8581: PHASE 1/2 TRIAL OF LURBINECTEDIN (L) IN COMBINATION WITH PEMBROLIZUMAB (P) IN RELAPSED SMALL CELL LUNG CANCER (SCLC): THE LUPER STUDY

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MEDSIR MEDICA SCIENTIA INNOVATION RESEARCH

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BACKGROUND

- Lurbinectedin (L) inhibits trans-activated transcription and modulates the tumor microenvironment.
- L is approved by the FDA for metastatic SCLC patients (pts) with progressive disease (PD) on or after platinum-based chemotherapy (CT).
- The LUPER study is assessing for the first time the safety, tolerability, and preliminary efficacy of L + pembrolizumab (P) as second-line regimen for SCLC pts after failure of platinum-based CT.

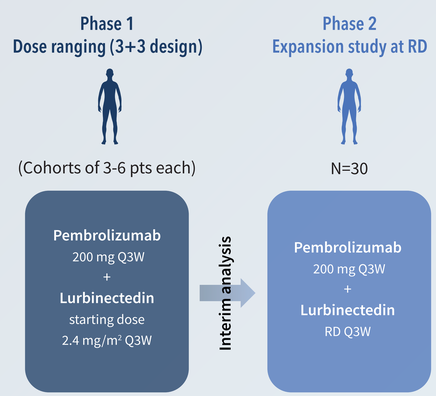
Baseline characteristics, n (%)		All, (N = 13)
Age, Median (Min; Max)		66 (43; 78)
Sex	Female	6 (46%)
	Male	7 (54%)
ECOG	0	5 (38%)
	1	8 (62%)
Disease stage at diagnosis	Extended	9 (69%)
	Limited	4 (31%)
CT-free interval	< 3 months, Resistant	6 (46%)
	> 3 months, Sensitive	7 (54%)
BMs	Yes	2 (15%)
	No	11 (85%)
LDH level	> UNL	5 (38%)
	< UNL	8 (62%)

METHODS AND STUDY DESIGN

Prospective phase I/II, multicenter, open-label study (NCT04358237)

Key inclusion criteria

- ≥18 years with confirmed SCLC
- ECOG PS 0-1
- Measurable disease as per RECIST v.1.1
- Progression to a CT-containing regimen (≥4 weeks before study initiation)
- Previous immunotherapy NOT allowed
- Pts with treated, stable, asymptomatic brain metastases (BMs) are allowed



The RP2D was the highest DL at which 0/3 pts or ≤1/6 pts experienced DLTs during the first cycle.
P and L will be administered Day 1 Q3W until disease progression, unacceptable toxicity, or consent withdrawal.

Primary endpoints

- Phase 1: MTD and RD of L in combination with P for phase II in pts with relapsed SCLC.
- Phase 2: Efficacy of L in combination with P in terms of ORR, according to RECIST 1.1, in pts with relapsed SCLC.

Secondary endpoints

- Safety as per CTCAE 5.0, preliminary efficacy, and pharmacokinetics.

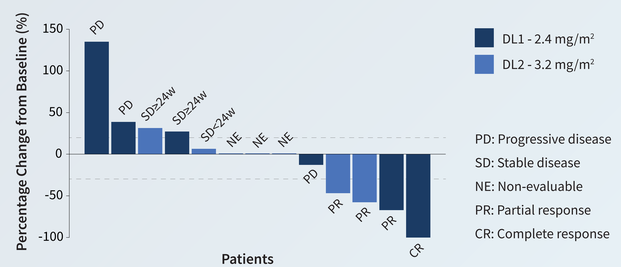
RESULTS (PHASE 1 PART)

- Thirteen pts were enrolled across 3 hospitals in Spain (DL1, n=7; DL2, n=6).
- At data cut-off (Mar 10, 2022), 4 (30.8%) pts remained on treatment (≥8 cycles).
- One DLT (G3 fatigue) occurred in the DL1. One non-clinically relevant DLT (G4 neutropenia) was reported at each DL.
- The RP2D was identified as 3.2 mg/m² L and 200 mg P i.v. Q3W.
- Total clearance of L was 13.0 L/h, therefore similar to that from a cohort of 101 patients with SCLC (11.7 L/h) (study B-005). A major effect of P on the pharmacokinetics of L is ruled out as anticipated based on the absence of common metabolic pathways.

Preliminary Efficacy

- Median duration of treatment was 3.1 (0–14.6) months.
- Median relative dose intensity of L and P were 90.6% and 90.8%, respectively.
- Responses were shown in both DLs, with ORR of 30.8%. (See Figure 1 for details).
- Median DoR was not reached; at 9 months 75% (95% CI: 42.6%-100%) pts were responding.

Figure 1. Best Overall Response according to RECIST v.1.1



Safety Analysis

Related TEAE

Overall (N=13)	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)
TEAEs*	11 (84.6)	7 (53.9)	2 (15.4)
Haematologic	8 (61.5)	3 (23.1)	2 (15.4)
Neutropenia	7 (53.9)	3 (23.1)	2 (15.4)
Thrombocytopenia	3 (23.1)	1 (7.7)	0 (0.0)
Anaemia	2 (15.4)	0 (0.0)	0 (0.0)
Non-haematologic**	11 (84.6)	4 (30.8)	0 (0.0)
Fatigue	10 (76.9)	1 (7.7)	0 (0.0)
Nausea	7 (53.9)	0 (0.0)	0 (0.0)
ALT increased	4 (30.8)	3 (23.1)	0 (0.0)
Decreased appetite	4 (30.8)	0 (0.0)	0 (0.0)
Vomiting	2 (15.4)	0 (0.0)	0 (0.0)
Constipation	2 (15.4)	0 (0.0)	0 (0.0)
AST increased	3 (23.1)	2 (15.4)	0 (0.0)
Dyspnoea	2 (15.4)	0 (0.0)	0 (0.0)

*TEAEs with incidence > 10%.
**One patient had a Grade 5 COVID-19 Adverse Event.
Immune-related AEs (G2 pneumonitis; G3 ALT increased) led to P discontinuation in 2 (15.4%) pts.

CONCLUSIONS

- Second-line L+P for relapsed SCLC pts have a manageable safety profile and demonstrate preliminary efficacy in phase 1/2 LUPER study.
- This combination warrants further confirmation in the ongoing expansion phase 2 with additional biomarker analysis of efficacy.

ACKNOWLEDGEMENTS

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Abbreviations: ALT: alanine aminotransferase; AST: Aspartate aminotransferase; BMs: brain metastases; DOR: Duration Of Response; ECOG: Eastern Cooperative Oncology Group; Q3W: Every-Three-Week; OS: overall survival; ORR: objective response rate; PFS: Progression-free survival; Pts: patients; RECIST: Response Evaluation Criteria In Solid Tumors; RD: Recommended Dose; RP2D: recommended phase II dose; SCLC: Small Cell Lung Cancer; DLTs: dose-limiting toxicities; N/n: number of patients; TEAE: Treatment Emergent Adverse Event; UNL: Upper Normal Limit

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