BARCELONA 2024 ESMO congress

Lenvatinib plus pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma: PECATI, single arm phase II clinical trial

Jordi Remon[1], Paolo Bironzo[2], Nicolas Girard[3], Laurence Bigay-Game[4], Oscar Juan-Vidal[5], Javier de Castro[6], Noemí Reguart[7], Laurent Greillier[8], Sophie Cousin[9], Eric Dansin[10], Margarita Majem[11], Reyes Bernabé[12], Joaquin Mosquera Martinez[13], Marta Díaz[14], Alba Meya [14], Daniel Alcalá-López[14], Alicia García-Sanz[14], Luisella Righi[15], Silvia Novello[2], Benjamin Besse[1].

[1]Department of Cancer Medicine, Gustave Roussy, Villejuif, France. [2]Department of Medical Oncology, University of Torino, San Luigi Gonzaga University Hospital, Orbassano, Italy. [3]Institut du thorax Curie Montsouris, Institut Curie Paris France UVSQ, Paris Saclay University, Paris, France.[4]Department of Pneumology and Thoracic Oncology, Centre Hospitalier Universitaire de Toulouse, Toulouse, France. [5]Department of Medical Oncology, Hospital Universitari I Politècnic La Fe, Valencia, Spain. [6] Department of Medical Oncology, Hospital Universitario La Paz, Madrid, Spain. [7]Department of Medical Oncology, Hospitla Clínic de Barcelona, Barcelona, Spain. [8]Department of Multidisciplinary Oncology and Therapeutic Innovations, Assistance Publique – Hôpitaux de Marseille, Aix Marseille University, Marseille, France. [9] Department of Medical Oncology, Institut Bergonié, Bordeaux, France.[10] Thoracic Oncology Unit, Centre Oscar Lambret, Lille, France.[11] Department of Medical Oncology, Hospital Sant Pau, Barcelona, Spain. [12]Department of Medical Oncology, Hospital Virgen del Rocío, Seville, Spain.[13]Department of Medical Oncology, Hospital Universitario de A Coruña, A Coruña, Spain.[14]Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil).[15]Department of Pathology, University of Turin, Turin, Italy.

DECLARATION OF INTERESTS

Dr. Jordi Remon

- **Receipt of grants / research support:** MSD, Astra-Zeneca (EORTC), Sanofi (EORTC).
- **Honoraria or consultant fees: Advisory boards (all institution):** AstraZeneca, EDIMARK. **Sponsored research (all institution):** MERCK
- **Other support / potential conflict of interest:** Speaker educational / webinars: AstraZeneca, Sanofi, Takeda Roche, Janssen. Travel: MSD. Other (non-financial): Secretary of EORTC-LCG.

Background

- Thymic Epithelial Tumors (TET) are rare malignancies (incidence: ≤ 1 case / 100.000 inh. / year)[1] and heterogeneous diseases based on histologic classification (thymoma and thymic carcinoma).[2]
- The histologic classification has prognostic value and correlates with the risk of autoimmune disorders (AID), reported in up to one third of patients. Myasthenia gravis the most common AID.[3]
- For patients with advanced TET, platinum-based chemotherapy is the standard first-line treatment option with no standard treatment at progression.[3]
- In patients with advanced pre-treated TET, the immune checkpoint blockers (ICB) and antiangiogenic agents either as monotherapy or in combination have reported clinically meaningful activity.[4-7]

PECATI trial (NCT04710628) assesses the efficacy and safety of pembrolizumab plus lenvatinib in pre-treated advanced B3-thymoma and thymic carcinoma

1. Gatta- Lancet Oncol 2017 * 2. Marx – JTO 2022 * 3. Girard – Ann Oncol 2015 * 4. Remon – Eur J Cancer 2023 * 5. Sato – Lancet Oncol 2020 * Niho – lung Cancer 2024 * Conforti –Lancet Oncol 2022

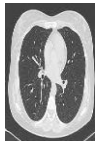
PECATI phase II: Study design

- Metastatic B3-thymoma or thymic carcinoma
- At least one previous line of platinum-based chemotherapy
- No autoimmune disorders
- Measurable disease
- No intratumor cavitation, invasion of blood vessels, or previous bleeding
- ECOG PS 0-1
- No previous treatment with sunitinib

