untreated patients with extensive-disease (ED) SCLC has not been established.
Purpose: To determine the maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of amrubicin and carboplatin in ED-SCLC.
Patients and Methods: Eligibility criteria were chemotherapy-naive ED-SCLC patients, performance status 0−1, age <75, and adequate hematological, hepatic, and renal function. Patients received escalating amrubicin doses under a fixed target AUC 5 of carboplatin (Chatelut formula). Amrubicin and carboplatin were administered by intravenous (i.v.) infusion on days 1, 2, and 3, and day 1, respectively. The initial dose of amrubicin was 30 mg/m^2, and the dose was escalated to 35 and 40 mg/m^2.
Results: Sixteen patients were enrolled and 15 eligible patients were evaluated. One of 6 patients in level 1, 1 of 6 in level 2, and 3 of 3 in level 3 experienced DLT. The presentation of DLTs included neutropenia, leukopenia, thrombocytopenia, febrile neutropenia, and liver dysfunction. The MTD doses of amrubicin and carboplatin were determined as 40 mg/m^2 and AUC 5. Evaluation of responses were 2CR, 9PR, 3SD, and 1PD (response rate 73%), and the median survival time was 13.6 months.
Conclusions: A dose of 35 mg/m^2 amrubicin and carboplatin AUC 5 were recommended. This regimen is associated with an acceptable tolerability profile, and warrants evaluation in the phase II setting.

9118 POSTER

Effect of chemotherapy (CT) in patients (pts) with resected small-cell (SCLC) or large-cell neuro endocrine carcinoma (LCNEC)

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Background: CT and concurrent radiotherapy is the current standard of treatment for limited-stage (LS) SCLC. The role of surgery is limited and remains a matter of controversy. Surgical resection of undiagnosed lung lesion may lead to unintentional removal of SCLC. The benefit of peri-operative CT in resected SCLC or large cell neuroendocrine tumors is unknown.
Material and Methods: This retrospective analysis included LS-SCLC and LCNEC surgically removed between 1979 and 2007 at Surgical Centre Marie Lannelongue. Logrank test was used to compare overall survival.
Results: Among 74 total pts identified, 29 pts (25 male, 4 female, median age of 64 years) underwent surgery (S) and 45 (38 male, 7 female, median age of 58 years) underwent surgery plus chemotherapy (S+C). Four and 21 pts had pre- and post-operative radiotherapy respectively. Pathological diagnosis was as follow: (1) group S: 25 SCLC, 4 LCNEC, 15 pN0 and 10 pN+, and only 2 resections were incomplete (2) group S+C: 34 SCLC, 11 LCNEC, 15 pN0, 27 pN+ and only 3 resections were incomplete. CT was preoperative in 9 pts and postoperative in 37 pts; 62% of the pts received etoposide/platinum, 13% platinum/other agent, 25% other. 15 pts were excluded from the survival analysis, 3 pts alive whose follow-up did not exceed 6 months, 12 pts died within 6 months postoperative, including 4 within 1 month in group S. Among the patients alive at 6 months or followed at least 6 months (n = 59), 33 died, with an overall median follow-up of 5.8 years (range 0.6−19.6). It is 4.5 years (1.4−7) for the group S and 5.8 years (0.6−19.6) for the group S+C. The median survival of the group S (n = 20) and S+C (n = 39) were 2.3 and 6.1 years respectively. The hazard ratio of death was 0.48 (95% CI [0.24–0.99], p = 0.04) for the group S+C compared to the group S. The overall survival at 3 years was 48% in the group S compared to 59% in the group S+C.
Conclusion: These results suggest that peri-operative chemotherapy may be beneficial in pts with resected SCLC or LCNEC.

