OVERALL SURVIVAL WITH LURBINECTEDIN PLUS DOXORUBICIN IN RELAPSED SCLC: RESULTS FROM AN EXPANSION COHORT OF A PHASE IB TRIAL.

Martin Forster1, Víctor Moreno2, Emilio Calvo1, María Eugenia Olmedo3, María Pilar López Criado3, José Antonio López-Vilarío4, Rafael Núñez5, Carmen Kahatt6.

1 University College of London Hospital and UCL Cancer Institute, London, UK. 2 START Madrid – FID (Hospital Fundación Jiménez Diaz), Madrid, Spain. 3 START Madrid - HM CIIOC, Hospital Madrid Norte Sanchinarro, Madrid, Spain. 4 Hospital Ramón y Cajal, Madrid, Spain. 5 M.D. Anderson Cancer Center, Madrid, Spain. 6 Pharma Mar, S.A., Colmenar Viejo, Madrid, Spain.

BACKGROUND

Lurbinaectedin (Lzpa-189, FR181684 Li) is a new investigational drug that is thought in block transcription to selectively inhibit a subset of transcriptional protein-protein interactions in transcriptionally-active tumour cells, like SCLC. Lzpa creates a detachment of transcription factors from their promoters initiating its anti-tumour activity (1).

METHODS

SCLC patients ≥18 years with relapsed or resistant disease had Lzpa-189 (Lzpa) and doxorubicin (DOX) offered in a phase Ib expansion cohort. Eligibility criteria: CTFI ≥ 90 days (Sensitive) or CTFI < 90 days (Resistant). A total of 21 patients were included, 18 at CTFI ≥ 90d and 3 at CTFI<90d (n=3).

RESULTS

SCLC patients ≥18 years with relapsed or resistant disease had Lzpa-189 (Lzpa) and doxorubicin (DOX) offered in a phase Ib expansion cohort. Eligibility criteria: CTFI ≥ 90 days (Sensitive) or CTFI < 90 days (Resistant). A total of 21 patients were included, 18 at CTFI ≥ 90d and 3 at CTFI<90d (n=3).

- Cohort B: OSI 40 mg/m² + 2 mg/m²/day 1st day and continue with L at 4 mg/m² after DS with cumulative dose of 600 mg/m² reached.

-- Objective response rate in SCLC and according to CNS involvement:

- Cohort A: Objective responses in SCLC excluding pts with CTFI <90d day 1 and day 2 according to CTFI/chemotherapy-free interval (CTFI; sensitive vs resistant).

- Cohort B: Objective responses in SCLC excluding pts with CTFI <90d day 1 and day 2 according to CTFI/chemotherapy-free interval (CTFI; sensitive vs resistant).

- Waterfall 3D Cohort B, showing maximal tumor variation in 3D according to CTFI and PFS (n=27).

- Spreader plot showing tumor variation over time during treatment with L/DOX in 3D cohort in cohort B patients (n=27).

CONCLUSIONS

- Lzpa/DOX combination showed remarkable activity as second line in SCLC, especially in sensitive patients (CTFI<90d).

- Activity is higher than that reported for CAV or topotecan.

- OS shows a remarkable improvement in this second-line setting, especially when excluding refractory pts. (CTFI>90d).

- Main hematologic toxicity was myelosuppression well-managed with G-CSF and dose reductions.

- A phase II clinical trial (ATLANTIS, NCT02566993) evaluating this combination in relapsed SCLC patients has recently completed recruitment.

ACKNOWLEDGEMENTS

- To all the patients and their families

- To all the investigators involved in this trial

- To Ana García Salas and Mariano Siguero for their help and support