1053 POSTER

Interim report of a phase I study of docetaxel (Taxotere®) in combination with vinorelbine in chemotherapy naive patients with metastatic or inoperable non small cell lung cancer (NSCLC)

T. Le Chevalier[1], A. Monnier[2], M. Aapro[3], J.Y. Douillard[4], S. Nahon[1], X.S. Sun[2], T. De Pas[3], C. Loret[5], N. Bougon[5], J. Bérille[5]. [1]*Institut Gustave Roussy, Villejuif;* [2]*C.H.G. Boulloche, Montbéliard;* [4]*Centre René Gaudducheau, Nantes;* [5]*Rhône-Poulenc Rorer, Antony, France;* [3]*Istituto Europeo di Oncologia, Milano, Italy*

Because of the potential synergism between docetaxel (D) and vinorelbine (V) a phase I study was initiated in order to determine the dose limiting toxicity (DLT), the maximum tolerated dose (MTD), the optimal dose and sheduling: (V) i.v. d1 and d8, (D) i.v. d8, q3 weeks. Eligible patients (pts) had histologically proven NSCLC, at least one measurable lesion, no previous chemotherapy, WHO PS ≤ 2, normal hematologic-hepatic-renal functions, no brain involvement. To date 34 pts were treated: 79% male; median age: 53 years (31–68); median PS: 1; adenocarcinoma 53%; squamous cell 23%; large cell 18%; other 6%; metastatic 81%. Pts received a mean of 4 cycles (1–9). Main toxicities were:

	Vd1-Vd8-Dd8[2] mg/m^2	Pts Treat/Elig	DLT Nb	DLT Type	N G-4	FN	M G-3	NS G-3	D G-4	V G-4	AL G-4	A sev.
1	20-20-75	8/7	2	1M/1N+I	8	2	2	–	–	–	–	–
2	25-20-75	3/3	0	–	2	–	–	–	–	–	–	–
3	25-20-85	7/5	1	1FN	7	2	–	1	1	–	–	1
4	25-25-85	7/7	1	1FN	5	2	–	–	–	–	1	–
4b	25-20-100	4/4	2	1FN+M/1TD	4	1	1	–	1	–	–	–
5	25-25-100	5/5	3	1FN/1NS 1N+I	5	2	–	1	–	1	–	1

* N neutropenia – FN febrile neutropenia – M mucositis – NS neurosensory – D diarrhea – V vomiting – AL allergy – A asthenia – I infection – TD toxic death.

At the dose-level 4b, 2 pts developed DLT. It is now considered the MTD. This combination appears feasible at close to the recommended dose for single agents D and V.

1054 POSTER

Gemcitabine and etoposide in chemonaive patients with extensive small cell lung cancer (SCLC): Preliminary phase II results

J.v. Pawel[1], U. Gatzemeier, J. Vansteenkiste, P. Weynants, A. Hanauske, L. Bosquée, K. Mansouri, S. Znamensky, J. Blatter, Chr. Manegold[2]. [1]*Zentralkrankenhaus, Gauting;* [2]*Thoraxklinik, Heidelberg-Rohrbach, Germany*

Purpose: Single-agent GEMZAR® (Gemcitabine HCl) produced an objective response rate of 27% in chemonaive patients with extensive SCLC. Etoposide also shows activity against SCLC. In a phase I study MTD was achieved with gemcitabine 1000 mg/m^2 given on days 1, 8, 15 of a 28 day cycle and etoposide 80 mg/m^2 given on days 8, 9 and 10. We report here the preliminary results of a subsequent phase II study using this combination.

Methods: Schedules and dosages were as above. Patients were eligible for inclusion if they had histological or cytological confirmation of extensive SCLC, PS > 60%, and adequate bone marrow reserve (baseline WBC > 1500/mL, platelets >100,000/mL, haemoglobin >10 g/dL). Patients were excluded if they had CNS metastases, serious concomitant systemic disorders, or any prior chemotherapy.

Results: 42 patients (pts) with progressive extensive SCLC have entered the study. 27 pts (9 F, 18 M) are evaluable for toxicity, response and demographics: median age, 58 (41–74) years; median Karnofsky PS 90% (70–100%); median number of involved organs, 5: liver (51.9% of patients), lung metastases (66.7%), lymph nodes (59.3%), adrenal (37.0%) and bone (14.8%). Of 22 evaluable pts, there were 9 PRs, 8 SDs, 5 PDs. The incidence of WHO grade 3 and 4 toxicity per cycle was: 17.0/2.4% leukopenia, 7.3/7.3% neutropenia (without febrile neutropenic sepsis), 4 9/0% thrombocytopenia, 2.4/2.4% AST, 7.3/0% nausea/vomiting, 0/2.4% mucositis, 32.7/0% alopecia, 0/2.4% cutaneous.

Conclusion: These preliminary data suggest that gemcitabine is both effective and well tolerated in combination with etoposide in patients with extensive SCLC.

