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Hypofractioned Prophylactic Radiotherapy for Pleural Malignant Mesothelioma − a Review of a 7-year Single Institutional Experience

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Background: Patients (p) with pleural malignant mesothelioma (PMM) who undergo invasive diagnostic procedures (DIP) tend to develop tract metastases. Hypofractioned prophylactic irradiation (HFPRT) of intervention tracts is still controversial.
The aim of this study is to assess the effectiveness of HFPRT and its biological equivalent doses (BED) in preventing tumour seeding.
Materials and Methods: Between December 1997 and January 2010, 34p (7 females) with a median age of 68 years (range 49−80), with histologically proven PMM were referred to our department, after DIP. Histological subtypes of PMM were epithelial in 18p (52.9%), sarcomatous in 10p (29.4%), mixed in 3p (8.8%) and unknown in 3p (8.8%). Stages distribution was IA 12p, IB 6p, II 1p, III 8p, IV 4p and 3p were unknown. Diagnostic and therapeutic invasive procedures were combined as needed in each patient, resulting in 20 thoracocentesis, 15 pleurodesis, 12 thoracoscopy biopsies, 7 thoracotomy biopsies, 2 CT-guided biopsies and 14 other pleural samples non specified. Only in 4p surgery was performed as 2 atypical resections, one extrapleural pneumonectomy and one pleurectomy. In all cases HFPRT was delivered to the instrumentation tract and scar sites, and was performed after a delay of 1−2 months after chest manipulation. HFPRT schemes used were 7 Gyx3 fractions (fr) (26p); 3 Gyx10fr (5p); 3 Gyx9fr (1p); 8 Gyx3fr (1p) and 6 Gyx3fr (1p). Treatments were grouped by BED using α/β=3 for PMM as greater than 40 Gy (7x3 BED 42 Gy and 8x3 BED 52.8 Gy) or lower than 40 Gy (6x3 BED 32.4 Gy, 3x9 BED 32.4 Gy and 3x10 BED 36 Gy). Almost all patients received pemetrexed chemotherapy alone or in combination with platinum-based agents, during or after HFPRT.
Results: After a median follow up of 11 months (m) from the beginning of HFPRT, only 3p had HFPRT field-in tumour progression, with a field-in progression free survival at the intervention site of 13.9 m; 23p died of disease with thoracic progression free survival of 8.5 m and distant progression free survival of 18 m; 3p are alive with disease; and 1p is alive without evidence of disease after a follow up of 12 m. The overall and cancer specific survival were 11.7 and 15.9 m respectively. No differences in relapses and survivals were found ($p < 0.884$) between HFPRT schedules in BEDs groups.
Conclusions: To prevent malignant seeding at drain sites after DIP the recommended HFPRT is effective in our patients. HFPRT with higher BEDs didn't influence relapses.

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Increased Number of Skip Mediastinal Nodal Metastases in the IIIA/N2 NSCLC Detected Using Intraoperative Ultrasound for Mediastinal Lymphadenectomy