N = 43 pts

LENVATINIB 20 mg orally daily
+
PEMBROLIZUMAB 200 mg IV D1 every 3 weeks

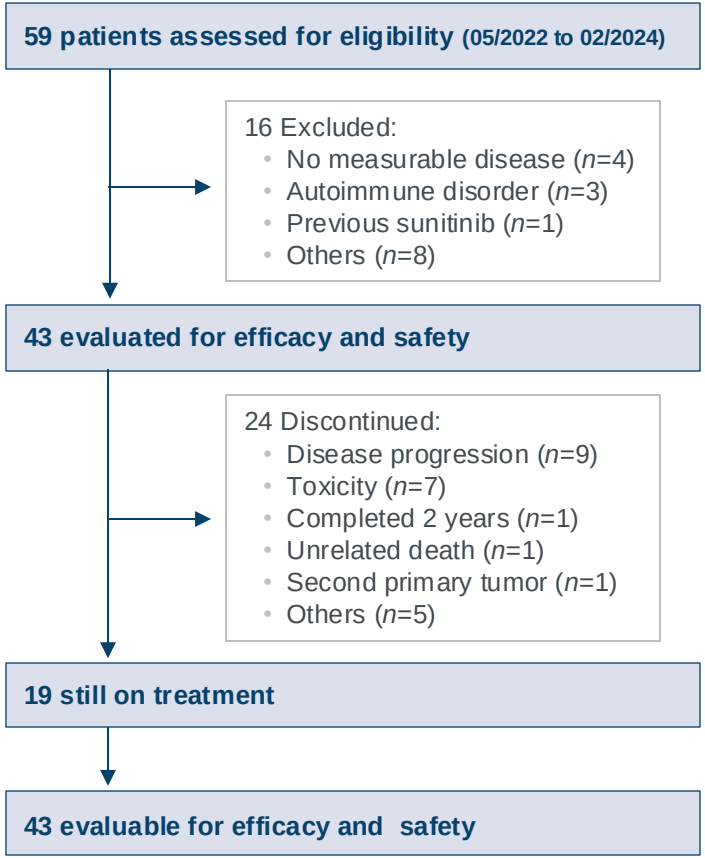
until PD, toxicity or up to 2 years



RECIST v.1.1 assessment with thorax, abdomen CT-scans Q6W for the first 12 weeks, then Q9W up to 1 year, then Q12W until the 2 years

- **Primary Endpoint:** 5-month Progression-Free Survival by INV as per RECIST v.1.1 (H_0 ≤50%; H_1 68.6%)
- **Secondary Endpoints:** Overall response rate, Overall survival, and Safety as per CTCAE v.5.0.

