Lung Cancer UPDATES
IASLC HIGHLIGHTS
San Diego, USA
ESMO HIGHLIGHTS
Barcelona, Spain

Iniciativa científica de:
GECP
lung cancer research

Otros tumores torácicos

Enric Carcereny Costa

Institut Català d'Oncologia Badalona-Mataró

Disclosures

- **Advisory / Consultancy :** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda

- **Speaker Bureau / Expert testimony:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda

- **Travel / Accommodation / Expenses** :Bristol-Myers Squibb, Pfizer, Roche, Takeda, Astra Zeneca

AGENDA

Iniciativa científica de:
GECP lung cancer research

- Phase I Trial of DLL3/CD3 IgG-Like T-Cell Engager Obrixtamig* (BI 764532) in Patients with DLL3-Positive Tumors: Patients with LCNEC-L

- PEMbrolizumab Plus Lenvatinib In Second-Line Pleural MEsotheLiomA Patients: A Single Arm Phase II Study - PEMMELA (second cohort)

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

TAKE AWAY ...

Iniciativa científica de:
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- Obrixtamig Safety & Efficacy: Manageable safety profile in LCNEC-L. CRS (36%) was grade 1/2 and controlled with standard care. Promising efficacy with ORR of 70% at doses ≥90 µg/kg

- Pembrolizumab plus lenvatinib shows promising clinical activity in patients with pleural mesothelioma who progressed after nivolumab plus ipilimumab

- Pembrolizumab plus Lenvatinib in pre-treated B3-T and TC reported a 5-months PFS rate of 88%.. Toxicity profile is manageable but close monitoring is advised.

Otros tumores torácicos

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Phase I Trial of DLL3/CD3 IgG-Like T-Cell Engager Obrixtamig (BI 764532) in Patients with DLL3-Positive Tumors: Patients with LCNEC-L*

LCNEC-L is a rare and highly aggressive form of lung cancer that shares similarities with SCLC and NSCLC[1]

- Treatment strategies are extrapolated from those used in patients with SCLC[2,3]
- Histological similarities with NSCLC and SCLC increase the difficulty of diagnosis[4]
- Clinical management remains controversial and standardized treatment methods are lacking[1,5]
- Prognosis remains poor, with a median OS of 8–12 months[1]

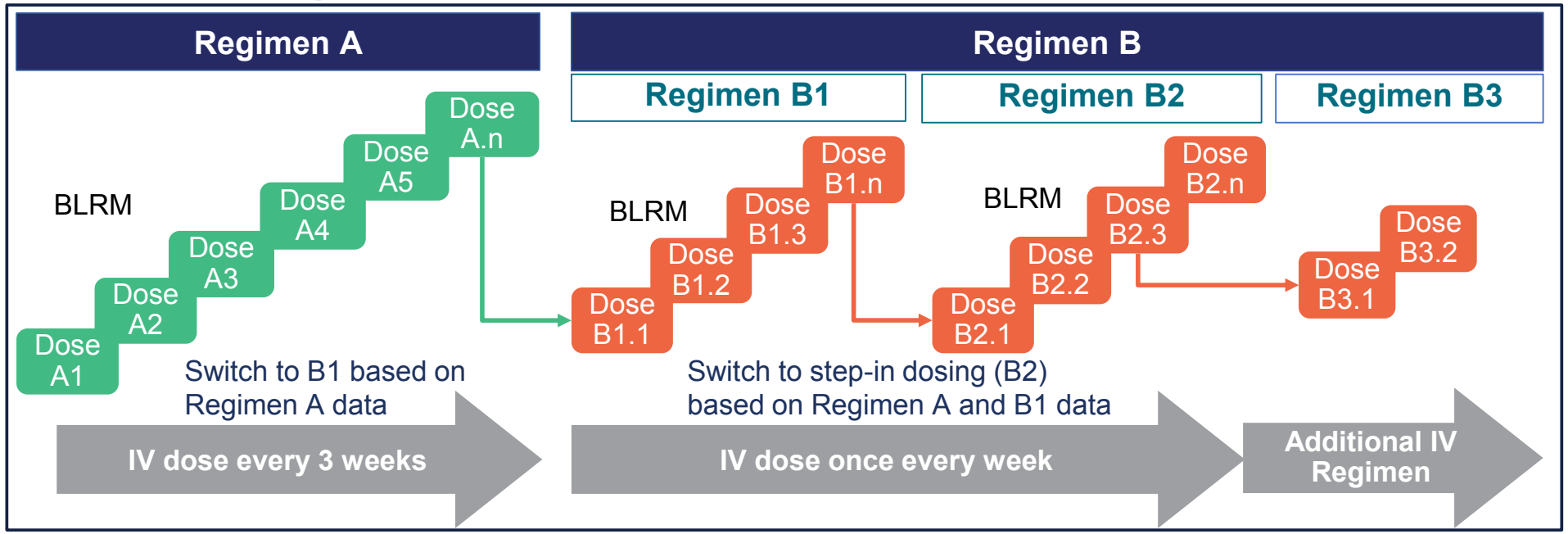
~70% of LCNEC-L tumors express DLL3[6,7]

