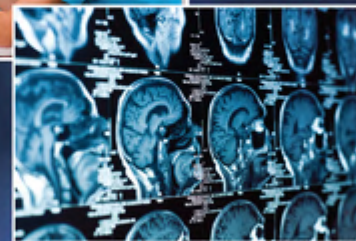


E2212: A randomized, double-blinded, placebo-controlled Phase II study of adjuvant everolimus following the resection of metastatic pancreatic neuroendocrine tumors to the liver

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Background

- Cytoreductive strategies (i.e. hepatic resection or ablation) for advanced pNET improve overall survival.¹⁻⁴
- For patients undergoing an R0 or R1 resection of liver metastases, median RFS is 15 months. Yet, the majority of patients recur (94% at 5 years).¹
- Everolimus confers a statistically significant 6-month prolongation in PFS compared to placebo in advanced pNETs (4.0 vs. 11.0 months)⁵

1. Mayo, Annals Surg Onc. 2010. 2. Elias, Surgery. 2003. 3. Knigge, Surgeon. 2008. 4. Yao, Surgery. 2001. 5. Yao, NEJM. 2011.

Schema and Study Design

Low and intermediate
grade advanced
pNETs following R0 or
R1 resection of hepatic
metastases
n=150

R
A
N
D
O
M
I
Z
E

Everolimus 10 mg po daily
for 12 months
n=75

Placebo po daily for 12
months
n=75

- Primary Endpoint: DFS (response assessment Q 3 months)
- Secondary Endpoints: OS, toxicity
- Stratification (to ensure balance between arms):
 - R0 vs. R1 resection
 - Primary tumor resected with metastectomy vs. primary tumor resected prior to metastectomy
 - Use of RFA or Microwave Ablation in addition to resection

Key Eligibility Criteria

- Patients with metastatic low or intermediate grade pancreatic neuroendocrine tumors to the liver who recovered from an R0 or R1 resection of all disease (including resection of a primary PNET if present) or resection plus microwave or radiofrequency ablation to R0 or R1 status
- Tissue available for central review to be done after patient enrollment not for eligibility (to include Ki-67 and mitotic index, NANETS grading system will be employed core biopsy preferred over FNA)
- Prior treatment with sunitinib and/or cytotoxic chemotherapy are allowed; no prior everolimus.
- ECOG performance status ≤ 2 .

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