#ESMOUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

ESMO HIGHLIGHTS

27 SEPTIEMBRE - 1 OCTUBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

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Mesotelioma no inmunoterapia y Carcinoma Tímico

Dr. Manuel Dómine Gómez

Con la colaboración de:
Bristol-Myers Squibb
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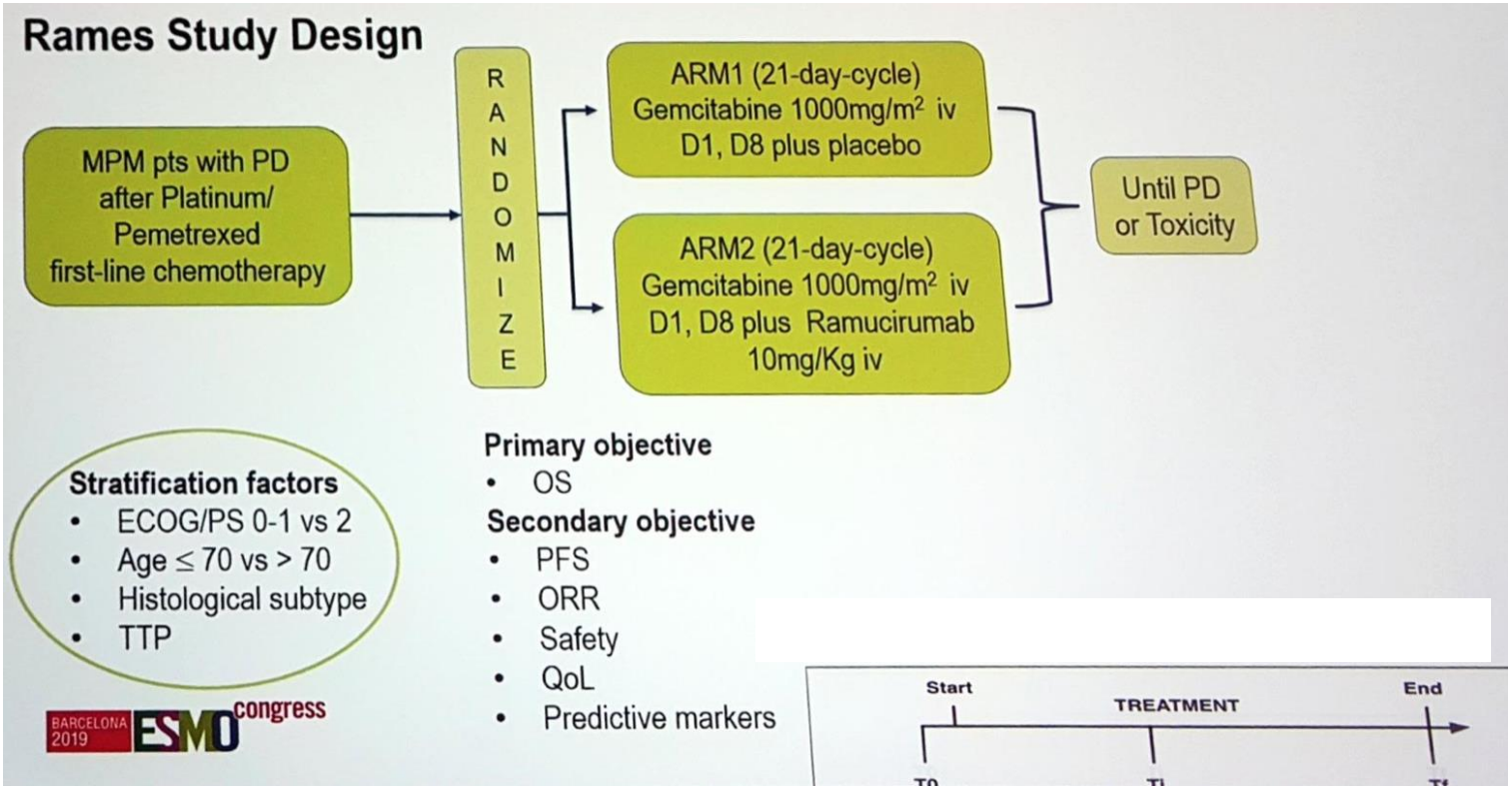
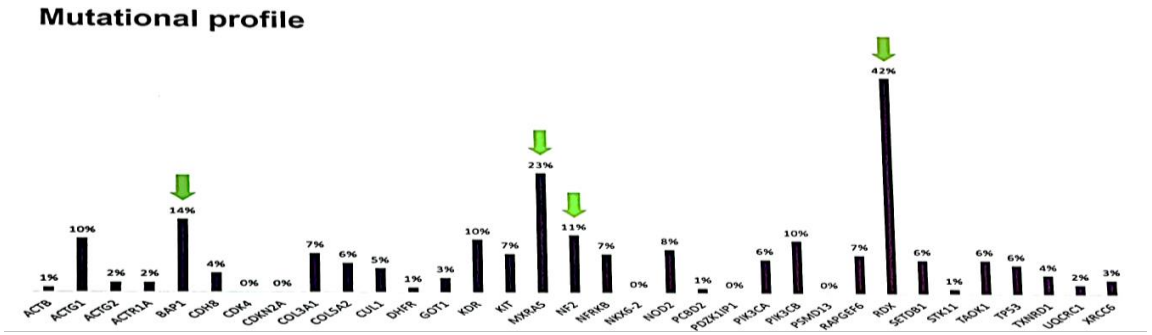
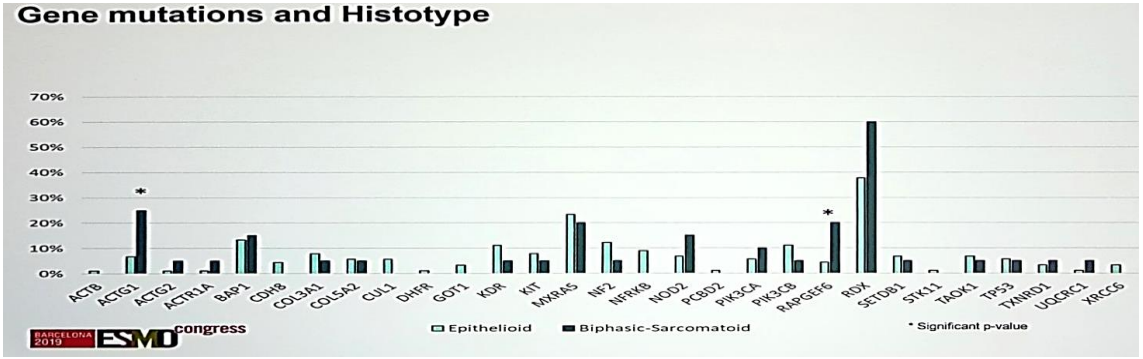
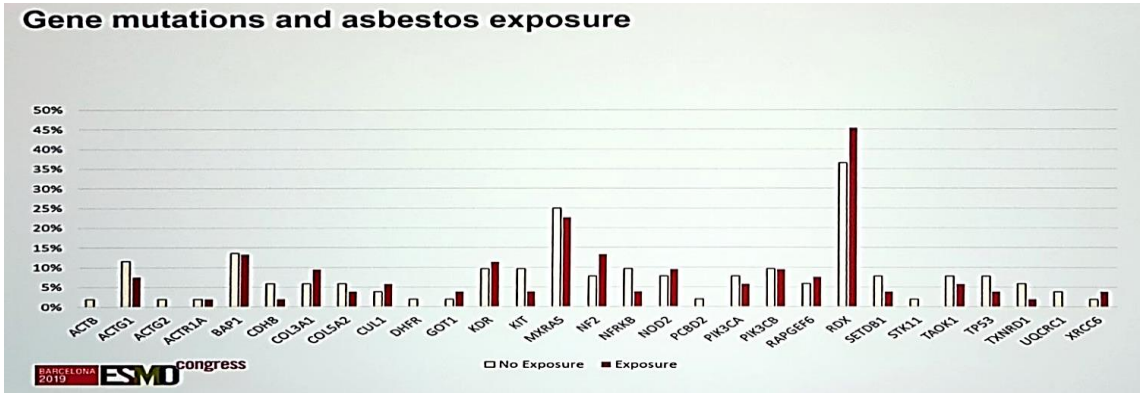
Mutacional Profile of MPM in the phase II RAMES Study