1. Andrini E, et al. J Clin Med 2022;11(5):1461; 2. Corbett V, et al, Front Oncol. 2021;11:653162; 3. Lo Russo G, et al. Tumour Biol 2016;37(6):7047–7057; 4. Zhu S, et al. Front Med (Lausanne) 2024;11:1326426; 5. Lantuejoul S, et al. Transl Lung Cancer Res 2020;9(5):2233–2244; 6. Hermans BCM, et al. Lung Cancer 2019;138:102–108; 7. Lima CF, et al. Abstract 5305 at AACR; Apr 8–13, 2022; New Orleans

DLL3, delta-like ligand 3; LCNEC-L, large cell neuroendocrine carcinoma of the lung; NSCLC, non-small cell lung cancer; OS, overall survival; SCLC, small cell lung cancer

Phase I Trial of DLL3/CD3 IgG-Like T-Cell Engager Obrixtamig (BI 764532) in Patients with DLL3-Positive Tumors: Patients with LCNEC-L*

First-in-human dose-escalation trial of obrixtamig in patients with SCLC, epNECs or LCNEC-L: NCT04429087



Primary endpoints	Secondary endpoints
• MTD • DLTs in the MTD evaluation period	• Objective response (RECIST v1.1) • PK parameters

BLRM, Bayesian Logistic Regression Model; DLTs, dose-limiting toxicities; epNECs, extrapulmonary neuroendocrine carcinomas; IV, intravenous; LCNEC-L, large cell neuroendocrine carcinoma of the lung; MTD, maximum tolerated dose; PK, pharmacokinetic; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SCLC, small cell lung cancer

