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Thymic Neuroendocrine Neoplasia: Therapy with Everolimus

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Introduction Neuroendocrine neoplasia (NEN) of the thymus, also referred as thymic carcinoid, has a less favorable prognosis than NEN of other localization. With an estimated incidence of 2 per 10 million it is a very rare entity. Therefore no standard treatment is established. Usually therapy protocols for pulmonary carcinoid are used. So far no data exist on the effect of mTOR-inhibitors.

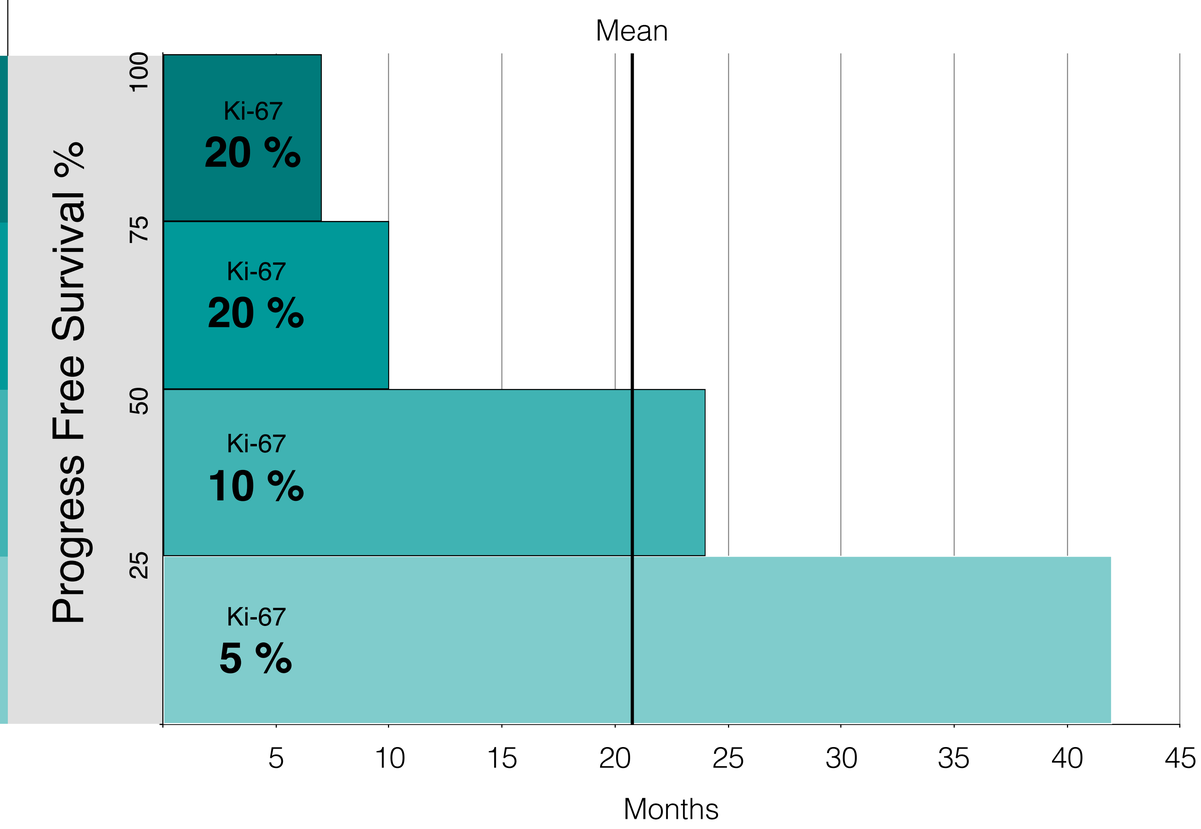
Material and Methods To address this issue, 4 patients with thymic NEN were treated with everolimus 10 mg/d after failure of at least one previous medical therapy. Everolimus was applied after a mean interval of 32.4 months (range 5 - 56) after first diagnosis.
The mean age at first diagnosis was 46 years (range 37 - 55).Thymectomy was performed in 3 cases. All patients developed bone metastasis. All patients were non smokers. No hormonal hypersecretion was observed, 1 patient had multiple endocrine neoplasia type 1.
The follow up included clinical examination, imaging (according RECIST criteria), and chromogranin A testing in 3 or 6 monthly intervals.

Results We observed stable disease for a mean of 20,8 months (7 - 42), median 17. Both patients with progress after 7 and 10 months had a Ki-67 index of 20 % and more previous therapies (3 and 6) than the others. No severe side effects occurred. In comparison to SEER database results[1] our patients had a better outcome despite a more advanced stage of disease.

Patient characteristics

Age & Gender	Tumor Size	Initial Symptoms	Disease Duration Before Everolimus	Prev. Medic. Therapies
38♂	13 cm	None	56 months	3
54♀	11 cm	Thoracic Pain	35 months	6
37♂ MEN-1	22 cm	Thoracic Pain	52 months	1
55♀	9 cm	Thoracic Pain	7 months	1

Kaplan-Maier Plot



Conclusions

- **Everolimus showed promising results in 4 thymic NEN**
- **The effect lasted longer, the lower the Ki-67 index**
- **The mean progress free survival was 20.8 months (range 7 - 42)**
- **The outcome was better than expected from SEER database results**

[1] Gaur P, Leary C, Yao J: Thymic Neuroendocrine Tumors: A SEER Database Analysis of 160 Patients. Annals of Surgery. 251(6):1117-1121, June 2010

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