Baseline characteristics

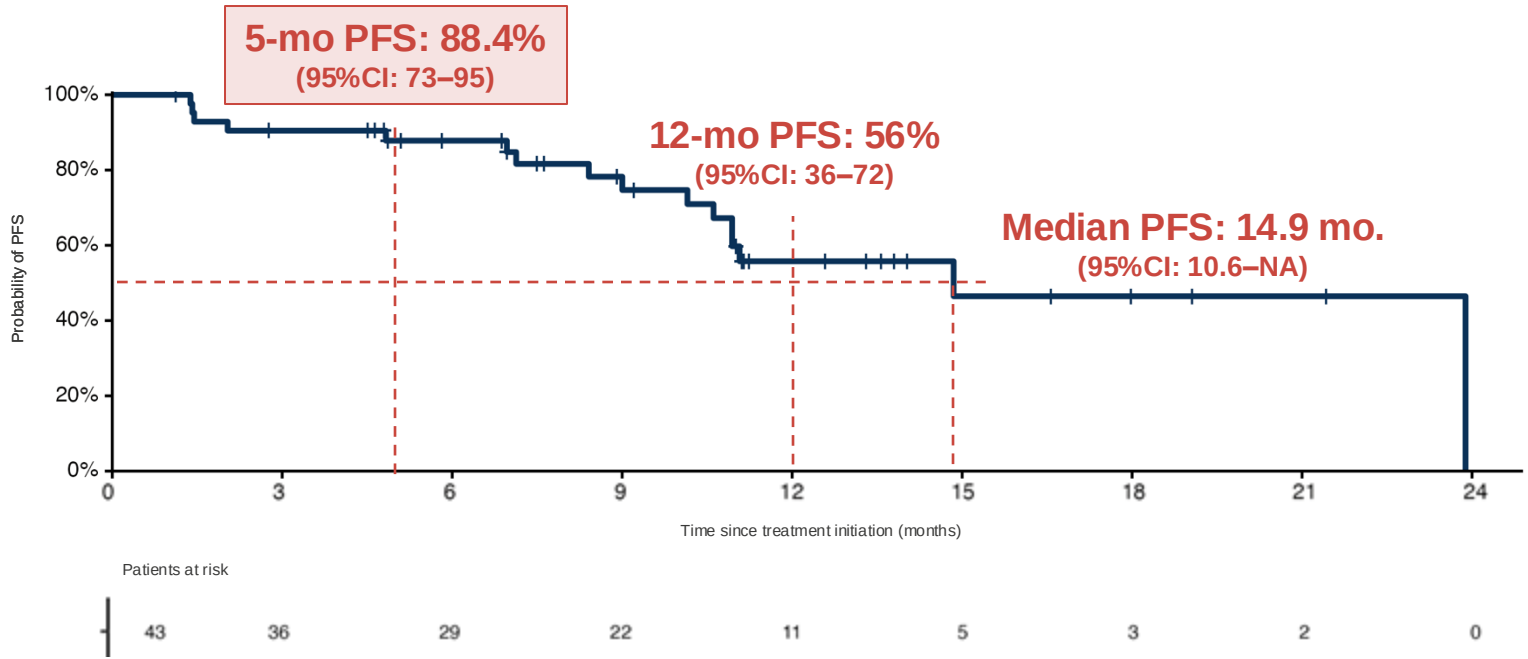


Characteristic	N = 43 (%)
Age, Median years (range)	57 (33-80)
Female	18 (42)
ECOG Performance status	
• 0	17 (40)
• 1	26 (60)
TET subtype	
• Thymic carcinoma	36 (84)
• B3-thymoma	7 (16)
Masaoka-Koga stage	
• IVA	15 (35)
• IVB	28 (65)
Previous lines of treatment	
• 1	23 (54)
• 2	17 (39)
• ≥3	3 (7)
≥ 3 metastatic sites	24 (56)
Liver metastases	16 (37)
Median sum of target lesions (mm)	86 (11-204)
PD-L1 expression (22C3), *N* = 32	
• <1%	17 (53)
• ≥1%	15 (47)
• ≥50%	5 (16)

