Conclusion: Weekly schedule of docetaxel and cisplatin in the first-line treatment of NSCLC demonstrated good efficacy and manageable toxicities.

9083 POSTER

Oral vinorelbine in elderly or unfit patients with metastatic NSCLC

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Background: Standard treatment for unfit or elderly patients (PTS) with NSCLC often includes single-agent (not platinum-based) chemotherapy or best supportive care (BSC), rather than a classical chemotherapy doublet. The Elderly Lung Cancer Vinorelbine Italian Study (ELVIS) stated that vinorelbine (VNB) provides both a survival and symptomatic benefit over BSC in elderly pts with NSCLC. The currently available oral formulation of VNB should be handier, with activity and safety profile similar to intravenous formulation.
We aimed to investigate efficacy and safety of oral VNB and its role as the next best in pts with advanced NSCLC not tolerating a classical combination chemotherapy.
Materials and Methods: We enrolled 55 consecutive patients (M/F = 41/14) with median age of 71 years (range 59−84), ECOG PS=1−2, major comorbidities and stage IIIB (n = 23) or IV (n = 32) NSCL (Adenocarcinoma = 51%, Squamous = 31%, NOS = 18%). Patients received oral VNB 60 mg/mq day 1.8 q21 as first-line chemotherapy until progression or unacceptable toxicity, evaluated according to NCI-CTC scale. Time to progression (TTP) was defined as the time between the beginning of treatment and the first evidence of tumor progression. Clinical benefit was evaluated according RECIST score.
Results: The 7% of treated pts had a partial response (RP), 41% stable disease (SD) until the regular treatment suspension and 52% showed a progression disease (PD), with a total clinical benefit of 48%. The median observed TTP was 6 months (range 2−23).
Treatment was well tolerated from the great part of pts and the main toxicities were low-grade (G1-G2). Few pts reported severe (G3-G4) adverse events such as fatigue 4% (n = 2), diarrhea 4% (n = 2), neutropenia 4% (n = 2), vomiting 2% (n = 1), anemia 2% (n = 1).
Conclusions: In our experience, oral VNB represents a safe first line chemotherapy in elderly, unfit pts with metastatic NSCLC not suitable for combination chemotherapy. The oral formulation allows a good compliance to treatment, optimal nausea/vomiting control by oral antiemetics and no required dose adjustment. Furthermore, oral VNB seems to preserve quality of life in the half of treated patients.

9084 POSTER

Pemetrexed vs docetaxel as second-line in NSCLC: is there a difference between adenocarcinoma and squamous cell carcinoma? – a retrospective analysis of a single institution

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Background: Emerging data suggest that chemotherapy with pemetrexed is more effective in patients with adenocarcinoma compared to those with squamous histology, with a longer survival. So the tumor histology should be carefully evaluated in second-line chemotherapy for patients with relapsed or metastatic non-small lung cancer. We retrospectively analysed patients with metastatic NSCLC divided in subgroups on the basis of histology, to evaluate the differential efficacy of pemetrexed and docetaxel.
Materials and Methods: From July 2000 to December 2008 we evaluated 368 patients with NSCLC, treated with pemetrexed or docetaxel, of whom 238 with adenocarcinoma and squamous cell carcinoma. One hundred and ninety-nine (83%) pts were evaluable for PFS and OS. Patients with histology not specified were excluded. Patients characteristics were: median age 63 years, F/M 23/77%, ECOG PS 0−1 86%, current/former/never smokers 37/45/13% (unknown 5%). The most part of pts were previously treated with platinum-based chemotherapy. One hundred and twenty-one pts were treated with pemetrexed, of whom 93 with adenocarcinoma and 28 with squamous cell carcinoma; 78 pts were treated with docetaxel, of whom 53 with adenocarcinoma and 25 with squamous cell carcinoma. Docetaxel was administered at 75 mg/sqm every three weeks (median 3 cycles, range 1−6). Pemetrexed was administered at 500 mg/sqm every three weeks (median 3 cycles, range 1−10).
Results: We analysed the two histologic subgroups and the different type of chemotherapy. The median follow-up is 14 months, median PFS and OS were 2.2 and 8.5 months. The median PFS and OS are presented in the tables below:

	Median PFS (mos)		
	Pemetrexed	Docetaxel	
Adenocarcinoma	2.1	2.3	p = 0.877
Squamous cell carcinoma	2.2	2.3	p = 0.627

	Median OS (mos)		
	Pemetrexed	Docetaxel	
Adenocarcinoma	9.4	8.0	p = 0.860
Squamous cell carcinoma	7.2	9.0	p = 0.636

Conclusions: Our retrospective analysis of adenocarcinoma and squamous cell carcinoma treated with pemetrexed or docetaxel, did not show a statistically significant differences in PFS and OS. Further analyses are needed to validate these data.

