## ACTIVITY AND TOLERABILITY OF CISPLATIN (CDDP) AND FOTEMUSTINE (FTM) COMBINATION IN THE TREATMENT OF PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC) WITH BRAIN METASTASES (BM): A MULTICENTRIC PHASE II STUDY OF THE GRUPPO ONCOLOGICO DELL'ITALIA MERIDIONALE (GOIM)

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*Background*: NSCLC is the most common primary solid tumour responsible for brain metastases (50–60% of all cases). Patients (pts) with untreated BM have a very poor prognosis with a median survival of approximately 1 month. Death of these pts can be attributed to neurologic complications only in around half of cases. Therefore, treatments directed toward extracranial metastases appear essential in the management of these subjects. Standard therapy for symptomatic multiple BM is whole-brain radiation therapy (WBRT). The role of systemic therapies for the treatment of BM is still under investigation due to concerns about the penetration of chemotherapeutic agents across brain barrier (BBB). Fotemustine (FTM) shows to be able to cross BBB whilst CDDP remains the key drug for systemic treatment on NSCLC.

*Methods*: Patients with advanced NSCLC, PS 0-1 ECOG and multiple BM not amenable to locoregional treatment received 2 cycles of FTM 80 mg/m$^2$ d1,8 and CDDP 80 mg/m$^2$ d1 every 3 weeks followed by WBRT 30 Gy/3 Gy daily; 2 other cycles were included for responding pts. Radiological response using Recist Criteria would be allowed before WBRT to assess the role of chemotherapy both for cranial and extra-cranial disease. Barthel ADL index was administered every 2 cycles. This trial was designed with a two step evaluation. After 30 pts is established first evaluation with the aim to verify if this combination is associated with more than 25% of response rate; subsequently, if this first step is reached, enrolment will go on till 81 pts according to the optimal two stage design of Simon.

*Results*: At 2/2008 21 patients were enrolled (M/F: 15/6, squamous 3, adenocarcinoma 11, large cell 1 NSCLC 6). First interim analysis is awaited to go on with this study

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## FIRST-LINE CISPLATIN (P) WITH DOCETAXEL (TXT) OR VINORELBINE (VNR) IN PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER: A PHASE II RANDOMIZED TRIAL OF GRUPPO ONCOLOGICO ITALIA MERIDIONALE

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Platinum-based doublets are considered standard therapy for pts with advanced NSCLC. The GOIM considered P/VNR as a reference treatment. P/TXT has been reported to be active but its not well known its real impact on quality of life. In this study patients received either six courses of TXT/P or VNR/P with activity/safety being the primary end-points. Secondary end-point included time-to-progression, overall survival, and tolerability. Patients with stage IV/IIIB, age $\leqslant$70 and ECOG PS 0–1, were eligible for the study. Sample size was calculated according to Fleming's single-stage procedure. Responses and toxicity were assessed according to the RECIST and NCI-CTC criteria. Patients were randomized to receive: TXT 75 mg/m$^2$ over 60 min followed by P 75 mg/m$^2$ on day 1 every 21 d, or VNR 30 mg/m$^2$ on days 1 and 8 and P 80 mg/m$^2$ on day 1 every 21 days. From 12/06 to 3/08 86 patients were enrolled: Arm A 42 patients, M/F: 32/10, IIIB/IV:8/34, squamous/not-squamous: 13/29 median age 61 (range 41–70); Arm B 44 patients, M/F: 35/9, IIIB/IV: 10/33, squamous/not-squamous: 14/30, median age 62 (range 44/70). To date available toxicity data of 49 patients are the following:

| Type of toxicity (49 patients) | TXT/P | VNR/P |
|---|---|---|
| Neutropenia total/G3-4 (%) | 34/30 | 67/46 |
| G-CSF (%) | 26 | 35 |
| Hemoglobin total/G3-4(%) | 39/0 | 58/16 |
| Darbopoetin (%) | 9 | 19 |
| Platelets total/G3-4 (%) | 9/0 | 39/4 |
| Vomiting total/G3-4 (%) | 34/4 | 12/0 |

Preliminary data show an equivalence among the two treatment arms regarding activity but with more hematological toxicity in the VNR arm.

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