Out-Patient Chemotherapy for Lung Cancer
—Principles and practice—

JMAJ 46(12): 542–546, 2003

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Abstract: Recent emphasis on the importance of quality of life (QOL) has led to an increase in the demand for out-patient chemotherapy for lung cancer. Patients with no prospect of a cure, including patients with stage IV non-small cell lung cancer, those with relapsed cancer, and aged patients, can benefit from long-term outpatient chemotherapy at modest doses, which is expected to lengthen survival and help maintain QOL. Combinations of antineoplastic agents other than cisplatin, such as carboplatin, paclitaxel, docetaxel, irinotecan, gemcitabine, and vinorelbine, require shorter time for infusion, cause milder side effects such as nausea and vomiting, and can be controlled more easily on an out-patient basis. Attention has recently been directed to an oral antineoplastic agent gefitinib. Neutropenia caused by chemotherapy should be treated with G-CSF, and the patients showing febrile neutropenia should be hospitalized and treated with intravenous infusion of antibiotics. Oral serotonin antagonists are useful for preventing nausea and vomiting. Current problems include the facts that out-patient chemotherapy has not been assigned sufficient national health insurance reimbursement and that home care places burden on family members.

Key words: Cisplatin; Carboplatin; Paclitaxel; Docetaxel

Introduction

Recent emphasis on the importance of quality of life (QOL) in cancer treatment has led to an increase in the demand for out-patient chemotherapy for lung cancer.

Prognosis of lung cancer is generally poor. About one-half of patients die within a year. The time left for patients with no prospect of cure (relapsed cases and the patients with stage IV non-small cell lung cancer) must be respected as much as possible. If we want to conserve the social life and family life of the patients, chemotherapy is better conducted on an out-patient basis, as is the case in Western countries. Because many patients with lung cancer remain ambulant and retain the ability to eat until the terminal stages, out-patient care
is more suitable for them than for patients with other types of cancer. However, sufficient attention must be paid, some patients develop complications such as pneumonia, carcinomatous pleurisy, and brain metastasis, and their conditions may aggravate suddenly.

Criteria for Performing Chemotherapy at Out-Patient Clinics

Among patients with small cell lung cancer and stage IV non-small lung cancer who are indicated for chemotherapy, those satisfying the criteria listed in Table 1 may be treated with out-patient chemotherapy, no matter whether they have received prior treatment or not. However, hospitalized care is the more convenient form of treatment, if we intend to cure the patient through multidisciplinary treatment such as concurrent chemotherapy and radiotherapy for LD (limited disease) small cell lung cancer and that for stage III non-small cell lung cancer. The patient-side conditions for performing out-patient chemotherapy ((1) in Table 1) include good performance status (PS) and short distance from home to hospital (i.e., ambulance transportation is possible and the travel time is within 1.5 hours by car).

Outpatient chemotherapy is often requested by young patients who can visit the hospital by themselves and want to continue work during treatment. On the other hand, aged patients representing a large proportion of lung cancer patients are generally unsuitable for hospitalized active cancer therapies because of deterioration of the functions of various organs, and out-patient chemotherapy is recommended for these patients. This would also improve the prevention of senile dementia and depression. Moreover, chemotherapy has been reported effective in improving survival even in aged patients with non-small lung cancer.1)

As for the preparedness of hospitals ((2) in Table 1), we need space for the outpatient administration of drip infusion, because most antineoplastic agents are nowadays given by I.V. drip infusion. Our hospital has 44 beds in 6 rooms in a ward-type space called the daycare center,2) where outpatient chemotherapy and blood transfusion are performed. Drugs for injection are prepared promptly after the arrival of patients by pharmacists using the safety cabinet in the daycare center. The number of chemotherapy sessions performed here was 4,889 in 2001, and is increasing. Of this total, 1,156 sessions were given to patients of the Department of Pulmonary Medicine, mostly consisting of lung cancer patients.

Patients need to be hospitalized quickly after sudden aggravation or other emergencies. In our hospital, the introduction of a clinical path system and the increase in out-patient chemotherapy have shortened the mean length of hospitalization to about 16 days and accelerated the turnover of beds. Because of this improvement, we are able to arrange emergency hospitalization when needed.

Selection and Administration of Antineoplastic Agents

Out-patient chemotherapy does not differ from hospitalized chemotherapy in that the main purposes are the reduction/elimination of tumors and the elongation of survival. We

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Table 1 Conditions for Performing Out-Patient Chemotherapy

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<th>(1) Conditions on the patient side</th>
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<tr>
<td>• The patient has self-motivation to fight the disease and informed consent can be obtained.</td>
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<td>• Performance status is good.</td>
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<tr>
<td>• The patient lives near the hospital.</td>
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<td>• It is desirable that the patient’s family is cooperative.</td>
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<th>(2) Conditions on the hospital side</th>
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<tr>
<td>• The hospital has the space for I.V. drip infusion and an efficient system for nursing.</td>
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<tr>
<td>• Patients showing sudden aggravation can be admitted.</td>
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<td>• The data for blood counts are reported promptly.</td>
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<th>(3) Content of chemotherapy</th>
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<td>• Side effects can be controlled.</td>
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<td>• Only a short time is needed for drip infusion.</td>
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need procedures that can be performed in outpatient clinics without compromising the efficacy of treatment.

Cisplatin has come to be used for not only non-small cell lung cancer but also small cell lung cancer. It has been recently demonstrated that the combination of cisplatin and irinotecan is effective for ED (extensive disease) small cell lung cancer. However, the administration of cisplatin at 60 to 80 mg/m² requires the use of large quantities of infusion to prevent renal damage, and accompanies severe side effects such as nausea and vomiting. For this reason, it is difficult to administer this regimen on an outpatient basis. A solution to this problem is the weekly administration of small divided doses of cisplatin (30 mg/m²). This regimen can be administered to out-patients because of its relatively mild side effects (mostly gastrointestinal) and high safety.