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Objectives: To study the incidence and characteristics of mediastinal nodal metastases without N1 nodal metastases ("skip-N2 metastases") in patients with resected pIII/A/N2 non-small cell lung cancer (NSCLC) using intraoperative ultrasound (US) for mediastinal lymphadenectomy.
Methods: A total of 240 NSCLC patients who underwent RO surgical resection followed by systemic mediastinal nodal dissection in four years time period (2005–2008) were retrospectively reviewed. Intraoperative hand held ultrasound probe was used for systematic mediastinal nodal dissection in a group of 120 patients and compared with the group of 120 patients who underwent lung resections and standard systematic mediastinal nodal dissection. Mapping of the lymph nodes by their number and station followed by histopathologic evaluation was performed. Median follow-up was 38 (range, 10−52) months. Patients data were statistically analyzed.
Results: The surgical procedure used depended on the extent of the disease, as well as the cardiopulmonary reserve of the patients and was comparable in both groups of patients. Operating time was prolonged for 12 (6−20) minutes in patients with US guided mediastinal nodal dissection, but number and stations of evaluated lymph nodes was significantly higher ($p < 0.001$) in the same group of patients. Skip nodal metastases were found in 24% of patients without N1 nodal involvement in the patients using standard systematic mediastinal nodal dissection. We found 35% of skip nodal metastases in the group of patients using US guided mediastinal lymphadenectomy. The incidence of N2 metastases seemed to be more frequent in adenocarcinoma patients ($p < 0.005$), but skip N2 metastases were significantly higher ($p < 0.001$) in squamous cell carcinoma patients. Although skip metastases involved more often upper mediastinal lymph nodes and one station level, the difference was not found statistically significant ($p < 0.227$). Complications rate showed no difference between analyzed groups of patients.
Conclusion: Higher number and location of analyzed mediastinal nodal stations in patients with resected NSCLC using hand held ultrasound probe suggested to be of great oncology significance. Procedure showed absolute safety and high accuracy. Our results indicated that intraoperative US may have important staging implication. Further clinical studies should be carried out in order to improve intraoperative staging in NSCLC patients.

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Incidence and Management of Adverse Events (AEs) in Patients Receiving Different Types of Treatment for Non-small Cell Lung Cancer (NSCLC) Across Europe − EPICLIN-Lung Study

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Background: The EPICLIN-Lung study (NCT00831909) describes clinical management of NSCLC across Europe, and its impact on outcomes and overall health care resource use.
Materials and Methods: This non-interventional, prospective cohort study was conducted in eight European countries. Patients (pts) with confirmed NSCLC attending the relevant hospital for the first time between 1 January and 31 March, 2009 were enrolled, and followed for a minimum of 12 months or until death. Incidence and severity of spontaneously mentioned AEs were recorded according to the CTCAE v3.0 scale. In the presence of an AE, investigators were asked to select from the following: blood, dermatological, gastrointestinal, neurological, pain, pulmonary, other. Information on clinical management of reported AEs was also collected.
Results: 3508 pts were enrolled in the study; spontaneously mentioned AE data are available for 2243 pts (Table 1). CTCAE $\leqslant$2 were reported in all treatment regimens. Pts receiving cisplatin (Cis)-based regimens experienced the highest incidence of severe (CTCAE >2) events (19.7%). The most frequently-reported AEs >grade 2 were blood (16.0%) and pulmonary (7.8%). Dose reductions and treatment interruptions were most frequently required with Car + paclitaxel + investigational (30.0%) and Car + vinblastine (Vib) (15.2%), respectively. Patients receiving Cis + docetaxel experienced the highest mean number of therapy-related events (2.8 ± 6.3) resulting in a hospital visit, following initial treatment. Patients receiving Car + pemetrexed or Cis + Vib required the highest mean number of blood-specific resources (0.4; transfusion, EPO or G-CSF).
Conclusions: Patients receiving treatment for NSCLC experience a high incidence of AEs. Cis-based chemotherapy is associated with the highest incidence of severe AEs, whereas Car-based regimens require more frequent dose reductions. EPO, transfusion or GCSF are mostly required with Car-pemetrexed and Cis-Vib.

Table 1

	No. pts treated	No. (%) pts with CTCAE $\leqslant$2	No (%) pts with CTCAE >2
Cis-based doublets	960	363 (37.81)	189 (19.69)
Car-based doublets	689	268 (38.90)	125 (18.14)
Bevacizumab-containing triplets	25	7 (28.00)	3 (12.00)
Gemcitabine or vinorelbine	114	37 (32.46)	17 (14.91)
Erlotinib	84	23 (27.38)	12 (14.29)
Investigational regimens	87	30 (34.480	14 (16.09)
Best supportive care	6	1 (16.67)	0 (0.00)
Other	278	122 (43.88)	73 (26.26)
Total	**2243**	**851 (37.94)**	**433 (19.30)**