Mutational profile







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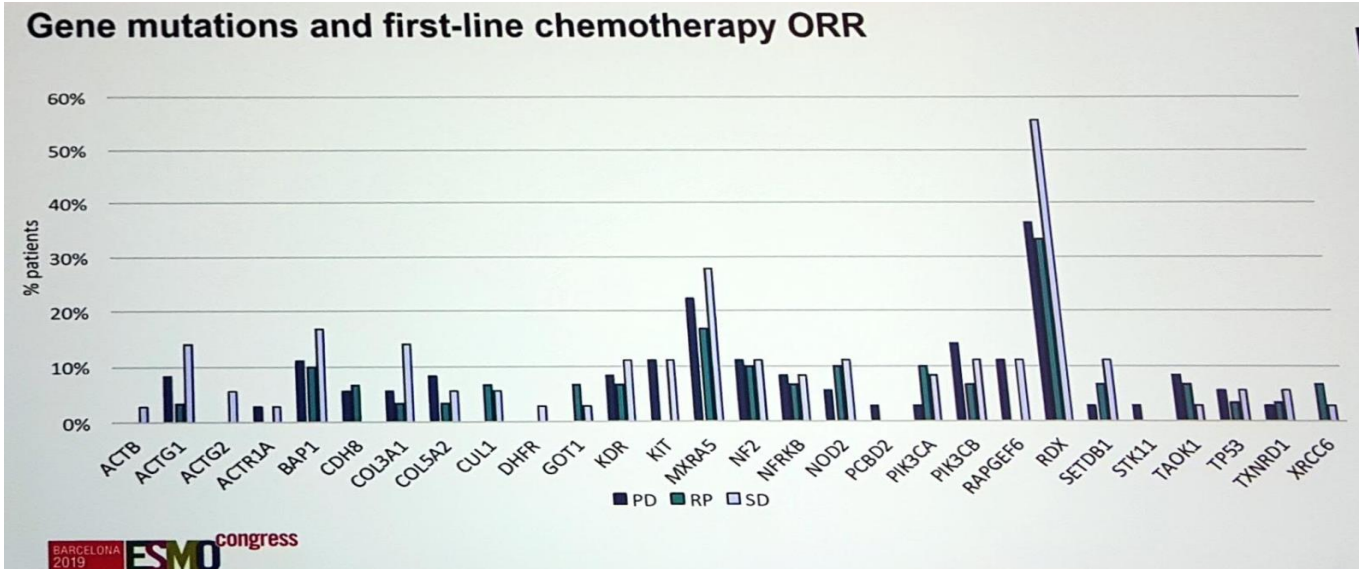

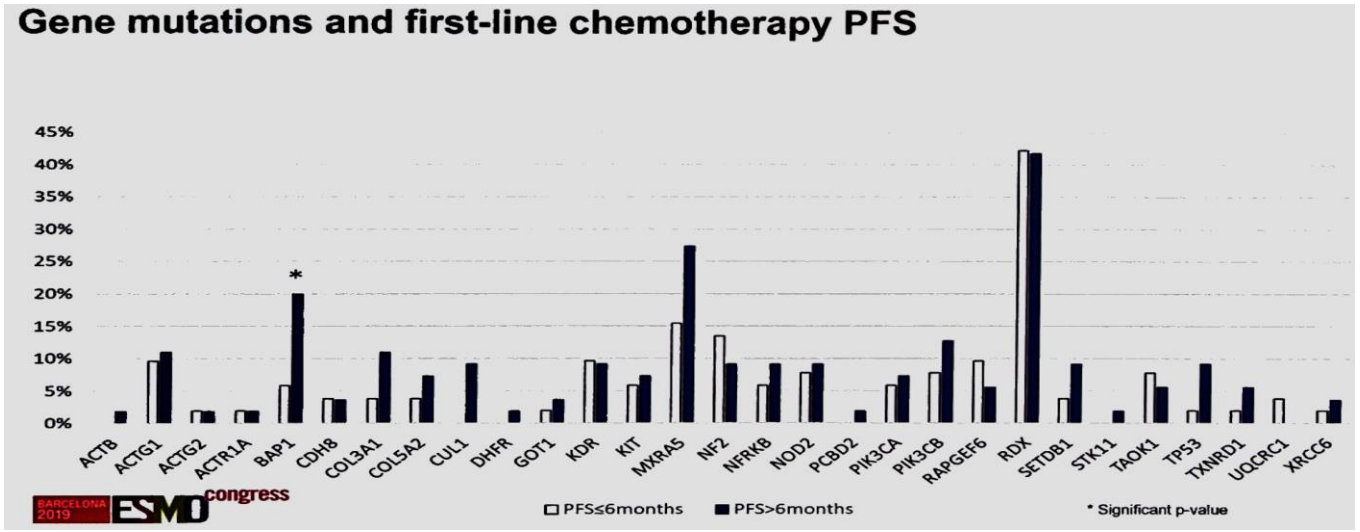

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Conclusions

A total 275 mutations were performed in 34 analyzed genes (74% missense variant)