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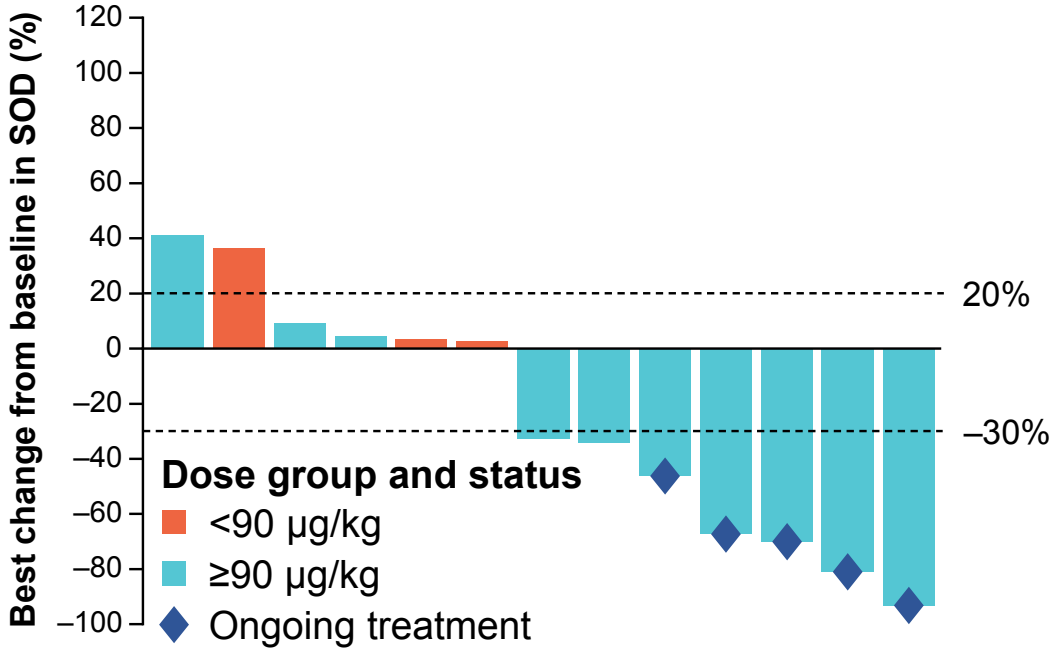
Phase I Trial of DLL3/CD3 IgG-Like T-Cell Engager Obrixtamig (BI 764532) in Patients with DLL3-Positive Tumors: Patients with LCNEC-L*

Efficacy in patients with LCNEC-L



Response n, (%)*	LCNEC-L (≥90 µg/kg) n=10†
PR	7 (70)
SD	2 (20)
PD	1 (10)
DCR	9 (90)
Missing‡	0

*Best overall response is reported regardless of confirmation; †Efficacy population: started treatment ≥7 weeks prior to data cut-off (responses evaluated per RECIST v1.1 criteria); ‡Assessable patients who did not have any tumor assessment due to early toxicity, start of subsequent anti-cancer therapy, death or any other reason

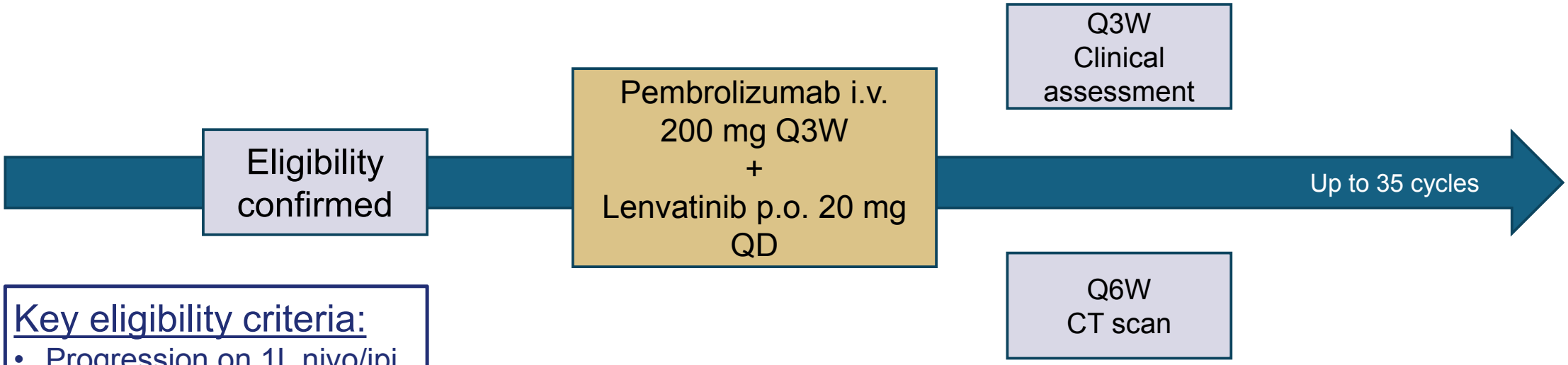
Data cut-off: Feb 21, 2024

DCR, disease control rate; LCNEC-L, large cell neuroendocrine carcinoma of the lung; PD, progressive disease; PR, partial response; RECIST v.1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; SOD, sum of diameters