1055 POSTER

Post operative high dose conformal radiation therapy with multileaf collimator for non small cell lung cancer (NSCLC)

S. Vuillermoz[1], I. Martel[2], L. Falchero[3], M. Vincent[4], D. Boutry[5], D. Arpin[6], C. Carrie[2]. [1]*Hôpital de la Croix Rousse, Dpt Pneumologie, Lyon;* [2]*Centre Léon Bérard Dpt Radiothérapie, Lyon;* [3]*Hôpital Louis Pradel, Dpt Pneumologie Lyon;* [4]*Hôpital St Joseph, Dpt Pneumologie, Lyon;* [5]*Hôpital de Villefranche/Saône, Dpt Pneumologie;* [6]*Hôpital de Mâcon, Dpt Pneumologie, France*

Purpose: Between 02/95 and 12/96, 13 patients with NSCLC were postoperatively treated by high dose conformal radiation therapy (4 after pneumonectomy, 6 after lobectomy and 3 after bilobectomy). Eight had nodal involvement, 4 surgical margin involvment, and 1 was T3.

Methods: No patient received concomitant or postradiation chemotherapy. The planified target volume (PTV) encompassed homolateral hilum and supraclavicular area for upper tumor until 50 Gy (25 fractions/5 weeks) through at least 6 portal entrances collimated by multileaf collimator; the PTV was then reduced with a safety margin of 0.5 cm until 66 Gy. The mean PTV n°2 was 220 cm^3. Dose-volume histogramms were done for normal tissues and tumor for each patient.

Results: After a mean follow-up of 10 months, no acute or late radio-induced pneumonitis occurred. One patient died of widespread disease and no local failure has yet been observed.

Conclusion: Postoperative high dose conformal radiation therapy is well tolerated and seems to allow an excellent local control rate but more follow up is needed.

1056 POSTER

Neoadjuvant cisplatin- vindesine/vinorelbine based combination chemotherapy (CT) for stage III non-small cell lung cancer (NSCLC)

T.E. Ciuleanu[5], A. Chahine[4], N. Todor[5], I. Monnet[1], N. Azli[1], S. Voisin[2], M. Riggi[1], J.C. Saltiel[2], J.P. Armand[1], P. Ruffié[1], H. de Cremoux[3], E. Cvitkovic[4]. *Association pour le traitement des tumeurs intrathoraciques (ATTIT[1-4]):* [1]*IGR La Grange;* [2]*CHI Créteil;* [3]*CHU Corbeil;* [4]*Hôp. Paul Brousse, France;* [5]*Oncol Inst Cluj, Romania*

Purpose: To assess results with neoadjuvant Cisplatin/Vindesine or Vinorelbine based CT in unresectable st III NSCLC.

Methods: From 4/87 to 2/96, 158 untreated pts received median 3 cycles of ATTIT 1, 2, 3, 5 or 6 protocol (ASCO 89–94). *Results: Pts charact.:* age 57 [37–72]; 91% males; Karnofsky (KI) 60–70% 29, >70% 129 pts; histology (H): squamous 91, adeno 37, large cell 25, adenosq. 5 pts; AJCC stages: IIIA 74, IIIB 84 pts. *Activity:* 73 pts had objective response (OR) (46%, CI [38%–54%] 7 CR, 66 PR); st IIIA vs IIIB: 54% vs 39% OR (p = 0.06). *Further trt:* 35 pts (22%), 24 IIIA and 11 IIIB ($p < 0.01$), became operable after CT (19 lobectomies, 16 pneumonectomies), with 7 pCR (4%). Surgical complications: 5 fatal broncho-pleural fistula. After surgery, 20 N+ pts and 36 non resectable CT responders received RT. Duration of response: 15 months (m) [2+..44+]. OR after all local trt: 55%. *Follow-up:* 36 m [3–66], *Survival* (S): median 17 m; KI > 70% vs 60–70%: 19 vs 12 m ($p < 0.01$); CT responders vs non responders: 26 vs 13 m ($p < 0.01$); adeno vs epidermoid vs large cell: 27 vs 16 vs 13 m (p = 0.04). S at 36 m resected vs irradiated CT responders: 42% vs 29% (p = 0.79). *Multivariate analysis:* A prognostic score (PS) was defined using Cox model: PS = 2*KI + 2*OR + H. The prognostic groups (good 7–10; intermediate 5–6; poor ≤ 4) had a median S of 29vs 17 vs 9 m ($p < 0.01$). To date, 59 pts are alive (25 in CR) and 99 have died: 93 pts disease progression (62 pts locoregional (LR), 8 pts metastases (M) only, 23 pts LR+M), 5 pts surgical complications, 1 pt other disease. Brain was the main site of metastatic relapse (19 pts).

Conclusions: 1) 46% OR rate with Cisplatin-Vinca combinations confirm single institution experiences. 2) There was no difference in 3y S between resected and irradiated CT responders. Controlled trial comparing surgery + RT vs RT alone for CT responders is needed. 3) Main prognostic factors for S were performance status and response to neoadjuvant CT.