The most frequently altered genes identified were RDX (42%), MXRA5 (23%),BAP1 (14%) and NF2 (11%)

Cul-1 and DHFR mutations were related to ephitelioid subtype, low stage and PFS1 > 6 months

ACTG1 and RAFGEF6 high expressions were observed in biphasic/sarcomatoid subtypes

No correlation was detected between asbestos exposure and gene alterations

BAP1 mutations were associated to a better PFS after platinum/pemetrexed first-line treatment

In the final analysis of RAMES Study the OS impact of the gemcitabine/ramucirumab second-line treatment and the molecular subgroups will be evaluated

SAKK17/16 LURBINECTEDIN AS SECOND OR THIRD LINE PALLIATIVE CHEMOTHERAPY IN MPM, A MULTICENTER SINGLE-ARM PHASE II TRIAL

PATIENTS AND DESIGN

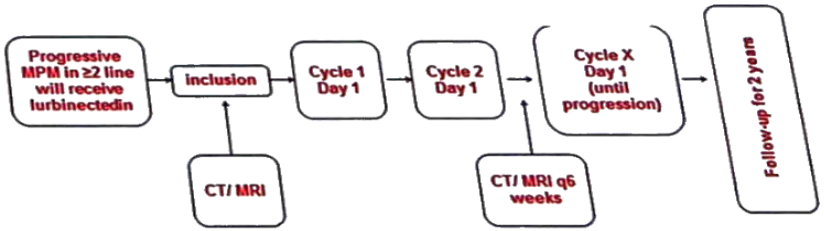
INCLUSION CRITERIA

- Histologically or cytologically confirmed MPM
- Progression on previous platinum-pemetrexed
- One additional line of immunotherapy allowed
- ECOG 0-1, adequate bone marrow and chemistry

EXCLUSION CRITERIA

- >1 prior chemotherapy lines
- CNS disease
- Prior malignancy
- Grade ≥2 AEs on prior treatment

- Prospective 2-stage single-arm open-label multicenter phase II trial
- Lurbinectedin 3.2mg/m² i.v. q3 weeks (one cycle) until progression, unacceptable toxicity or patient's withdrawal

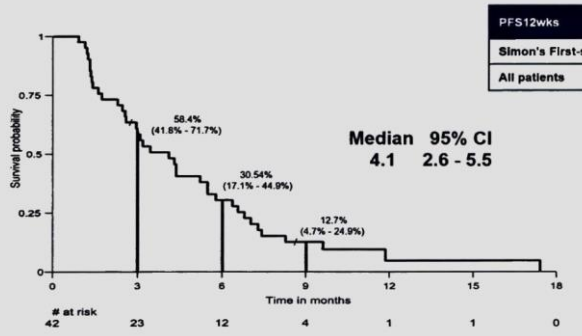


Primary endpoint:
Progression-free survival (PFS) at 12 weeks (PFS12wks)

Secondary endpoints:
PFS
Overall survival (OS)
Adverse events (as per CTCAE v4.03).

SAKK17/16 AS SECOND OR THIRS LINES PALLIATIVE CHEMOTHERAPY IN MPM, A MULTICENTER SINGLE-ARM PHASE II TRIAL

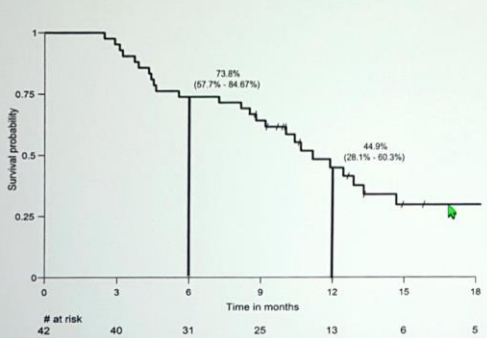
RESULTS: PFS



PFS12wks	N (%)
Simon's First-stage	11/21
All patients	22/42 (52.4%) (90%CI: 38.7%-63.5%)

Median 95% CI
4.1 2.6 - 5.5

RESULTS: OS



N=42	
No of events (death)	n 26

Median 95% CI
11.1 8.8 – 14.7

RESULTS: TREATMENT OVERVIEW

	N=42
Data downloaded on	21st August 2019
Follow-up, median (95% CI)	14.9mo (10.6mo - 18.6mo)
Cycles administered, median (range)	5 (1 - 22)
Duration of treatment, median (range)	98 days (22 - 525)
Best overal response	CR: 1 / PR: 1 / SD: 20
Treatment ongoing	1 pt
Treatment discontinued	41 pts
Reason for discontinuation	
Progressive disease	32 pts
Other*	9 pts
Toxicity	0 pts