PEMbrolizumab Plus Lenvatinib In Second-Line Pleural MEsotheLiomA Patients:
A Single Arm Phase II Study - PEMMELA (second cohort)

Trial Design

Single-arm, single-center, phase II study



Key eligibility criteria:
- Progression on 1L nivo/ipi
- Measurable disease
- ECOG PS 0-1

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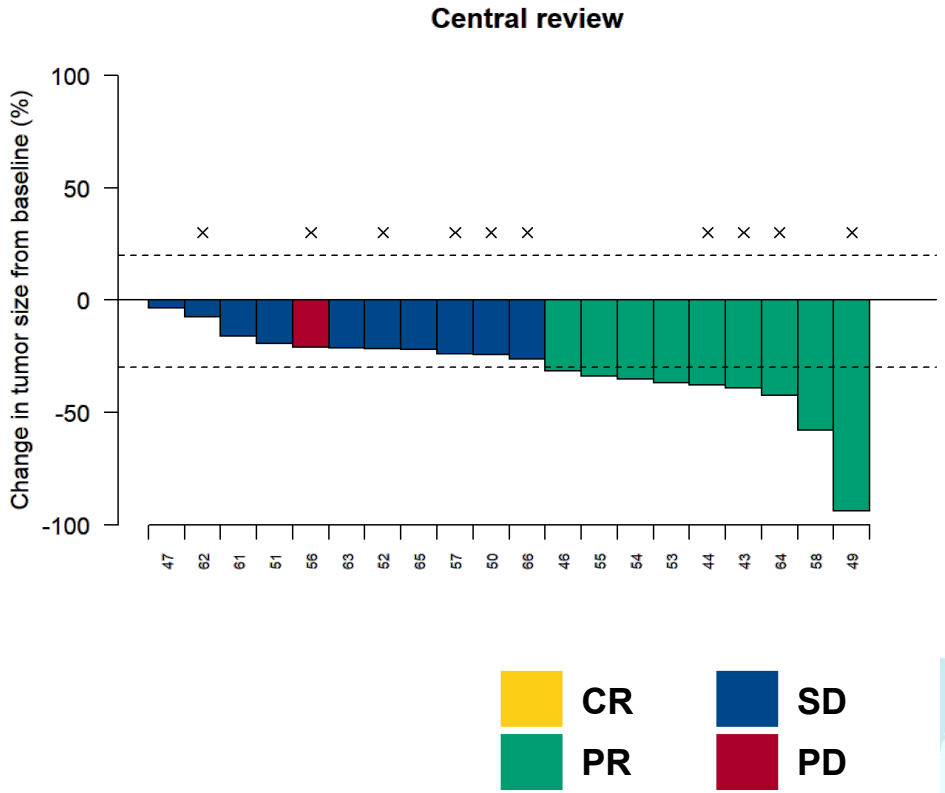
PEMbrolizumab Plus Lenvatinib In Second-Line Pleural MEsotheLiomA Patients: A Single Arm Phase II Study - PEMMELA (second cohort)