9085 POSTER

A platinum based second line rechallenge chemotherapy improves survival in small cell lung cancer patients

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Background: Patients with SCLC that progress after first-line (FL) chemotherapy have a poor prognosis and the evidence of a benefit of SL is still limited. This retrospective analysis evaluates the clinical outcomes of patients who received SL treatment for SCLC.
Methods: Retrospectively we reviewed 166 consecutive patients who progressed after FL and received a second or third-line treatment, between 1993 and 2008 in 17 institutions. In our analysis we divided patients in four subgroups, according to the type of SL treatment: 1) Platinum-based rechallenge (P), 2) Non platinum-based polichemotherapy (NP), 3) Non topotecan monochemotherapy (NT), and 4) topotecan monochemotherapy (T). Our endpoints were Overall survival (OS), Progression free survival (PFS) and Response Rate (RR). Survival curves were designed with Kaplan-Meier method and Cox proportional hazard model was used for investigating factors which influence survival.
Results: Median age was 63 (range 25−86). Median OS from the SL was 6.2 months and PFS 2.9. 163 patients received a platinum based chemotherapy as FL, among them 67% obtained a response (CR = 14%, PR = 53.7%) and 19% had progressive disease (PD). 30% of the complete responders and 22% with partial response after FL had a response in SL, whilst only 16% of patients with SD/PD after FL had a response with SL (test for trend p = 0.03). No statistical differences among regimens groups were found. However, patients receiving platinum-based rechallenge did better than others if they had a long PFS after FL (p = 0.02).
Conclusions: The clinical benefit of SL therapy for SCLC is poor and strictly dependent on response and on duration of response with FL treatment. Consistently with published data, our retrospective analysis confirms that median OS for patients receiving SL is about 6 months and median PFS is 2.9 months. Rechallenge with platinum could be the best options in patients with a long PFS in FL. Single agent topotecan did not show evidence of superiority against other chemotherapy regimens.

9086 POSTER

Pralatrexate plus vitamin B12 and folic acid supplementation in patients with previously-treated, advanced non-small cell lung cancer: safety and efficacy in a phase 1 trial

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Background: Pralatrexate showed activity in previously treated patients (pts) with advanced non-small cell lung cancer (NSCLC) at doses of

135−150 mg/m^2 every 2 weeks (q2w) without vitamin supplementation (Krug, Clin Cancer Res 2003;9:2072−8). This phase 1 study evaluated the safety of higher pralatrexate doses with vitamin supplementation to minimize toxicities in pts with advanced NSCLC.
Materials and Methods: Pts age ⩾18y with stage IIIB or IV NSCLC received pralatrexate q2w in 4-wk cycles with folate and vitamin B_{12}. Outcomes in this report include adverse events, pharmacokinetics (PK), and investigator reports of treatment response.
Results: 39 pts were treated (23 female, 34 White, median age 62y [range, 40−77y]). The number of prior chemotherapy treatments was 1−2 in 20 pts and 3+ in 19 pts. Pts received a median of 2 pralatrexate cycles (range, 1−12). Rates of treatment-related grade 3−4 adverse events at any time were (doses ⩽ 190 mg/m^2, > 190 mg/m^2) stomatitis/mucosal inflammation (22%, 33%), fatigue (0%, 13%), and hand-foot syndrome, headache, increased ALT, back pain, dehydration, thrombocytopenia, and neutropenia (0%, 3% each). Treatment-related serious adverse event rates were 0% and 23% for doses ⩽ 190 and > 190 mg/m^2, respectively. The table summarizes dose-limiting toxicities (DLTs) during cycle 1 (cohorts in chronological order).

Dose, mg/m^2	Infusion duration, min	N	No. of Pts with DLT
150	3−5	1	
190	3−5	1	
230	3−5	1	
270	3−5	6	1 Mucositis (Gr3)
325	3−5	3	2 Mucositis (Gr3)
270	3−5	10	2 Mucositis (Gr3)
			1 Mucositis+fatigue (Gr3+3)
			1 Mucositis+fatigue+headache (Gr3+3+3)
			1 Hand-foot syndrome (Gr3)
			1 Elevated ALT+back pain (Gr3+3)
230	3−5	5	3 Mucositis (Gr2)
			1 Fatigue+hemorrhagic mucositis (Gr3+4)
230	60	5	1 Mucositis (Gr3)
			1 Mucositis+neutropenia (Gr2+3)
			1 Dyspnea (Gr3)
			1 Syncope+somnolence (Gr3+3)
190	3−5	2	2 Mucositis (Gr3)
190	60	5	1 Fatigue+dyspnea+mucositis (Gr3+3+2)

PK was dose-proportional and was not altered significantly by extending the infusion to 60 min. ORR by RECIST was 8% (3/39; 95% CI: 0.7%-16%), with 2 CR (22+ and 16+ months) and 1 PR (10 months). Disease control rate (CR, PR, or SD and TTP > 2 months) was 49% (95% CI: 33%-64%).
Conclusions: Pralatrexate in combination with vitamin B_{12} and folate was safe and active in pts with previously treated NSCLC, with durable CRs in this phase 1 trial. Mucositis remained the DLT. Pralatrexate 190 mg/m^2 with vitamin supplementation is being compared to erlotinib treatment in a randomized phase 2b trial (NCT00606502) in pts with previously treated NSCLC.

