(SCLC) tumor cells. In patients with SCLC, IL-2 secretion is significantly impaired at the time of diagnosis. Reconstitution of cytokine secretion correlated with reduction of tumor load. Thus, the immune system was suppressed by the tumor.

Methods: Using the Kaplan-Meier method, the log-rank test and the cox-regression model, we analysed the relation of IL-2 secretion in whole blood cell cultures from 52 patients with SCLC at diagnosis to established prognostic factors and survival.

Results: Impairment of IL-2 secretion influences survival in SCLC ($p = 0.004$). This prognostic factor is independent from stage of disease, NSE, LDH, age, and sex. The prognostic value of IL-2 secretion is comparable to the most predominant prognostic factors identified for SCLC. In the final model of cox regression, p-value for IL-2 and stage of disease was 0.012 and 0.019, respectively. High level of IL-2 predicts for improved survival after complete response (CR) to chemotherapy. With 45/52 failures at the last follow up, median survival was 1290 days (d) in CR/IL-2 > 1550 pg/ml (high), 330 d in CR/IL-2 < 1550 pg/ml (low), 390 d in PR/high IL-2, 300 in PR/low IL-2 ($p = 0.00005$).

Conclusion: Prognosis in SCLC may be predicted from IL-2 level at diagnosis. Long term survival seems to be partly characterized by CR to chemotherapy and high IL-2 level at diagnosis. As IL-2 secretion is suppressed by SCLC-derived TGF β1, immunobiological interactions may influence the clinical course of this disease.

1032 ORAL

Preliminary results of a randomised comparative phase III trial of topotecan versus CAV as second-line therapy of small cell lung cancer

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Purpose: To compare single agent topotecan (T) with the commonly used regimen CAV for the second-line therapy of small cell lung cancer (SCLC) in an ongoing international randomised trial.

Methods: Eligible patients (pts) with measurable disease, who responded to first-line chemotherapy & were off-treatment ≥60 days before relapse receive either T (1.5 mg/m^2/d iv. d1–5 q 21 d) or CAV (cyclophosphamide 1000 mg/m^2, doxorubicin 45 mg/m^2 & vincristine 2 mg, iv., d 1 q 21d). At interim analysis 161 pts received ≥1 treatment; 125 pts are evaluable for efficacy with up to ≥20 weeks follow-up. 64 pts were treated with T (total 239 courses [crs], median 3.5/pt); 61 pts were treated with CAV (total 195 crs, median 3/pt).

Results: Partial responses were seen in 16/64 (25%) T pts & 9/61 (15%) CAV pts (confirmed by independent radiological review). Median time to progression for T pts is 11.1 wk & 11.9 wk for CAV pts. Median survival for T pts is 21.7 wk & for CAV pts is 23.1 wk. Grade 3/4 haematological toxicities: neutropenia in 63% of T crs & in 67% CAV crs; anaemia in 18% of T crs & 6% of CAV crs; thrombocytopenia in 32% of T crs & 9% of CAV crs. Neutropenic fever, infection with neutropenia, or sepsis have been associated with 7.5% of T crs & 9.7% of CAV crs. Grade 3/4 non-haematological toxicities related to study drug occurred in 19 (30%) T pts & in 20 (33%) CAV pts. Related adverse events caused 11 pts to withdraw from the study, (5 T[8%] & 6 CAV[10%] pts).

Conclusion: Preliminary results suggest that single agent T has similar efficacy, with manageable toxicity, to CAV in pts with SCLC who responded to first-line therapy.

1033 ORAL

Preliminary results of a randomised phase III trial of an established chemotherapy (CT) regimen with or without lenograstim (rHuG-CSF) in small cell lung cancer (SCLC): Impact on survival

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Purpose: to investigate the potential survival benefit of the CT optimisation due to lenograstim support in previously untreated SCLC patients (pts).

Methods: up to 6 cycles of ACE (Doxo 45 mg/m^2, day 1 (d1), Cyclo 1000 mg/m^2, d1 and VP16 100 mg/m^2 iv d1 and 240 mg/m^2 po or 100 mg/m^2 iv d2–d3) with (lenograstim arm: L) or without (control arm: C) rHuG-CSF, were planned to be administered every 3 weeks Lenograstim was administered at a daily dose of 50 μg/m^2 sc, starting on d4.

Results: 280 pts were randomised. (L arm: 141; C arm: 139), 276 were treated. An intent-to-treat analysis was performed. A total of 859 cycles was administered. Twenty seven percent of pts in both arms completed 6 CT cycles. The number of pts with CT delay was lower in the L arm (39% vs 47%). The recovery of ANC > 1.5 × 10^9/l at d14 was significantly higher in the L arm over cycles. Non haematological toxicity was identical in both groups as well as infections. The assessment of tumoural response was stratified according to the tumour status at baseline (limited [LD] or extensive [ED] disease). The objective response (CR + PR) and complete response rate in the 268 evaluated pts were not different.

With a median follow-up of 25 months, the median survival was 11 months in the L arm and 9 months in the C arm (not significant).

Conclusion: in this chemotherapy optimisation trial, the survival improvement did not reach statistical significance. However, considering the good neutrophil recovery at d14 in the L arm, CT intensification seems feasible as was demonstrated by Thatcher et al (EJC, 1995) and could lead to further survival benefits as was proposed by Woll et al (JCO, 1995). This is being explored in further studies.

1034 ORAL

Randomized trials evaluating radiotherapy adjuvant to chemotherapy for small cell lung carcinoma (SCLC): Qualitative evaluation before meta-analysis

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The role of adjuvant radiotherapy for limited disease SCLC remains controversial. In 2 recent meta-analyses, survival was significantly prolonged when radiotherapy was added to chemotherapy. Chalmers et al have elaborated qualitative criteria evaluating publications methodology and Marino et al tested that scale in a meta-analysis in non small cell lung cancer. Our group elaborated a more complete qualitative scale, including 51 criteria. The quality score of the article was expressed in percentage of a maximal theoretical score. We compared the results obtained by our method with these of Chalmers-Marino. A quantitative meta-analysis, based on the available published data (8 studies) was performed. Chest radiotherapy combined to chemotherapy was associated to a non significant advantage (odd ratio = 0.82; 95%CI 0.63–1.07). The qualitative ELCWP score of the 14 eligible articles ranged from 29.5% to 73%. A good correlation could be established between our score and that of Chalmers-Marino ($r = 0.87$, $p < 0.001$). No significant difference in quality score was observed between the studies according to eligibility for quantitative meta-analysis, date of publication, date of the first patient inclusion and reported radiotherapy efficacy. Few studies mentioned important criteria like definition of the primary endpoint (14.2%) and β error (0%). In conclusion, quality scores should be taken into account when publishing quantitative meta-analyses in order to reduce heterogeneity in the studies quality.