Objective Response Rate

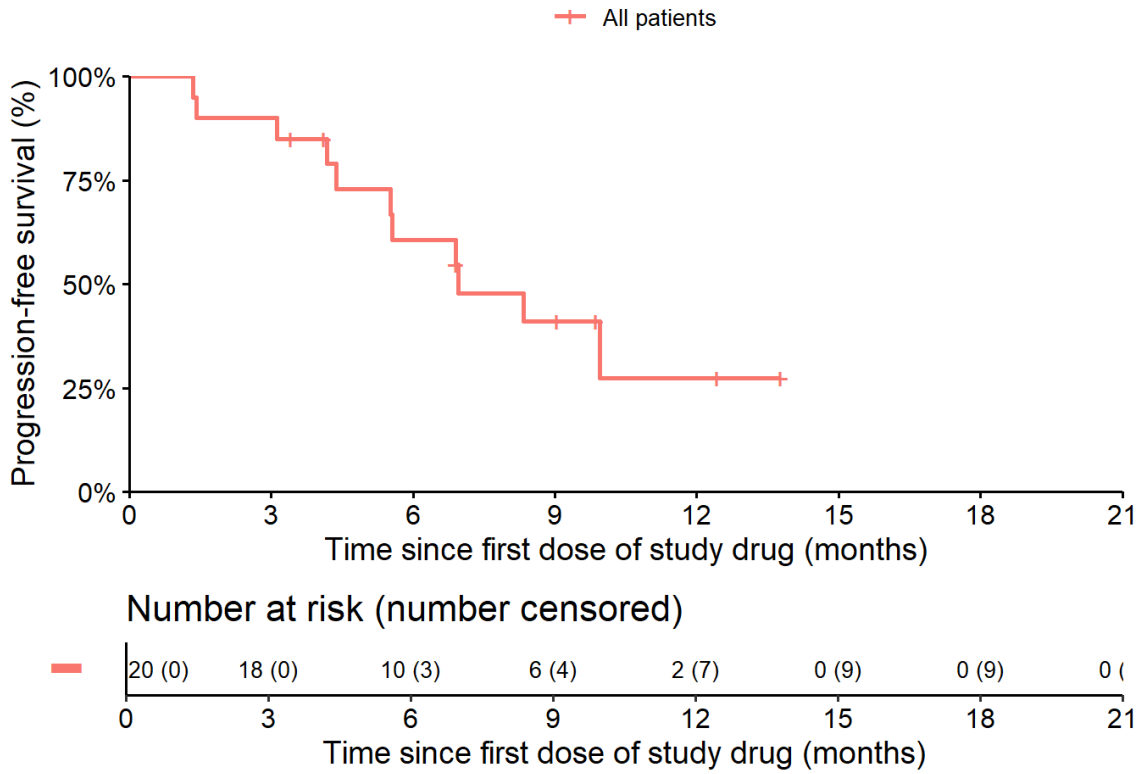
	Local investigator	Independent central reviewer (2nd endpoint)
	PEM+LEN (N=20)	PEM+LEN (N=20)
Objective response (95% CI) -%	60 (39-82)	45 (23-67)
Best overall response – n(%)		
CR	1 (5)	0 (0)
PR	11 (55)	9 (45)
SD	6 (30)	10 (50)
PD	2 (10)	1 (5)



X= PD as best response nivo/ipi

PEMbrolizumab Plus Lenvatinib In Second-Line Pleural MEsotheLiomA Patients: A Single Arm Phase II Study - PEMMELA (second cohort)

Progression-Free Survival



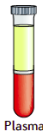
mPFS 7.0 months (95% CI 5.5 – NA)

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

PECATI phase II: Study design

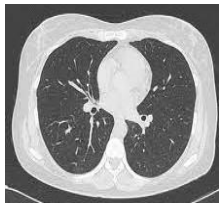
- **Metastatic B3-thymoma or thymic carcinoma**
- **At least one previous line of platinum-based chemotherapy**
- **No autoimmune disorders**
- **Measurable disease**
- **No intratumor cavitation, invasion of blood vessels, or previous bleeding**
- **ECOG PS 0-1**
- **No previous treatment with sunitinib**

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.

