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Immunotherapy in Thymic carcinoma- Adding quality years to cancer saga!!!

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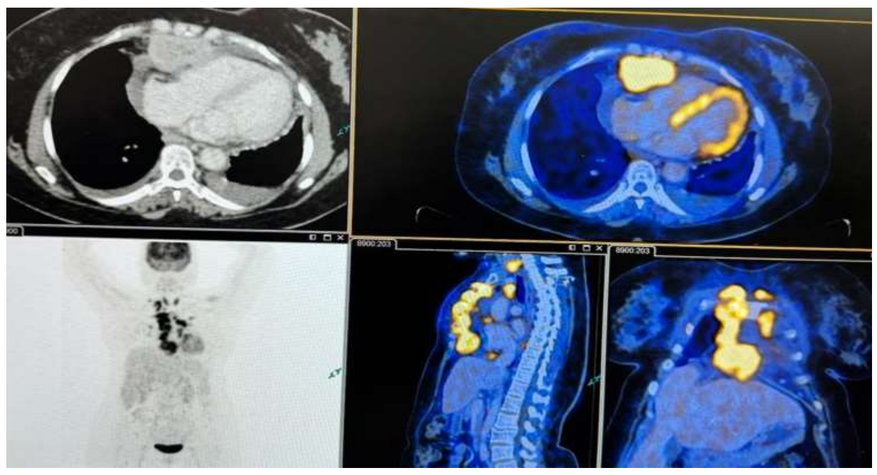
INTRODUCTION & AIM

- Limited treatment options exist for patients with thymic epithelial tumor (TET) whose disease progresses after platinum-based chemotherapy.
- Only a few prospective studies have investigated potential therapies in this setting.
- Recent studies have reported that PD-L1 is expressed in upto 70% of patients with TETs.
- The median progression-free survival even with pembrolizumab was 6.1 months in these relpased refractory thymomas.
- However, we present a case of relapsed thymoma with longer PFS benefit with pembrolizumab.

METHOD

- 54yr old female was initially diagnosed with Locally advanced Thymic carcinoma in Jan 2020.
- She received 3 cycles of gemcitabine + cisplatin followed by concurrent chemoradiation 66Gy/33# with weekly cisplatin.
- She developed dilated cardiomyopathy and was started on cardiac medications.
- She had very minimal disease progression in Jan 2021 and was started on OMCT with Tab Endoxan and Tab Methotrexate.
- After 6 months, due to further metastatic disease progression she received 9 cycles of Nabpaclitaxel+carboplatin last in Oct 2021.
- In Oct 2021, PET CT showed new metastatic nodes in the mediastinum, interval increase in pericardial effusion and bilateral pleural effusion. She was initiated on pembrolizumab 3weekly once (from 16/11/2021). Post 3 cycles she had partial response and was clinically better. She went on to receive total of 17 cycles, close to one year of pembrolizumab.
- She further developed oligoprogression in lymph nodes and hence received 40GY/10 fractions of IMRT.
- On further disease progression she received tab Lenvatinib and capecitabine. Finally, she succumbed to illness after 52 months of diagnosis.

OCT 2021



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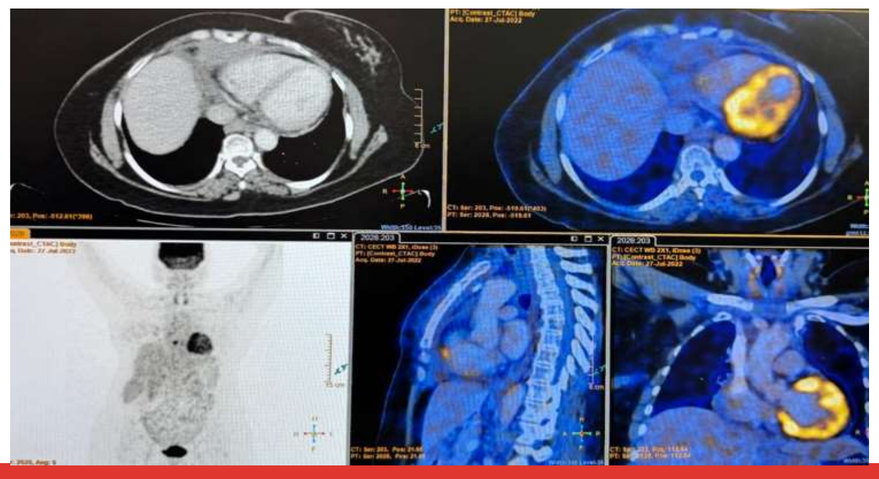

RESULTS & DISCUSSION

- Thymomas, thymic carcinomas, and thymic neuroendocrine tumors, collectively referred to as thymic epithelial tumors (TETs) are rare cancers.
- Molecular features include a low tumor mutation burden and lack of actionable genomic aberrations (1,2).
- TETs exhibit relatively high degrees of PD-L1 expression, with frequencies of 23–92% in thymomas and 36–100% in thymic carcinomas, providing a rationale for use of immune checkpoint blockade in recurrent TETs (3).
- However, the utility of PD-L1 expression as a predictive biomarker for ICI therapy in advanced or recurrent TETs is questionable due to high frequency of PD-L1 expression in non-neoplastic thymus and the potential effect of prior systemic therapies on PD-L1 expression in recurrent TETs (4).
- Among other well-recognized markers of response to ICIs, TETs have a low TMB and rarely exhibit MSI, documented in 0.3% of thymomas and 2.3% of thymic carcinomas (2).
- Emerging data suggest that autoimmune regulator (AIRE) deficiency, frequently observed in thymomas, increases sensitivity to immune checkpoint blockade (5).
- These observations highlight the role of less well-recognized features of TET biology that have the potential to increase responsiveness to immune checkpoint blockade and could provide an explanation for the activity of ICIs observed in clinical trials

INTERVENTION (REFERNCE)	TET HISTOLOGY	ENDPOINTS	NO OF EVALUABLE PATIENTS	ORR(%)	MEDIAN PFS(mo)	MEDIAN OS (mo)	GRADE 3or 4 irAEs (%)	All Grade Muscle or NM irAEs (%)
Pembrolizumab (6)	TC	ORR	40	22.5	4.2	25.5	15	7.5
Pembrolizumab (7)	T TC	ORR	7 26	28.6 19.2	6.1 6.1	NR 14.5	71.4 15.4	42.9 7.7
Nivolumab (8)	TC	ORR	15	0	3.8	14.1	20	20
Nivolumab (9)	B3T TC	PFS-6	49	12	6	21.3	57	3.7
AVelumab (10)	T TC	ORR and Safety	12 10	17 20	6.4 14.7	NR NR	58 45	25 9

CONCLUSION

- Pembrolizumab has showed encouraging antitumor activity in patients with advanced TET.
- Given the high incidence of autoimmunity, additional studies are needed to identify those who can benefit from pembrolizumab without immune-related adverse events.
- Also median survival of stage 4 thymic carcinoma is around 20-24months, however it can be prolonged to a greater extent with immunotherapy.

FUTURE WORK / REFERENCES

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