Activity of lurbinectedin as single agent and in combination in patients with advanced small cell lung cancer (SCLC) 

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Background

Lurbinectedin (Zeprovin®; PMH101) is a novel anticancer drug that inhibits activated transcription. Unlike DNA double-strand breaks generating agents, and includes tumor microenvironment. Pharmacological modulation of active transcription is a valid approach to tumor targets that are dependent on transcription activation. Small Cell Lung Cancer (SCLC) cells are addicted to transcriptional rogue transcription factors that support their growth. Resistant SCLC still remains an unmet medical need.

Methods

Antitumor activity and safety of lurbinectedin in SCLC was reviewed in three clinical trials (multi-patient) 1-3: randomized phase II/III study with lurbinectedin in combination with Paclitaxel (L+TAX), and a phase I single arm study with lurbinectedin L+DOX (L+DOX) (Cohort A and B).

Trials design and schedule

A. PMH13-069-15 (L+DOX)

• Phase 2: 3+3 dose escalation followed by dose expansion at RD in selected lines, including SCLC.
• Phase 3: 3+3 dose-challenge 5 mg/m² lurbinectedin daily 5 days/week or placebo (L+TAX), and a single arm single agent lurbinectedin L+DOX (L+DOX) cohort.

Treated patients

- Lurbinectedin dose escalation: 50 mg/m² + Lurbinectedin 15 mg/m² drug (FD) daily qw and continue with lurbinectedin 7 mg/m² RD after DOX cumulative dose of 400 mg/m². RD dose escalation 50 mg/m² lurbinectedin 2 mg/m² qw.
- Lurbinectedin dose expansion: 10 mg/m² qw and continue with lurbinectedin 4 mg/m² RD cumulative dose of 450 mg/m².

B. PMH13-067-11 (L+TAX)

• Phase 1-3 dose escalation followed by dose expansion of RD in selected lines including SCLC.
• Phase 3: 2+2 dose-challenge lurbinectedin l+TAX daily 10 mg/m² qw and 25 mg/m² qw.

Treatment Schedule

- liquor weekly for the continued with lurbinectedin alone; lurbinectedin day 1 qw.
- RD-Full at 60 mg/m² D1 and 60 mg/m² T1 qw.

C. PMH13-068-14 (Lurbinectedin single agent)

• Phase 1: Multifunctional open label, exploratory, basket trial.
• Phase 2: 3+3 dose-challenge lurbinectedin for selected disease lines.

Treated patients

- lurbinectedin dose escalation 3.2 mg/m² qw 1h infusion qw.
- lurbinectedin dose expansion 6.4 mg/m² qw.

No activity in this indication

SCLC Subgroup

1 response in 15 patients

Conclusions

- Lurbinectedin shows strong and consistent activity as a single agent and in combination with other agents (DOX and TAX) in relapsed SCLC.
- Results were remarkable in terms of DRR, PFS and OCR, especially in platinum-sensitive SCLC.
- Toxicity mainly consisted of transient myelosuppression, which was manageable with dose reductions and G-CSF use.
- A randomized Phase II with L+DOX is ongoing (ATLANTIS Study - NCT02566693).

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