

## New findings on thymic epithelial tumors: Something is changing

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### Abstract

Thymic epithelial tumors (TETs) are uncommon neo-

plasms with a wide range of anatomical, clinical, histological and molecular malignant entities. To date the management of TETs within clinical practice is based on a multimodal therapeutic strategy including surgery, chemotherapy and radiotherapy with a multidisciplinary approach and prognostic evaluation is mainly based on Masaoka staging and World Health Organization classification. Therefore novel strategies are needed, especially for refractory and/or recurrent TETs and for thymic carcinomas that present a poor prognosis. Personalized approaches are currently being developed and molecular targets are emerging from recent integrated genomic analyses. Targeted therapy will represent an important treatment option for TETs with an aggressive histology. To date, data indicate that vascular endothelial growth factor molecules, insulin-like growth factor 1 receptor, cyclin-dependent kinases and mammalian target of rapamycin may be potentially useful as targeted biological therapies.

**Key words:** Thymic epithelial tumors; Thymoma; Thymic carcinoma; Targeted therapy; Programmed cell death-1

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**Core tip:** Thymic epithelial tumors (TETs) are uncommon neoplasms with a wide range of anatomical, clinical, histological and molecular malignant entities. To date the management of TETs within clinical practice is based on a multimodal therapeutic strategy including surgery, chemotherapy and radiotherapy with a multidisciplinary approach and prognostic evaluation is mainly based on Masaoka staging and World Health Organization classification. Targeted therapy will represent an important treatment option for TETs with an aggressive histology.

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## INTRODUCTION

Thymic epithelial tumors (TETs) are uncommon neoplasms with a wide range of anatomical, clinical, histological and molecular malignant entities<sup>[1,2]</sup>.

## AVAILABLE TREATMENTS

To date the management of TETs within clinical practice is based on a multimodal therapeutic strategy including surgery, chemotherapy and radiotherapy with a multidisciplinary approach and prognostic evaluation is mainly based on Masaoka staging and World Health Organization classification.

## NEW EVIDENCES

Therefore novel strategies are needed, especially for refractory and/or recurrent TETs and for thymic carcinomas (TC) that present a poor prognosis. Personalized approaches are currently being developed and molecular targets are emerging from recent integrated genomic analyses<sup>[3-5]</sup>.

However where does research aim and what could we expect for the future in this setting?

We believe that targeted therapy will represent an important treatment option for TETs with an aggressive histology.

To date, data indicate that vascular endothelial growth factor molecules, insulin-like growth factor 1 receptor (IGF1R), cyclin-dependent kinases (CDK) and mammalian target of rapamycin may be potentially useful as targeted biological therapies.

In this regard, Thomas *et al.*<sup>[6]</sup> in non-randomized phase II trial demonstrated efficacy of sunitinib in patients with pre-treated TC.

As IGF1R overexpression is a poor prognostic factor, Rajan *et al.*<sup>[7]</sup> recently reported that Cituxumumab, an IGF1-R directed monoclonal antibody, could produce a promising 90% disease control rate in refractory thymomas.

Therefore, Besse *et al.*<sup>[8]</sup> have initiated a single-arm Phase II study with Milciclib, an CDK inhibitor, in advanced TC/B3 thymomas based on good overall response rate, observed in a phase I study.

Also Zucali *et al.*<sup>[9]</sup> conducted a single arm, single-stage, open label, multicentre phase II trial with everolimus in pre-treated TETs and TC patients. Out of 35 enrolled patients, 71.4% achieved disease control with a median PFS was 12.1 mo, while median OS was 24.0 mo.

The main aim of ongoing trials and new studies is to increase knowledge about etiology and genetic alterations involved in various types of TETs, leading to

development and use of biological therapies that will be particularly useful for managing of refractory, recurrent tumors and for TC.

Additionally, STAT3 and PD-L1 protein expression level, both involved in bad prognosis, may have vital importance to evaluate the prognosis of TETs, especially precise for the highly malignant TETs.

## CONCLUSION

In our opinion, further investigations on these genes could increase our knowledge about molecular mechanisms responsible for the TETS heterogeneity, about tumor interactions with adjacent healthy tissue and as regard its variegated response to treatments, to guarantee the development of new promising therapies<sup>[10,11]</sup>.

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