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1640TiP - PECATI: A phase 2 trial to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma

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BACKGROUND

- First-line platinum-based chemotherapy is the standard of care treatment for advanced B3-thymoma (B3-T) and thymic carcinoma (TC) [1]. However, the optimal treatment in patients with platinum refractory tumors is not yet defined.
- In the setting of platinum-refractory thymic epithelial tumors; two phase 2 trials have reported a meaningful clinical benefit in patients with TC when treated with the multi-tyrosine kinase inhibitors with antiangiogenic properties sunitinib [2] and lenvatinib [3]. Recently, immune checkpoint inhibitors (ICI), such as pembrolizumab [4-6], nivolumab [7], and avelumab [8] have also demonstrated encouraging antitumor activity with durable response. Despite recent advances, many patients still have a poor outcome with lack of alternative treatment options.
- Combination of ICI and antiangiogenic drugs is a novel approach that may provide greater antitumor activity compared to single-agent alone. Indeed, combination of pembrolizumab and lenvatinib has reported synergistic activity in other solid tumors [9,10].

OBJECTIVE

- PECATI evaluates the safety and efficacy of lenvatinib combined with pembrolizumab in patients with advanced B3-T or TC who progressed on or after at least one previous line of platinum-based chemotherapy.

METHODS

- This is an international, investigator-initiated, open-label, single-arm, phase 2 trial (NCT04710628).
- Patients will be treated with lenvatinib in combination with pembrolizumab on each 21-day cycle until disease progression, unacceptable toxicity, or patient refusal. Maximum duration of treatment will be 35 cycles. In case of withdrawal of any of the agents due to toxicity, monotherapy is allowed as per investigator's criteria.
- Tumor assessment through computed tomography (CT) scan or magnetic resonance imaging (MRI) will be performed at screening, at weeks 6 and 12, then every 9 weeks during the first 12 months, and every 12 weeks thereafter.
- Response will be assessed as best response according to Response Evaluation Criteria in Solid Tumors (RECIST) version (v.)1.1.
- An overview of the study design is shown in Figure 1.

STUDY ENDPOINTS

Primary Endpoint

- To evaluate the efficacy in terms of investigator-assessed 5-months progression-free survival (PFS).

Secondary Endpoints

- To assess the efficacy in terms of investigator-assessed overall response rate (ORR), maximum tumor shrinkage, disease control rate (DCR), duration of response (DoR) as per RECISTv.1.1., and overall survival (OS).
- To evaluate the safety and tolerability of lenvatinib in combination with pembrolizumab as per National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) v.5.0.

Exploratory Endpoints

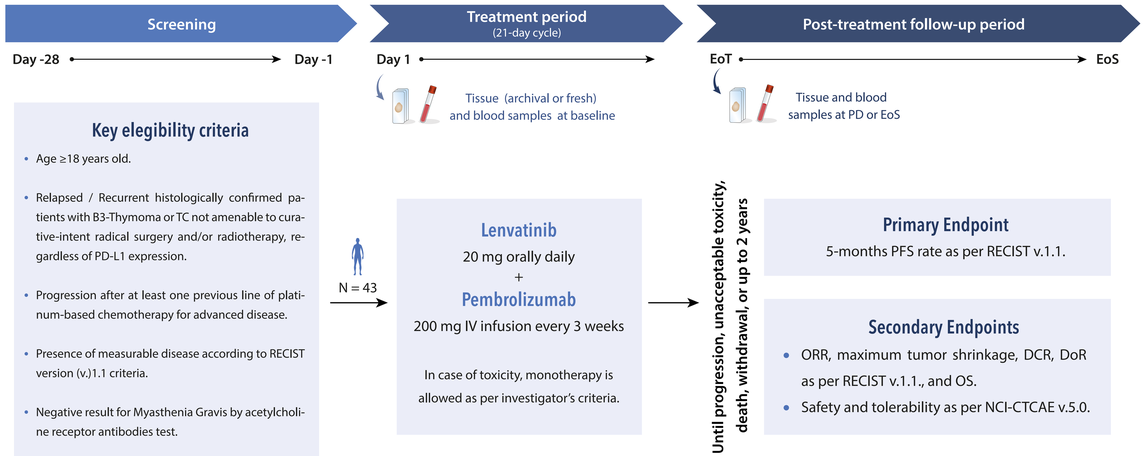
- To identify an optimal cut-off value by PD-L1 protein expression (22C3 anti-PD-L1 monoclonal antibody assay).
- To investigate blood tumor mutational burden by next-generation sequencing (NGS) at baseline and at the time of disease progression.
- To analyze genomic profile by NGS through a liquid biopsy test at baseline and at the time of disease progression.
- To determine immune-related gene signatures at baseline and at the time of disease progression.

STATISTICS

- A sample size of 43 patients who received at least 1 dose of study combination is planned.
- The primary analysis will estimate the 5-months PFS rate with the Kaplan-Meier method. The PFS rate will be compared to historical results for previous TC trials with pembrolizumab reporting PFS rates ranging from 4.2 to 6.1 months [4,6].
- The comparison will be conducted with exponential maximum likelihood estimation test (Null hypothesis: PFS rate ≤ 50%; Alternative hypothesis: PFS rate ≥ 68.6%).
- The design is planned to attain an 80% power at nominal level of one-sided alpha of 0.05.

STUDY DESIGN

Figure 1. PECATI Trial Design



Abbreviations: ECOG, Eastern Cooperative Oncology Group; EoS, End of Study; EoT, End of Treatment; IV, Intravenously.

TRIAL ENROLLMENT

- PECATI was opened to accrual in September 2021.
- There are currently 10 activated sites across Spain, France, and Italy.

ACKNOWLEDGEMENTS

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Presenter Author Conflict of Interest: Consultant / advisory role: MSD, BMS, Pfizer, Ose-Immunotherapeutics, Boehringer Ingelheim, Astra-Zeneca, Sanofi, Janssen, Takeda. **Talk in a company's organized public event:** MSD, Boehringer Ingelheim, Astra-Zeneca, Roche.

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