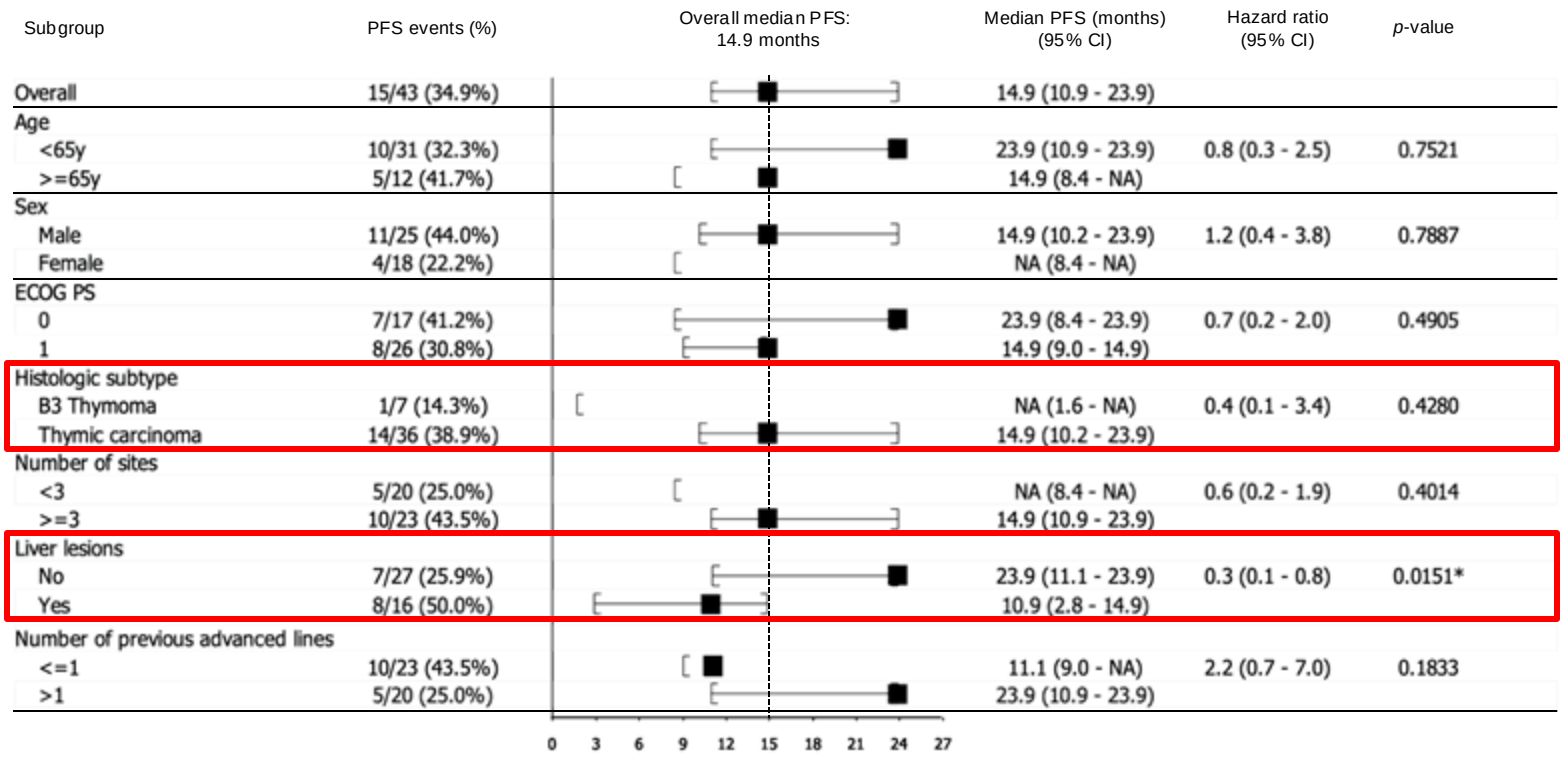
Primary endpoint: 5-months PFS rate by INV.