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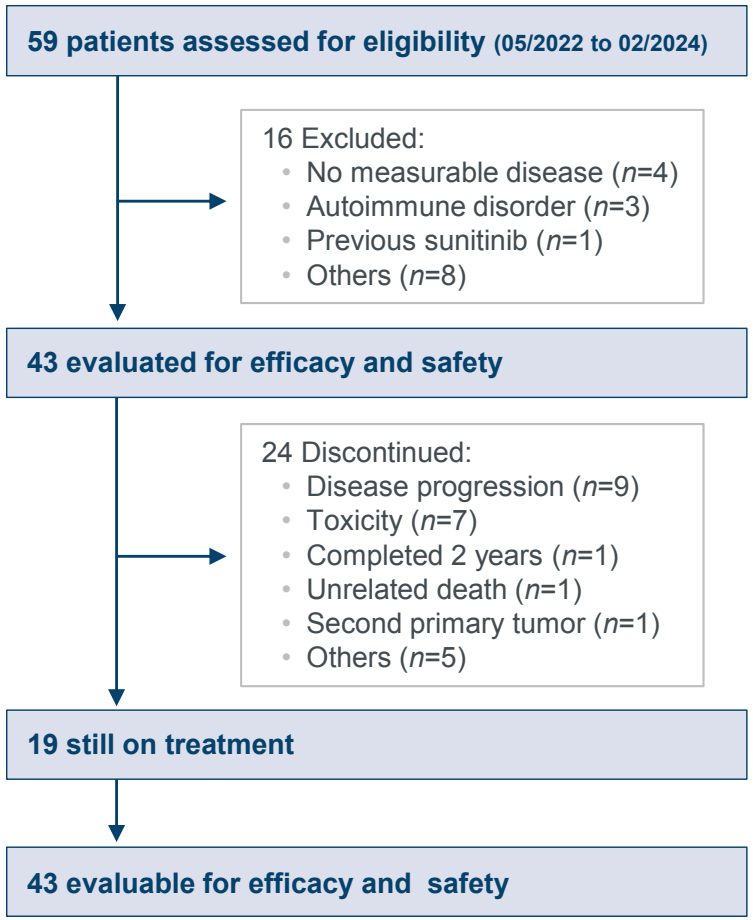
Lenvatinib plus pembrolizumab in pretreated advanced B3-thymoma and thymic carcinoma: PECATI, single arm phase II clinical trial