9119 POSTER

Reciprocal CD4+ T cell balance of Th17 and Treg in small cell lung cancer reflects disease stage

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Background: Small cell lung cancer (SCLC) possesses high tendency to disseminate. However, SCLC patients with paraneoplastic syndrome mediated by immunity against onconeural antigens remain in limited-stage disease (LD) without distant metastases. Cumulative evidence regulates that a balance between immune and regulatory T cells (Treg) determines the magnitude of immune responses to not only self-antigens but also tumor-associated antigens. The purpose of this study was to elucidate the immunological balance induced in SCLC patients.
Materials and Methods: We analyzed T cells in the peripheral blood of 35 consecutive SCLC patients, 8 long-term survivors, and 19 healthy volunteers.
Results: Purified CD4$^+$ T cells with down-regulated expression of CD62L (CD62L^{low}) produced IFN-g, IL-4, and IL-17, thus, considered to be immune effector T cells (Teff). Significantly more Teff numbers were detected in LD-SCLC patients than that of extended-stage (ED) SCLC. By contrast, induction of CD62L^{high}CD25$^+$ CD4$^+$ Treg was significantly higher in ED-SCLC patients. Long-term survivors of SCLC maintained a high Teff to Treg ratio, whereas patients with recurrent disease exhibited a low Teff to Treg ratio. Teff in LD-SCLC patients included more IL-17-producing CD4$^+$ T cells (Th17).
Conclusion: These results show that CD4$^+$ T cell balance may be a biomarker that distinguishes disease stages and predicts recurrence. This study also suggests the importance of inducing effector CD4$^+$ T cells, particularly Th17 cells, while eliminating Treg to control systemic dissemination of SCLC.

9120 POSTER

Second-line amrubicin vs topotecan in extensive-disease small cell lung cancer (ED-SCLC) sensitive to first-line platinum-based chemotherapy: updated results of a randomized phase 2 trial

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Background: Amrubicin (AMR) is a 3rd-generation synthetic anthracycline and potent topoisomerase II inhibitor that has shown an improved early cardiac safety profile relative to other anthracyclines. We compare the efficacy and safety of AMR for 2nd-line treatment of ED-SCLC sensitive to 1st-line chemotherapy with that of topotecan (Topo).
Methods: Randomized, phase 2, open-label, multicenter study (NCT 00319969). Eligible pts had ED-SCLC sensitive to 1st-line platinum-based chemotherapy (recurrence or progression $\geqslant$90 days from completion of 1st-line treatment), ECOG PS $\leqslant$2, and only 1 prior therapy. Pts were randomized (2:1) to IV AMR 40 mg/m^2/d (days 1−3) or IV Topo 1.5 mg/m^2/d (days 1−5) q21 days until progression, unacceptable toxicity, or withdrawal. The primary endpoint was overall response rate (ORR, by RECIST). Secondary endpoints were time to progression (TTP), progression-free survival (PFS), overall survival (OS), and safety. Left ventricular ejection fraction (LVEF) in AMR pts was measured by ECHO or MUGA at baseline (BL), cycles 3, 6, then every 2 cycles, and end of treatment.

Response	AMR (n = 50) n (%)	Topo (n = 26) n(%)
ORR*	22 (44)	3 (12)
CR	6 (12)	1 (4)
PR	16 (32)	2 (8)
SD	11 (22)	10 (39)
PD	13 (26)	9 (35)
N/A†	4 (8)	4 (15)

*AMR vs Topo, p = 0.005; †8 pts (4 each group) discontinued or died before first response assessment.

Results: 76 pts were randomized to AMR (n = 50) or Topo (n = 26). AMR was given for a median of 6 cycles (range 1−16); Topo 3 cycles (1−16). AMR significantly improved ORR vs Topo (p = 0.005 Table), including in older ($\geqslant$65 yrs) pts: 46% vs 7%, respectively. Median TTP was 5.6 mos (95% CI 2.8, 6.9) with AMR vs 3.0 mos (95% CI 1.4, 4.4) with Topo. Median PFS was 4.6 mos (95% CI 2.1, 6.1) with AMR vs 3.3 mos (95% CI 2.2, 5.4) with Topo. Median OS was 9.3 mos (95% CI 5.8, 12.2) with AMR vs 7.7 mos (95% CI 4.5, 14.0) with Topo. The most common grade $\geqslant$3 AEs with AMR vs Topo were neutropenia (61% vs 78%), thrombocytopenia (39% vs 61%) and leukopenia (39% vs 39%). Dose reductions were required in