BARCELONA 2024 ESMO congress

Median follow-up was 10.6 (range: 1.6–25.5) months at data cutoff

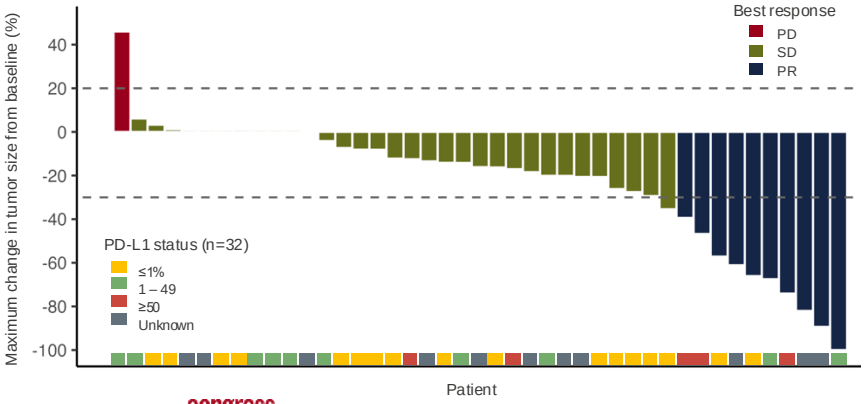


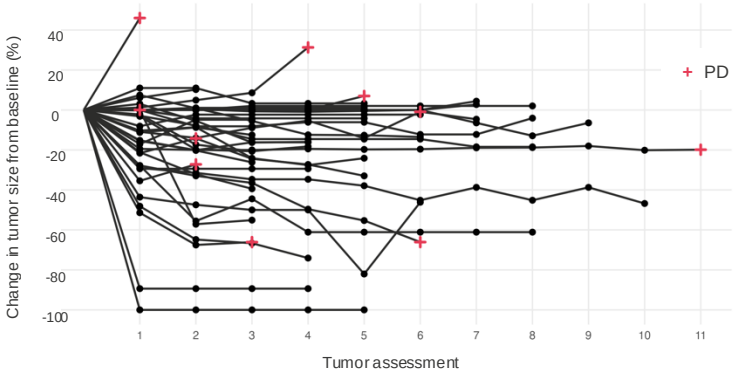
5-months PFS rate subgroup analysis



Secondary endpoint: Objective Response Rate

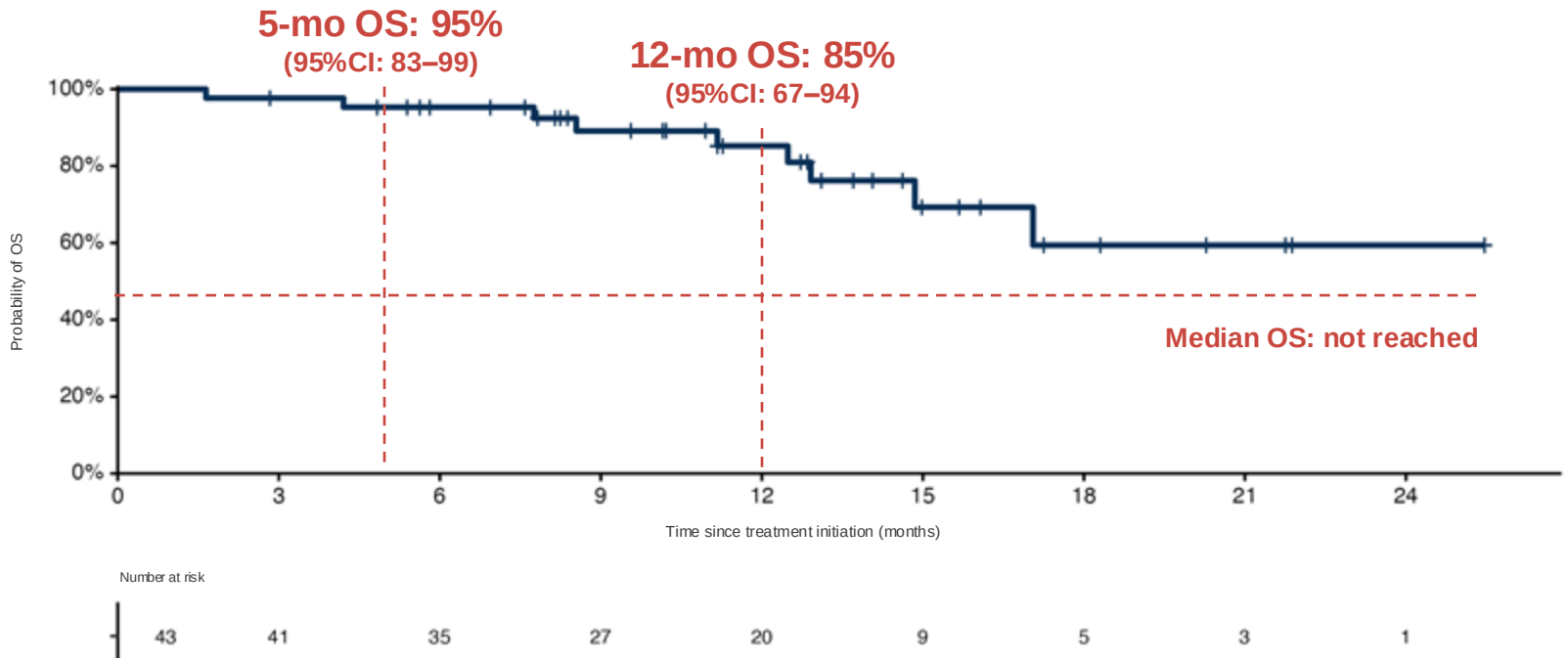
Response Rate	N = 43 (%)
Overall Response Rate	**23.3 (95% CI: 11.8–38.6)**
CR	0 (0)
PR	10 (23.3)
PD	2 (4.7)
NE	1 (2.3)
SD≥24w	22 (51.2)
SD<24w	8 (18.6)
Median Duration of Response, months (95% CI)	**8.2 (6.1–NE)**





