2SMALL (NCT04253145) PHASE I PART: LURBINECTIDINE (LUR) IN COMBINATION WITH ATEZOLIZUMAB (ATZ) FOR SECOND LINE EXTENSIVE STAGE SMALL CELL LUNG CANCER (ES-SCLC) PATIENTS (PTS)

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Background Current front-line treatment for ES-SCLC includes chemotherapy plus a PD-L1 inhibitor. FDA has recently approved LUR for pretreated patients with SCLC. 2SMALL is a two-part phase 1/2 study assessing the safety, tolerability and efficacy of LUR in combination with ATZ as second line treatment for ES-SCLC. Here we report data from phase I part of the 2SMALL trial (data cut off 14-07-2021)

Methods 2SMALL phase I was an open-label, single arm, dose exploration trial. Eligible patients had confirmed ES-SCLC, who progressed to first line platinum based treatment, ECOG performance status score 0-1 and adequate organ function; prior exposure to immunotherapy was not allowed. During dose finding phase pts received increasing doses of LUR (2.5 mg/m² - 3.2 mg/m²) on day (D) 1 plus a fixed dose of ATZ (1200 mg) every 3 weeks following a standard 3+3 dose escalation design. Study endpoints included the definition of the safety profile and the recommended dose. Additional objectives included efficacy (ORR and PFS).

Results 26 patients were treated, including male 14 pts (53.84%), with median age 60.6 years. Five pts received LUR 2.5 mg/m² + ATZ 1200 mg, and 3 pts were evaluable without DLT. Out of the 21 pts who received LUR 3.2 mg/m² + ATZ 1200 mg (6 pts with primary G-CSF), 5 pts (20.83%) developed DTLs: 2 pts G3 febrile neutropenia (9.52%) (1 pt with G4 thrombocytopenia), 2 pts G4 neutropenia lasting more than 72h (9.52%), 1 pt G4 thrombocytopenia (4.76%). Most frequent haematological adverse events ≥ grade 2 (21 pts) were neutropenia (42.86%), thrombocytopenia (28.57%), anaemia (19.05%); lymphopenia (4.76%) and febrile neutropenia (4.76%). The most common non-haematological TAEs ≥ grade 2 was asthenia 30.76%. No deaths treatment-related were reported. Objective responses were observed in 15 pts (ORR: 57.69%), including complete responses in 2 pts (7.69%), partial response in 13 pts (50%). 6 pts had stable disease (26.92%) and 3 pts progressive disease (11.54%). Disease control rate was 84.61%. With 8 pts censored for progression, median PFS was 4.93 months (range 3.37 - 7.67 months).

Conclusions The combination of LUR plus ATZ was well tolerated, without unexpected toxicities. Transient haematological toxicity was dose limiting. The RD for further studies is LUR 3.2 mg/m² on D1 + ATZ 1200 mg D1 with G-CSF. Preliminary anti-tumor activity is remarkable. 2SMALL trial part II is ongoing, and will provide further data regarding efficacy and safety of the regimen for second line SCLC.

Trial Registration NCT04253145

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