preferred because of severe neurological complications which occur in 15-25%.

In malignant mesothelioma, persistent resistant pain has been considered for percutaneous cordotomy, destruction of the contralateral spinothalamic tract in the neck. In five reports of 302 patients, pain relief was seen in 65%, respiratory depression in 0-4%, retention 6-10%, mirror image pain 7-55%, and hemiparesis 0.4-9%. The opioid dose can be reduced thereby. A skilled team is essential.

**Adverse Events**

Patients must be aware of these. Common errors are failure to prescribe early anti-emetics and bulk and stimulant laxatives when opioids are begun; to overlook the cholinergic side effects of tricyclics; the failure to decrease opioid doses in renal impairment; and the failure to use adequate opioids for fear of irreversible respiratory depression.

**Prevention**

Meticulous attention to analgesic management both intra and post operatively may reduce the incidence of post thoracotomy pain and accelerate recovery. Earlier palliative spine irradiation may postpone neurological problems and troublesome incident pain.

**References**

Ripamonti C and Fulﬁlaro F, Mechanisms of pain associated with respiratory disease. In Supportive Care in Respiratory Disease eds Ahmedzai SH and Muers MF Oxford OUP 2005 pp 413-426


Ahmedzai SH, Clayton H, Supportive and palliative care in mesothelioma In Malignant Pleural Mesothelioma, Eds O’Byrne K, Rusch V, Oxford OUP 2006 p403-33


Hanks GW, de Conno F, Cherny N et al Morphine and alternative opioids in cancer pain: The EPAC recommendations, Br J Cancer 2001: 95 587-93


Dwerkin RH, Backonja M, Rowbotham MC et al, Advances in neuropathic pain: Diagnosis, mechanisms, and treatment recommendations Arch Neurol 2003 60 1524-34


Breitbart W, Passik S, Payne D. Psychological and psychiatric interventions in pain control in The Oxford Textbook of Palliative Medicine op.cit. p437-454

Colvin L, Forbes K, Fallon M, Difficult pain BMJ 2006 332 1081-1083

Comprehensive symptom management in advanced lung cancer

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Although we have entered the era of targeted therapy in lung cancer, the back bone of initial treatment for most patients with either non-small cell (NSCLC) or small cell lung (SCLC) is myelotoxic chemotherapy. For patients receiving systemic treatment, platinum based regimens are used in the adjuvant setting, in combination with radiation for inoperable Stage III A/B and as primary therapy for advanced stage patients. While multiple different regimens have been developed and some alternative non-platinum based regimens are also used, all of these regimens have been developed with neutropenia as a limiting toxicity, which in fact has helped define the dose schedule of many of these regimens. Furthermore, these chemotherapy combinations were developed in younger, healthier patients, but are now applied worldwide across a population of older patients with more co-morbid disease and therefore, more at risk for complications of treatment. Thus, both neutropenia and anemia are common sequelae of treatment that impact the quality of life and outcomes of patients being treated. While thrombocytopenia can also be an issue, it is not generally limiting except in patients with significant bone marrow involvement, extensive prior chemotherapy and radiation and/or very advanced disease, particularly hepatic metastasis. While Interleukin 11 is available for treatment of patients with thrombocytopenia, its use has been limited. New thrombopoietic molecules have shown promising activity in immune thrombocytopenia and are just beginning to be studied as an adjunct to chemotherapy.

The risk of neutropenia and neutropenic complications varies significantly between patients with SCLC or NSCLC. In a prospective, nationwide registry in the United States, patients with SCLC receiving chemotherapy have nearly a 20% risk of developing febrile neutropenia at some point in their treatment course. At this level of risk, most patients with SCLC receiving standard platinum etoposide chemotherapy would be candidates for first cycle prophylaxis with colony stimulating factors as established by NCCN guidelines and subsequently supported by the EORTC and ASCO expert panels. By contrast, patients with NSCLC have a substantially lower risk of developing febrile neutropenia with an overall rate of less than 5-10% in unselected populations receiving platinum based chemotherapy. The differences in risk may have to do with the briefer periods of neutropenia seen with taxanes or weekly vinorelbine or gemcitabine, used in NSCLC, compared to etoposide or irinotecan, more commonly used in SCLC. There are also overall differences between SCLC and NSCLC patients in terms of age, functional status, extent of disease, bone marrow involvement that may also be associated with poorer tolerance of myelosuppressive chemotherapy for the small cell population.

SCLC was recognized as a rapidly fatal cancer and aggressive chemotherapy were developed decades ago that led to significant increase in survival, symptom improvement and quality of life benefit. Studies of high dose chemotherapy have been largely unsuccessful in further improving outcomes, while the delivery of dose dense chemotherapy with the use of colony stimulating factors has provided modest improvement. However, reducing the dose of chemotherapy clearly led to reduced benefit. With the availability of myeloid growth factors, neutropenic complications can be minimized for the majority of patients and standard dose intensity maintained in the extensive stage patients.

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For patients with potentially curable limited stage SCLC, concurrent administration of myeloid growth factors with chemotherapy and radiation has led to paradoxical worsening of cytopenias, presumably related to radiation damage of CSF mobilized peripheral blood stem cells. This remains a poorly studied area. Carefully done studies that vary the timing of myeloid growth factors in relationship to chemotherapy and radiation might be very informative.