9087 POSTER

The feasibility of weekly paclitaxel in combination with carboplatin for advanced non-small cell lung cancer with idiopathic interstitial pneumonias: a pilot study

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Background: Idiopathic interstitial pneumonias (IIP) appear to be associated with lung carcinogenesis. In lung cancer combined with IIP, acute exacerbation of interstitial pneumonias (AE) frequently occurs after the anti-cancer treatments. The AE was fatal and poor prognostic factor of these patients. However, no current consensus and evidence on whether aggressive anti-cancer treatments, such a chemotherapy, for advanced stage non-small cell lung cancer (NSCLC) with IIP was regarded as a serious clinical problem. This study was conducted to elucidate cumulative incidence of AE in NSCLC with IIP who had received standard chemotherapy.
Patients and Method: Advanced NSCLC with IIP who had never received chemotherapy or radiotherapy from 2004 to 2008 at Nippon Medical School Main Hospital were enrolled. Patients received paclitaxel (PTX) 100 mg/m^2 weekly for 3 of 4 weeks and carboplatin (CBDCA) area under the curve (AUC) = 5 on day 1 of each 4-week cycle. The safety and efficacy of PTX plus CBDCA was prospectively investigated.
Results: Eighteen patients [male/female, 14/4; median age 71 years (38−81); performance status 0/1, 7/11] were enrolled. The 6 of 18 patients were diagnosed idiopathic pulmonary fibrosis (IPF). The median number of cycles administered per patients was 4 (range 1−7). The median progressive free survival was 27 weeks. The overall response rate was 61%. The median survival was 46 weeks, and 1-year survival rate was 22%. During the follow-up period, AE was observed in 5 of 18 patients (28%). Treatment-related AE occurred in only one patient (6%) with histological confirmed usual interstitial pneumonia (UIP). Other main adverse events were; 33% of Grade 3 or 4 neutropenia, 22% of Grade 2 neuropathy.
Conclusion: The safety and anti-tumor response of PTX combined with CBDCA for advanced NSCLC with IIP were well acceptable. These results suggest that the chemotherapy of PTX plus CBDCA is candidate of treatment for NSCLC with IIP. Further large-scale prospective study for NSCLS with IIP should be performed.

9088 POSTER

Phase III study of Lipoplatin plus Gemcitabine versus Cisplatin plus Gemcitabine in advanced NSCLC; interim analysis

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Background: Lipoplatin is a liposomal formulation of cisplatin, designed to reduce its adverse reactions without reducing efficacy. This is a report of an ongoing randomized, multicenter, non-inferiority phase III trial (LipoGem-PIII-1L, 0−218b/6th/23−3−05) comparing OS/response, safety and QOL of Lipoplatin versus cisplatin, both combined with gemcitabine against advanced stage NSCLC.
Materials and Methods: Interim analysis of 101 patients' safety and response data, emphasizing the correlation of results with the histological subtype of NSCLC. Sixty patients were assigned to Lipoplatin arm (LipoGem) and 41 patients were assigned to the cisplatin arm (CisGem). Patients received Lipoplatin 120 mg/m^2 D1, 8, 15 or cisplatin 100 mg/m^2 D1, combined with gemcitabine 1,000 mg/m^2 D1, 8, in 3-week cycles, with disease evaluation after 3 and 6 cycles (LipoGem and CisGem arms, respectively).
Results: Response: Evaluable patients were 52 in LipoGem arm and 32 in the CisGem arm. The study meets the noninferiority goals with a slight superiority of LipoGem over CisGem across all histological subtypes combined. However, among patients diagnosed with adenocarcinoma PR, SD and PD were 48%, 38% and 14% for LipoGem and 32%, 36% and 32% for CisGem arms, respectively. Toxicity: Nephrotoxicity grade III occurred in 8.5% in LipoGem arm versus 12.5% in CisGem arm, while respective values for nausea and vomiting grade III were 1.7% versus 10%, neurotoxicity grade III were 0 versus 2.5% and asthenia grade III were 3.4% versus 17.5%. The remaining of safety parameters were comparable, although neutropenia grade III favored the LipoGem arm.
Conclusions: Lipoplatin appears more effective in advanced NSCLC when combined with gemcitabine, especially against adenocarcinomas, than cisplatin-gemcitabine, which appears to be more effective against squamous cell carcinomas. Lipoplatin has a more favorable safety profile than cisplatin, particularly regarding nephrotoxicity, neurotoxicity and asthenia.

9089 POSTER

Optimal duration of 1st- and 2nd-line chemotherapy (CT) for advanced non-small cell lung cancer (NSCLC)

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Background: Six vs 3−4 cycles of 1st-line CT do not offer an overall survival (OS) benefit to patients (pts) with advanced NSCLC and are associated with increased toxicity and potential for worse quality of life. No randomized, prospective data exist on the optimal duration of 2nd-line CT. This retrospective study aimed to: i) confirm the lack of impact of 1st-line treatment duration on efficacy outcomes; ii) evaluate the impact of treatment duration in the 2nd-line setting.