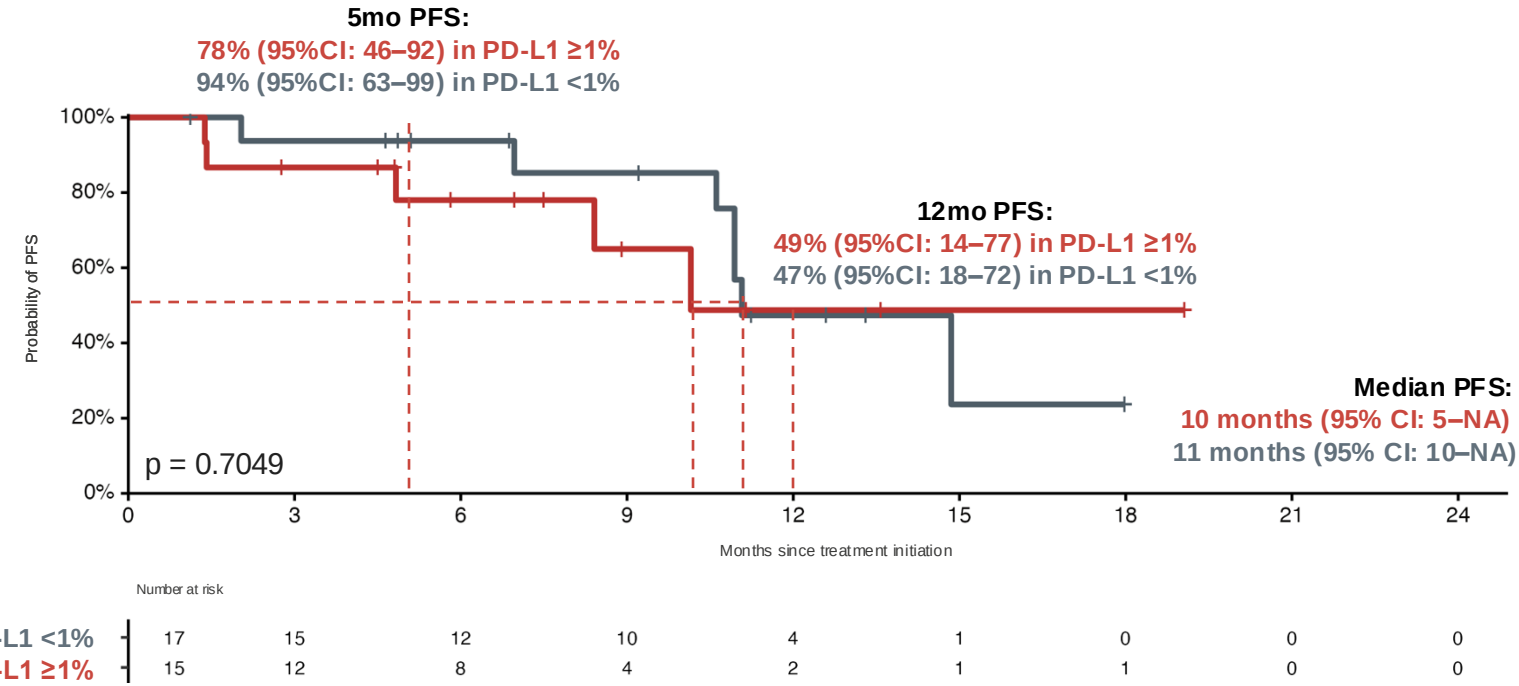
Secondary endpoint: Overall Survival

Median follow-up was 10.6 (range: 1.6–25.5) months at data cutoff



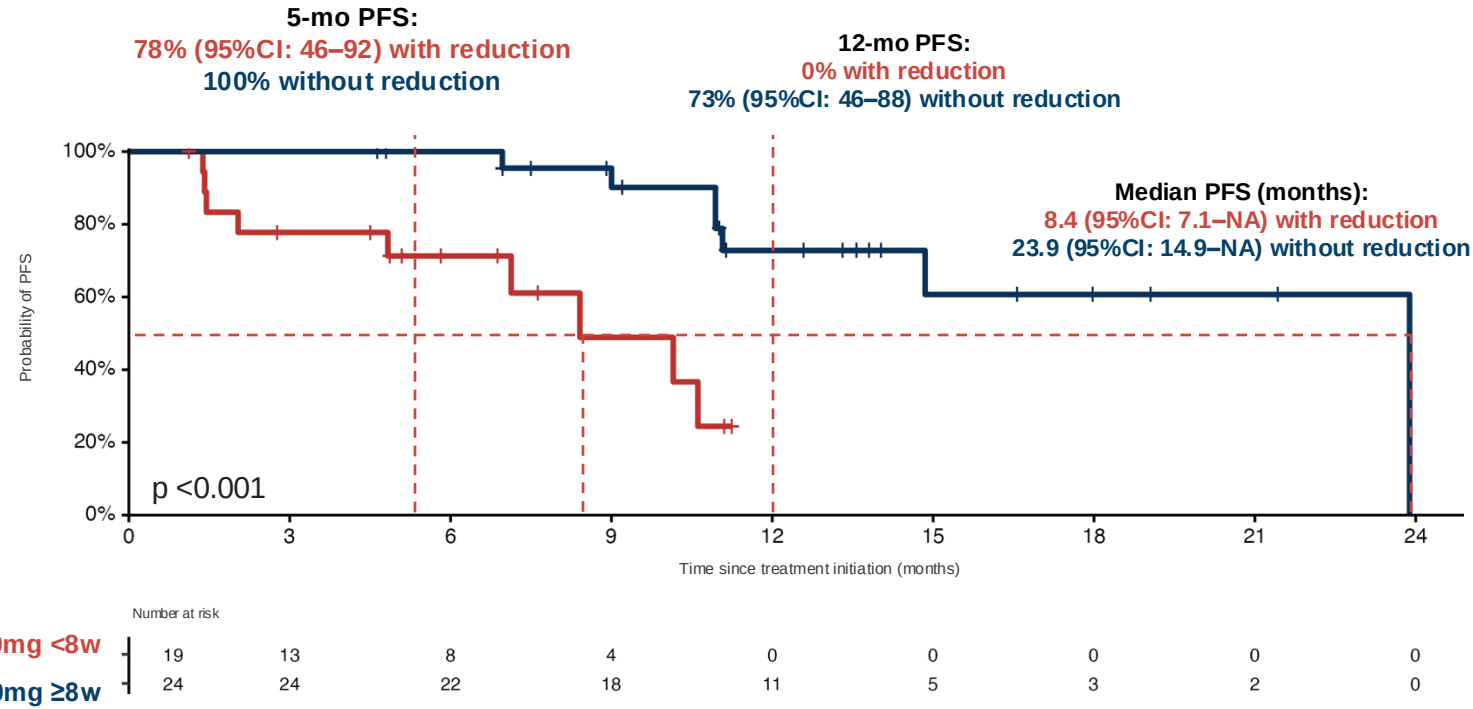
Exploratory analysis: PD-L1 expression

Centralized PD-L1 status by 22C3 assay (N = 32): PD-L1 ≥1% , PD-L1 <1%



Exploratory analysis: Lenvatinib dose intensity

PFS by dose intensity: Lenvatinib WITH reduction within the first 8 weeks (44%), Lenvatinib WITHOUT dose reduction (56%)