Baseline characteristics

BARCELONA 2024 ESMO congress

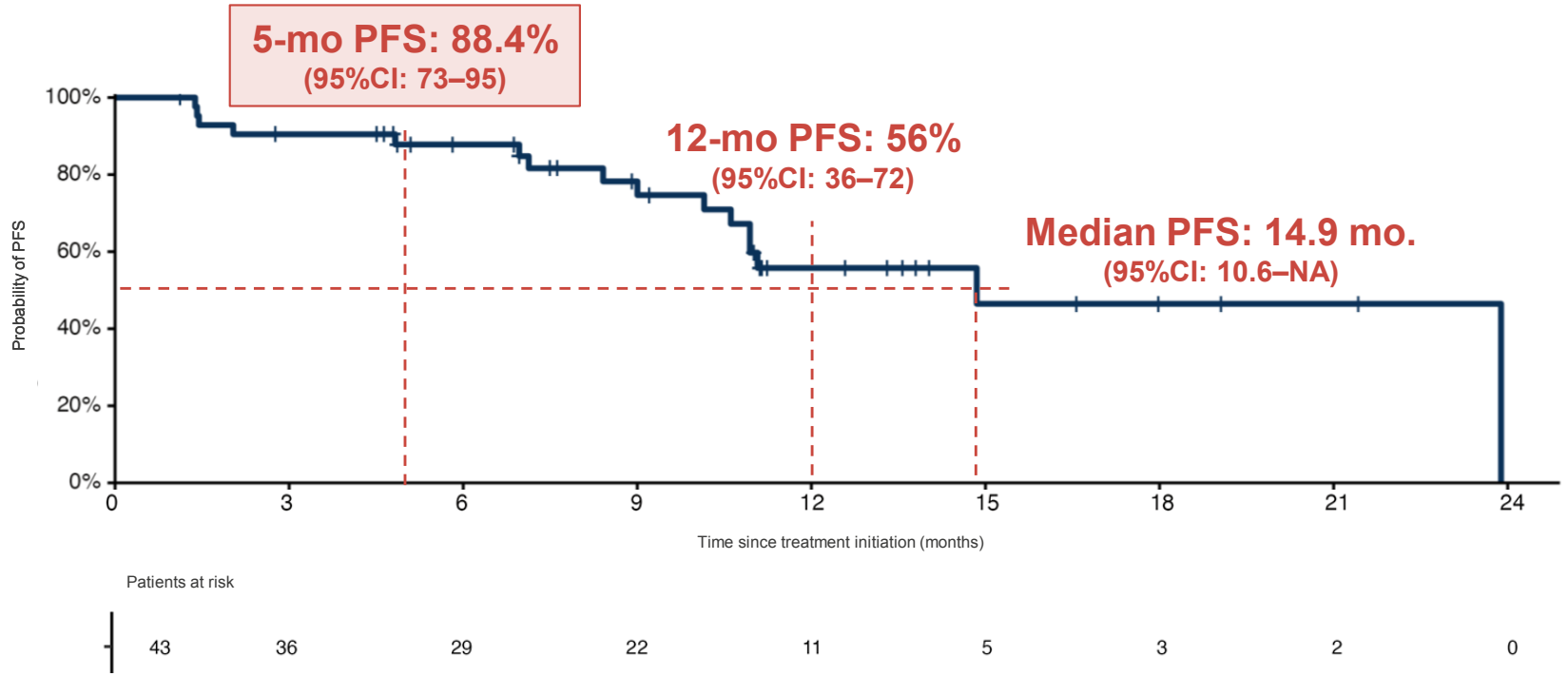


Characteristic	N = 43 (%)
Age, Median years (range)	57 (33-80)
Female	18 (42)
ECOG Performance status	
• 0	17 (40)
• 1	26 (60)
TET subtype	
• Thymic carcinoma	36 (84)
• B3-thymoma	7 (16)
Masaoka-Koga stage	
• IVA	15 (35)
• IVB	28 (65)
Previous lines of treatment	
• 1	23 (54)
• 2	17 (39)
• ≥3	3 (7)
≥ 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)

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

Primary endpoint: 5-months PFS rate by INV.

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



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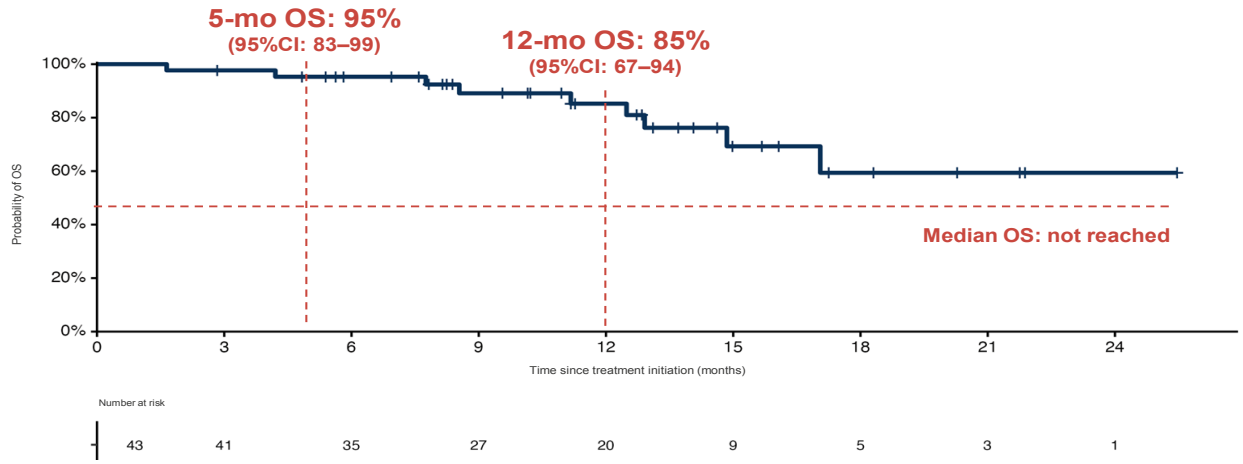
Secondary endpoint: Objective Response Rate

