7591 General Poster Session (Board #29A), Sat, 8:00 AM-11:45 AM

Phase I/IIa study of the novel combination of bendamustine (B) with irinotecan (I) followed by etoposide (E) and carboplatin (C) in untreated patients (Pts) with extensive-stage small cell lung cancer (ESSCLC).

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Background: Standard therapy for ESSCLC consisting of E and a platin drug (Plat) yields a median time to progression (TTP) of 4 months (m) and overall survival (OS) of 9 m. DNA damage from B is repaired by excision repair, akin to Plat. The activity of I, a topoisomerase (Top)-1 inhibitor, leads to increases in Top-2, the target of E. The sequence B+I → E+C was hypothesized to increase TTP by exploiting mitotic catastrophe. **Methods:** This is an open label trial enrolling pts with ESSCLC and evaluable disease. The phase I primary endpoint was to determine the maximum tolerated dose (MTD) of B+I; the phase IIa primary endpoint was TTP after B+I→E+C. Secondary endpoints were objective response rate (ORR) and OS. In the phase I (N=15), cohorts received I (150 mg/m^2, d 1) with B at 80, 100, or 120 mg/m^2/day (d 1,2) every 3 weeks for 3 cycles. Phase IIa Pts were treated at the recommended dose of B+I for 3 cycles followed by E (100 mg/m^2, d 1-3) + C (AUC 6, d 1) for 3 cycles. Restaging was performed after 3 cycles of each regimen. The phase IIa was powered to detect a 30% increase in TTP from 4 to 5.2 m with a of 0.1. The Kaplan-Meier method was used to calculate TTP and OS. Toxicities were evaluated using the NCI CTCAE. **Results:** The MTD of B was not reached. The recommended phase IIa dose of B was 100 mg/m^2; dose-escalation was allowed in subsequent cycles of therapy. Dose limiting toxicities were diarrhea, nausea, and vomiting. One treatment-related death from metabolic encephalopathy occurred in the phase IIa. The commonest grade 3/4 hematologic toxicity was neutropenia. Fatigue, nausea, vomiting, and diarrhea were common non-hematologic toxicities. **Conclusions:** B+I is an active regimen in ESSCLC and the treatment sequence B+I→E+C seems to improve the TTP and OS in ESSCLC compared to historic values for E+C. Toxicities were increased compared to historic values for E+C, but were manageable. Correlative studies with pre-treatment assessment of tumor ERCC-1, Top-1, and Top-2 as predictors of response are ongoing. Clinical trial information: NCT00856830.

Efficacy parameters (N=29).

Median TTP		**6.0 m (95% CI 5.0-7.0)**
Median OS	10.0 m (95% CI 8.3-11.7)	
ORR	75%	
Median tumor reduction after	B+I	65%
E+C	73%	