BARCELONA 2024 ESMO congress

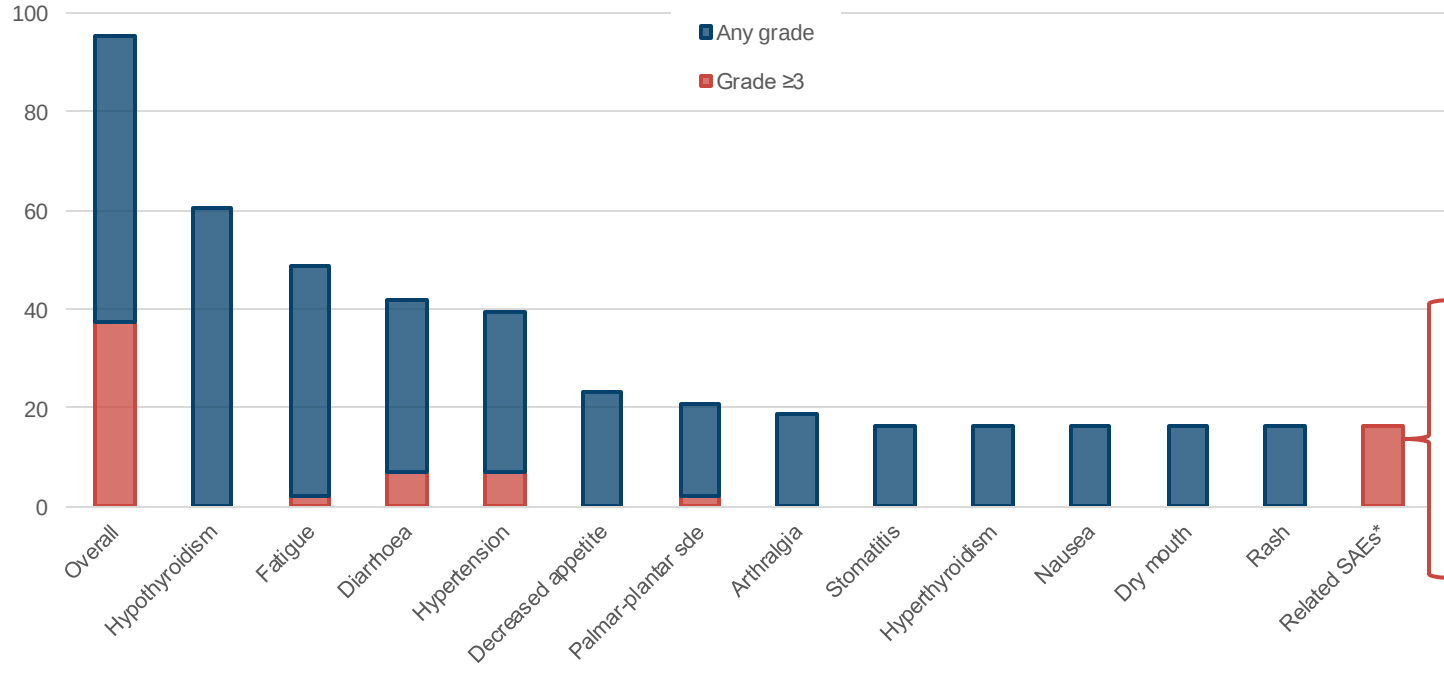
Safety analysis

Adverse events	*N* = 43 (%)	
Adverse events (%)	42 (97.7)	
Grade ≥3 TEAEs (%)	20 (46.5)	
Grade ≥3 TRAEs (%)	16 (37.2)	
Related grade ≥3 SAEs	7 (16.3)	
TRAEs leading treatment discontinuation (any drug)	11 (25.6)	
	Lenvatinib	Pembrolizumab
Median (range) number of cycles administered	13 (1–35)	12 (1–35)
Immune Related AEs (%)		6 (13.9%)*
Grade ≥ 3 TRAEs (%)	8 (18.6%)	4 (9.3%)
Dose temporary interruption due to TRAEs (%)	25 (58.1%)	21 (48.8%)
Dose permanent discontinuation due to TRAEs (%)	10 (23.3%)	8 (18.6%)

***irAEs:** Pneumonitis, myocarditis, Encephalitis, myositis, cardiac dysfunction, cytolysis (n=2)

Safety analysis

Treatment-related adverse events (TRAEs) in ≥15% of patients



SAEs Pembrolizumab:
- Pneumonitis
- Myocarditis / Encephalitis
- Cytolysis

SAEs Lenvatinib:
- Palmar-plantar syndrome
- Cardiac dysfunction
- Pulmonary abscess
- Colitis

Conclusions

- **Pembrolizumab plus Lenvatinib in pre-treated B3-T and TC reported a 5-months PFS rate of 88%.**
- **Higher dose intensity within the first 8 weeks with lenvatinib was associated with better outcome.**
- **Toxicity profile is manageable but close monitoring is advised.**
- **Outcome reported with the combination surpasses data reported with monotherapy of these agents.**

PECATI trial supports pembrolizumab plus lenvatinib as potential standard treatment in patients with pre-treated advanced B3-thymoma and thymic carcinoma

Acknowledgements

- All patients and families.
- Thanks to the investigators and staff at each site.
- Personal acknowledgement:
  - Dr. Paolo Bironzo
  - Pr. Silvia Novello
  - Dr. Liusella Righi
- Thanks to MSD for their financial support and drug supply for this Investigator Initiated Study.

Countries where PECATI trial was conducted

Presentation

Lay language summary

"Funding Source: Supported in part by a research grant from Investigator-Initiated Studies Program of Merck Sharp & Dohme LLC. The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck Sharp & Dohme LLC."