*patient's decision, physician's decision,

RESULTS: TOXICITY

Toxicity, n(%)	All grades	Grade 1-2	Grade 3-4
AEs	42 (100%)	10 (23.8%)	32 (76.2%)
Treatment-related AEs[1, 2]	38 (90.5%)	18 (42.9)	20 (47.6%)
Neutropenia	11 (26.2%)	1 (2.4%)	10 (23.8%)
Febrile neutropenia	4 (9.5%)		4 (9.5%)
Anemia	10 (23.8%)	7 (16.7%)	3 (7.1%)
Thrombopenia	6 (14.4%)	3 (7.2%)	3 (7.2%)
Hepatotoxicity[3]	20 (47.6%)	20 (47.6%)	0 (0%)
Renal toxicity	2 (4.8%)	2 (4.8%)	0 (0%)
Fatigue	25 (59.6%)	18 (42.9%)	7 (16.7%)
Anorexia	9 (21.4%)	7 (16.7%)	2 (4.8%)
Nausea	22 (52.4%)	20 (47.6%)	2 (4.8%)
Vomiting	11 (26.2%)	9 (21.4%)	2 (4.8%)
Diarrhoa	3 (7.1%)	3 (7.1%)	0 (0%)

Conclusions

- Trial showed **activity of lurbinectedin in progressive MPM**
- **Toxicity** was **acceptable**
- Lurbinectedin works **independently of histology** or prior **immunotherapy**
- **Both "slow" and "fast" progressive pts** on platinum-pemetrexed benefit respectively from lurbinectedin
- Our data support evaluation of lurbinectedin in a randomized, **Phase III trial**

Durable ant-tumor activity of the multitargeted inhibitor lenvatinib in patients with advanced or metastatic thymic carcinoma. Preliminary results from a multicenter phase II (REMORA) trial

Lenvatinib: multitarget inhibitor of FGFR, RET, C-Kit

STUDY DESIGN

- An open-label, single-arm, multi-center (8 institutions) phase II trial.

Patients with advanced or metastatic Thymic carcinoma (Any histology; n=42) → Lenvatinib 24 mg QD → Until PD, unacceptable toxicity or loss of clinical benefit

Inclusion Criteria
- Pathologically confirmed thymic carcinoma
- Measurable disease per RECIST v1.1
- ECOG PS of 0 or 1
- Disease progression after at least one previous line of platinum-based chemotherapy

Exclusion Criteria
- Uncontrolled hypertension
- Treatment history of TKIs targeted for VEGFR
- Active brain metastases requiring treatment

Primary endpoint
- Objective response rate (ORR) by independent radiological review

Secondary endpoints
- Efficacy endpoints: Progression-free survival (PFS), Over all survival (OS) and disease control rate (DCR)
- Safety endpoints: Treatment-related adverse events

Sample size consideration
- As per the SWOG two-stage design, the sample size of 40 had 80% power with one-sided alpha error of 5%; threshold ORR, 10%; and expected ORR, 25%

Durable ant-tumor activity of the multitargeted inhibitor lenvatinib in patients with advanced or metastatic thymic carcinoma. Preliminary results from a multicenter phase II (REMORA) trial

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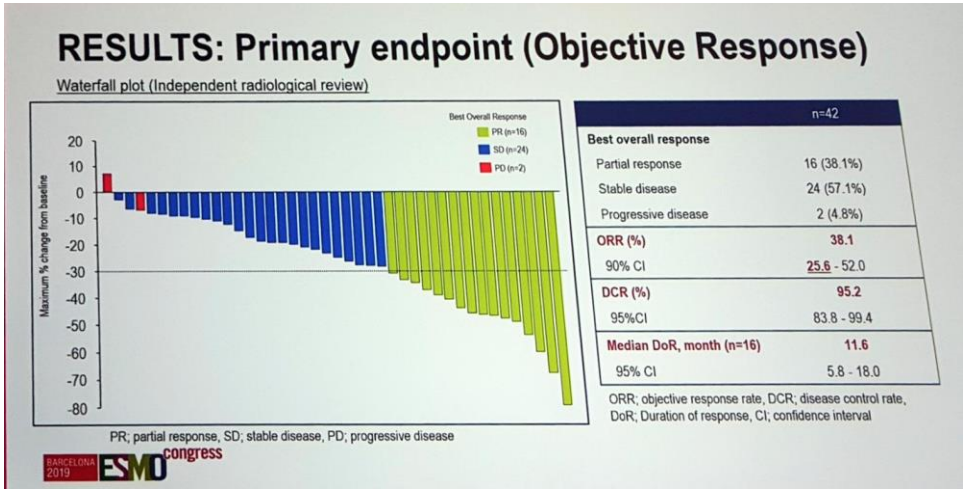