For NSCLC, in the era of platinum based treatment in patients with advanced disease, a survival benefit has clearly been shown, but it is quite modest in nature. Therefore, with the perceived lower benefit of chemotherapy in NSCLC, there has also been an intent to minimize toxicity, often by altering dose and schedule of chemotherapy. In the case of paclitaxel, switching from prolonged infusions to short infusions reduced the duration of neutropenia. Other regimens have moved to weekly administration rather than every three weeks which also allow one to titrate or eliminate the subsequent doses that may worsen myelosuppression. Interestingly, even in advanced stage NSCLC, the development of neutropenia is associated with a longer survival compared to patients who do not have neutropenia. While neutropenia may be telling us about pharmacogenomics, it suggests that dose may be an important variable, even on advanced stage lung cancer patients, and this may have implications for chemotherapy in earlier stage disease.

Now that adjuvant chemotherapy has become a standard part of practice in Stage IB, III NSCLC, it is important to fully understand the relationship of dose and schedule to outcome. In this curative setting, it is also important to understand which patients are most at risk for neutropenia and who might benefit from early intervention strategies. The ANC Study Group has developed a risk model for factors associated with the likelihood of neutropenic complications, febrile neutropenia and dose reduction. These models now need to be applied prospectively in selected populations. The need for such a prospective risk model is also important for patients with more advanced NSCLC. Because the individual risk is low, first cycle prophylaxis is not commonly applied. However, because a large number of patients treated with NSCLC have co-morbidities, the number of NSCLC patients hospitalized with febrile neutropenia is substantial. Furthermore, the clinical course for patients with febrile neutropenia in the setting of lung cancer is more similar to patients with hematologic malignancies than with other solid tumors such as breast cancer. Although the reasons for this are not fully explored, advanced age and co-morbidity may account for the higher mortality rate from febrile neutropenia, as well as need for prolonged hospitalization in many patients. Therefore, identifying patients at risk not only for febrile neutropenia, but for prolonged complications is another important area for study.

Session E11: Controversy in Small Cell Lung Cancer

E11-01 Controversy in Small Cell Lung Cancer, Tue, Sept 4, 16:00 – 17:30

Controversy in small cell lung cancer - staging

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Staging of cancers has traditionally been based on the requirement to accurately define patients with localised disease that can be treated with surgical resection with curative intent. For certain malignancies, this involves defining involvement of regional lymph nodes that can be resected in continuity with the primary or separately. The finding of metastatic disease beyond regional nodes alters the treatment to primarily systemic and in most solid tumours from cure to palliation. Small cell lung cancer challenges this paradigm. Prior to the introduction of systemic therapy, there was no realistic curative approach for localised disease, with case series reporting median survivals of less than 2 months with surgery and/or radiation. The introduction of multi-agent systemic chemotherapy substantially extended median survival both in patients with metastatic disease and in those with apparent localised disease. However, the finding that radiation therapy could significantly enhance the outcome of systemic chemotherapy, particularly the longer term survival chances, results in the primary goal of SCLC ‘staging’ being the determination on whether thoracic radiation therapy is appropriate or not. Thus ‘limited’ SCLC is not a staging that directly reflects T and N stage, but a definition based on the ability to treat a patient with radiation therapy fields that encompass the tumour volume. Determining the extent of intrathoracic disease is only important when it removes the possibility of ‘encompassing’ by radiation fields, for example finding a malignant pleural effusion. Minor nuances, such as whether contralateral mediastinal nodes are ‘limited’ or ‘extensive’, are not relevant.

The search for ‘extensive’ SCLC has progressively followed advances in diagnostic imaging. Since the 1970s, CT scanning, nuclear bone scans, MRI scanning, and F18-FDG-PET scanning have been applied to identify sites of disease in SCLC patients and all have reported the ability to detect disease otherwise missed and so ‘upstage’ patients to extensive disease. Integrated PET/CT scanning has not been reported in detail in SCLC but is likely to improve the accuracy of PET scanning in SCLC also. The replacement of multiple staging investigations by a single investigation is likely to reduce costs and patient inconvenience and PET/CT may provide this particularly if adequate images of the brain can be obtained. PET scanning can also potentially aid radiation therapy planning in SCLC, as in NSCLC, by defining central tumour mass versus collapsed lung, and detecting involvement of anatomically normal lymph nodes.

While routine bone marrow biopsies are no longer part of SCLC staging, studies that have examined bone marrow by more refined techniques than routine H & E staining have reported much higher detection of malignant cells than is otherwise the case. In the era when high dose therapy and stem cell transplant were being investigated for SCLC treatment, a high incidence of detecting circulating tumor cells in peripheral blood was reported. It is therefore likely that there is no such thing as truly ‘limited’ SCLC, but all patients have ‘extensive disease’ that could be detected by more refined diagnostic imaging and/or molecular pathology. Therefore the goal of staging a patient with SCLC is not defining anatomical disease parameters but deciding whether a sufficiently large percentage of the burden of tumour cells are anatomically situated where delivery of a sufficient dose of radiation therapy to potentially eradicate chemotherapy-resistant clones is possible. This is dependent not only on staging but to some extent on the judgement of the radiation oncologist and will alter with advances in techniques of radiation delivery and planning. Use of a TNM-type staging paradigm in SCLC does not reflect either disease biology or direct treatment, so is not appropriate.