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



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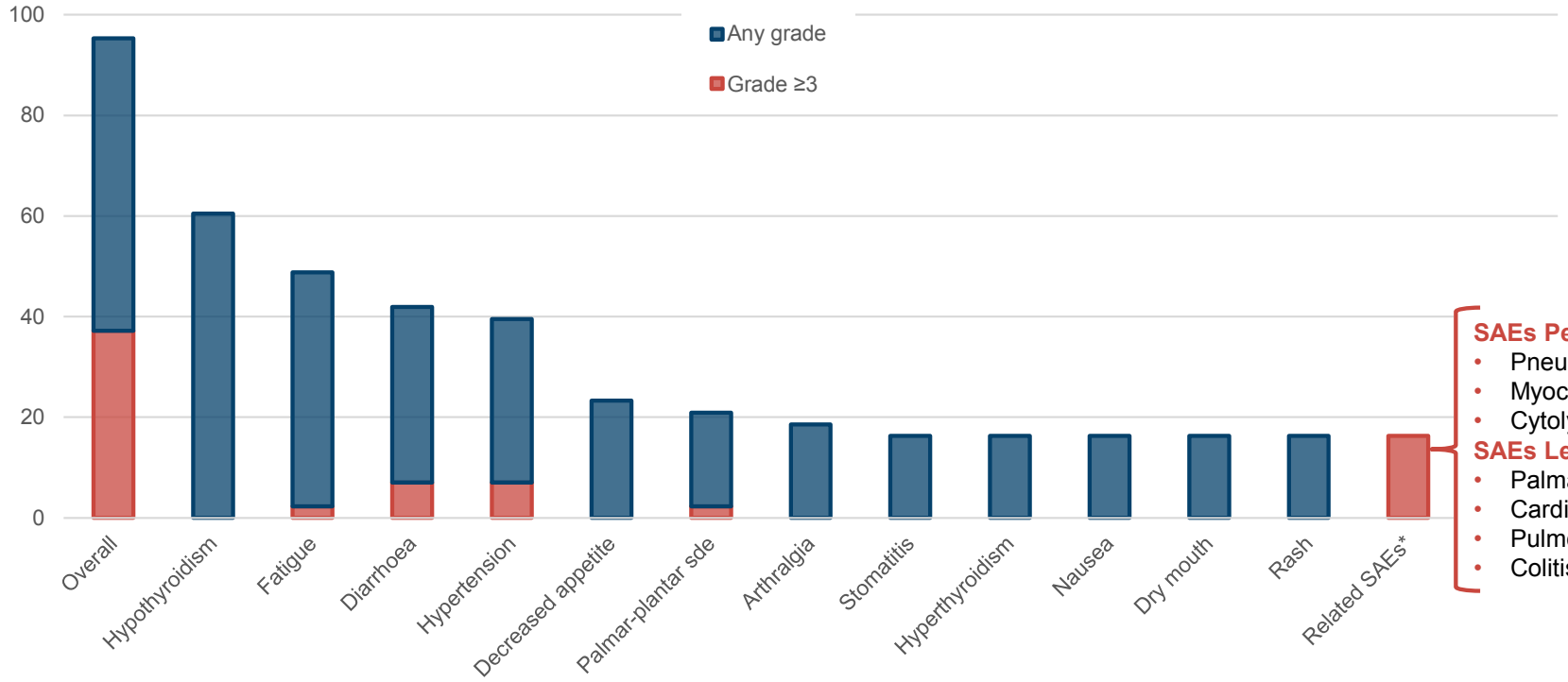
Safety analysis

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

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