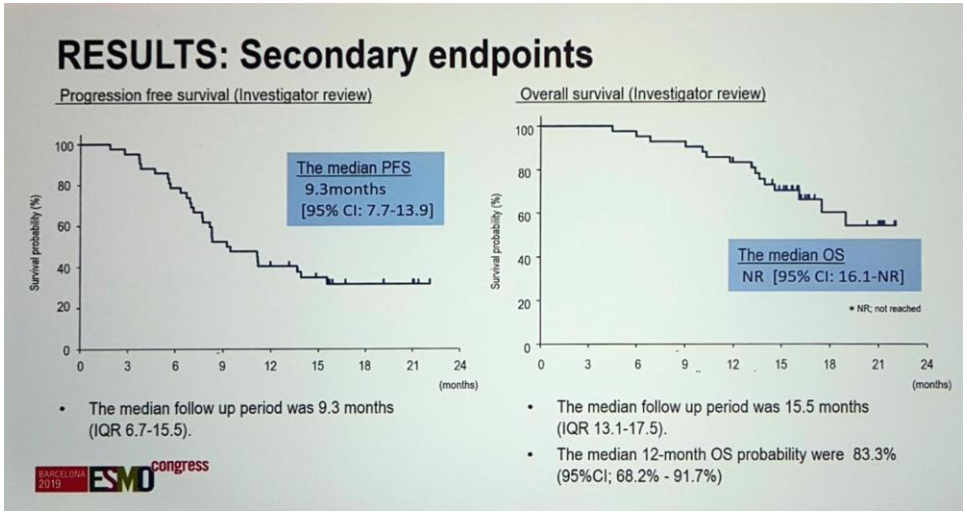

RESULTS: Treatment-related adverse events (AEs)

Characteristics	Grade 1-2*	Grade 3	Grade 4	Total
Hypertension	10 (23.8%)	27 (64.3%)	0 (0.0%)	37 (88.1%)
Hand-foot syndrome	26 (61.9%)	3 (7.1%)	0 (0.0%)	29 (69.0%)
Proteinuria	28 (66.7%)	0 (0.0%)	0 (0.0%)	28 (66.7%)
Hypothyroidism	27 (64.3%)	0 (0.0%)	0 (0.0%)	27 (64.3%)
Platelet count decreased	20 (47.6%)	2 (4.8%)	0 (0.0%)	22 (52.4%)
Diarrhoea	19 (45.2%)	2 (4.8%)	0 (0.0%)	21 (50.0%)
Malaise	14 (33.3%)	0 (0.0%)	0 (0.0%)	14 (33.3%)
Stomatitis	14 (33.3%)	0 (0.0%)	0 (0.0%)	14 (33.3%)
Aspartate aminotransferase increased	12 (28.6%)	0 (0.0%)	0 (0.0%)	12 (28.6%)
Alanine aminotransferase increased	11 (26.2%)	0 (0.0%)	0 (0.0%)	11 (26.2%)
Nausea	10 (23.8%)	0 (0.0%)	0 (0.0%)	10 (23.8%)
Neutrophil count decreased	6 (14.3%)	2 (4.8%)	0 (0.0%)	8 (19.0%)
Pneumonitis	0 (0.0%)	1 (2.4%)	0 (0.0%)	1 (2.4%)

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The highest grade per event per patient is shown. * Only grades 1 and 2 treatment-related adverse events that occurred in 10% of patients or more are shown.

Conclusiones

- Lenvatinib has shown the clinical efficacy in patients with advanced or metastatic thymic carcinoma.
- The safety profile of lenvatinib was generally tolerable as treatment-related adverse events were mild to moderate in severity with manageable through proper interruptions and dose reduction.
- Lenvatinib could become one of the standard treatment options in patients with advanced or metastatic thymic carcinoma previously treated with platinum-based chemotherapy.