	57.9	0.3
Males, %	23	9 (81%)	14 (80%)	0.5
Stage	all stage IV	all stage IV	all stage IV	
Grade				
1	8 (26%)	4 (36%)	4 (25%)	0.8
2	19 (61%)	6 (55%)	13 (65%)	0.8
Unknown	4 (13%)	1 (1%)	3 (15%)	
Familial syndrome	4 (13%)	1 (MEN-1)	3 (all MEN-1)	
Functional syndrome	10 (32%)	2 (18%)	8 (40%)	0.2

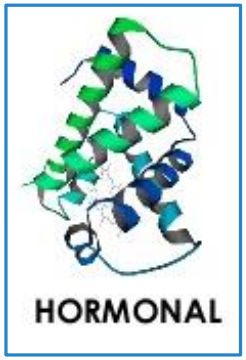
Θεραπεία με ΜΤΤ ανάλογα με μοριακό προφιλ

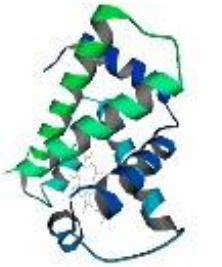
Figure 1 Study flow chart. CR, complete response; PR, partial response; SD, stable disease; PD, disease progression.



Paraneoplastic Syndromes (PNS)

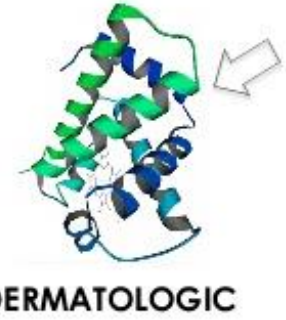
- Endocrine, Neurological, Mucocutaneous, Haematological, others

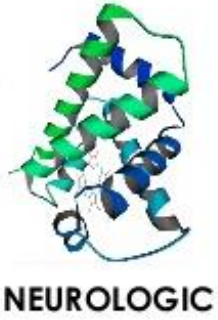




Polycythemia
Granulocytosis
Anemia

Dermatomyositis
Acanthosis nigricans





Lamber-Eaton Myasthenic syndrome
Cerebellar degeneration

Endocrine PNS

Dimitriadis et al; ERC 2017

Table 3 Endocrine and non-endocrine tumours causing paraneoplastic syndromes.

Paraneoplastic syndrome	Tumour types
Common	
Humoral hypercalcemia of malignancy (HHM)	Squamous cell (head and neck, lung, skin), breast, genitourinary (ovary, testis), lymphomas, renal, multiple myeloma, chronic lymphocytic leukaemia, lung (SCLC), colorectal, GI-NETs
Syndrome of inappropriate anti-diuretic hormone secretion (SIADH)	Lung (squamous, SCLC, LCLC, bronchial carcinoids), prostate, breast, adrenal, GI
Cushing's syndrome	Lung (SCLC, bronchial carcinoids, LCLC), thymus, MTC, pNET, pheochromocytomas, parangliomas, neuroblastomas
Less common	
Non-islet cell tumour hypoglycaemia (NICTH)	Mesenchymal tumours (sarcomas, GIST), renal, ovary, NETs
Gynaecomastia/virilisation (β-hCG)	Lung (SCLC, bronchial carcinoids), GCT (seminomas, teratomas, choriocarcinomas, yolk sac), pNETs
Rare	
Acromegaly	pNETs, lung (bronchial carcinoids), choristomas, hamartomas, gliomas, gangliocytomas
Hypertension	Lung (SCLC, bronchial carcinoids), paragangliomas, renal, DSRCT
Ovarian hyperstimulation syndrome/PCOS like	pNETs, lung (bronchial carcinoids)
Hyperprolactinaemia	Lung (SCLC), mesenchymal tumours
Hyperthyroidism	Ectopic pituitary adenomas, struma ovarii
Secretory diarrhoea	Lung (SCLC), MTC, pheochromocytoma, renal
Tumour induced osteomalacia (TIO)	Mesenchymal tumours, prostate, colon
Ileus	Glomus tumours (skull base)
Acute inflammatory reaction/pyrexia	Pheochromocytomas, mesenchymal tumours, angiomatoid fibrous histiocytoma

β-hCG, beta-human chorionic gonadotrophin; DSRCT, desmoplastic round cell tumours; GI-NETs, gastrointestinal neuroendocrine tumours; GIST, gastrointestinal stromal tumours; LCLC, large cell lung carcinoma; MTC, myeloid thyroid carcinoma; PCOS, polycystic ovary syndrome; pNETs, pancreatic neuroendocrine tumours; SCLC, small cell lung carcinoma.