During the 1990s, a series of new antineoplastic agents were developed mainly targeted at non-small cell lung cancer. Combinations of these agents excluding cisplatin are effective as cisplatin-containing chemotherapy, and they are superior with respect to the control of side effects. As a result, regimens excluding cisplatin are now the mainstream outpatient chemotherapy.

For example, we are now using the combination of docetaxel (30 mg/m²) or paclitaxel (110 mg/m²) and carboplatin [based on Calvert’s formula* with the AUC (area under the curve) target of 3] at half the normal dose. This treatment is given at 2-week intervals, if considered possible based on the monitoring of leukopenia and other side effects. Each course of drip infusion takes 2 to 4 hours. The use of Calvert’s formula enables us to correct for the individual difference in the AUC of carboplatin and improve safety. In addition, bone marrow side effects of paclitaxel and docetaxel are less prominent when they are given in divided doses. Thrombocytopenia due to carboplatin is also lower than expected. Other side effects are also slight because of the low dose per session. This regimen can be administered safely using hospital visits at intervals of 1 to 2 weeks.

Other combinations such as vinorelbine plus gemcitabine and docetaxel plus gemcitabin are also practiced. The administration of these regimens is simple and requires only a short time of I.V. drip infusion.

A tyrosine kinase inhibitor gefitinib (Iressa®) was authorized in July 2002. In addition, the indications of TS-1 (TS-1®), a combination drug containing tegafur, are going to be expanded to include non-small cell lung cancer. Both these drugs are administered orally. Iressa® has been reported to show response rates of 6 to 19% in cases of previously treated non-small cell lung cancer. The side effect profile of this agent is entirely different from that of conventional antineoplastic agents, and it hardly causes bone marrow suppression, nausea, vomiting, or alopecia. The use of oral agents eliminates the need for the space for outpatient I.V. infusion, facilitating the execution of outpatient chemotherapy.

**Side Effects and Prevention of Medical Accidents**

In our department (Department of Pulmonary Medicine, Saitama Cancer Center), the patients receiving chemotherapy usually visit the hospital at intervals of 1 to 2 weeks. At each visit, blood samples are collected and I.V. chemotherapy is given based on the measurement of blood counts. If neutropenia is noted, G-CSF is given according to the standards approved in the national health insurance system. When fever (38°C or higher) accompanies neutropenia, the patient is hospitalized, examined for causative bacteria, and treated

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*Calvert’s formula: carboplatin dose (mg/body) = target AUC × (GFR + 25), where GFR is usually based on the measured value of 24-hr creatinine clearance (Ccr).
with the combined use of G-CSF and I.V. antibiotics.\(^{10}\)

Even if neutropenia is not observed, signs of infection such as fever and purulent sputum should be responded to quickly, because lung cancer is often complicated with obstructive pneumonia or opportunistic infections, which are possibly fatal.

Oral serotonin antagonists were authorized several years ago, and this facilitated the control of nausea and vomiting due to chemotherapy on an out-patient basis. Although slight anorexia does not need special treatment, hydration is required when the condition is so severe that the patient is unable to drink water.

There are wide individual variations in the side effects of irinotecan, such as leukopenia and late-onset diarrhea, and these problems must be treated with the greatest care. Oral alkalization with control of defecation can be useful in preventing diarrhea.

Prevention of medical accidents is extremely important in busy out-patient clinics. First, errors in prescription and dispensing must be prevented through multiple checks by pharmacists and nurses. Care should be taken because shock may be caused infrequently by hypersensitive reaction to paclitaxel, docetaxel, other antineoplastic agents, and additives. The leakage of antineoplastic agents to the skin should be prevented by secure keeping of the I.V. route.\(^{11}\) If there is difficulty in keeping peripheral veins, use of an indwelling I.V. port is useful.

Sufficient informed consent must be obtained concerning the possibility of toxic death and the fact that alopecia is almost inevitable.

### Problems of Out-Patient Chemotherapy and Solutions

Outpatient chemotherapy eliminates the cost of hospitalization and reduces the overall cost of medical care. However, hospitals are not able to allocate sufficient staff needed for out-patient chemotherapy, because appropriate reimbursement has not been assigned in the national health insurance system. Although the revision of medical fees in April 2002 allowed hospitals to add the cost of out-patient chemotherapy to their invoices, the unit price of 300 points per day is grossly insufficient. In addition, hospitals are required to be accredited through medical performance evaluation conducted by the Japan Council for Quality Health Care or other authorized organizations.

The self-motivation of the patients is an important factor in out-patient care. Patients should be given not only information on the diagnosis but also the details of their disease including prognosis, and written consent must be obtained. However, physicians and other medical staff are too busy to allow sufficient time for explanation to patients, and they may overlook details of the situation of patients because of the inability to collect information from the patients. In particular, it takes a long time to understand the patient’s condition, the selection of treatment strategy, and obtaining informed consent at the time of the first introduction of chemotherapy. It is also necessary to take great care concerning possible side effects. At present, we are addressing these problems through educational hospitalization for about 1 week at the beginning of treatment.

Nurses and paramedical staff are playing important roles in the U.S. concerning the education of patients and the practice of I.V. infusion and other procedures. It is desired that Japan develop systems for the training of nurses specializing in chemotherapy and the division of roles to make the best use of the abilities of these nurses.

Another problem is the burden on the patients’ families, which might be severe in the case of aged patients requiring assistance and patients who are not able to visit hospitals by themselves because of brain metastases or other complications. It is necessary to expand further the system for supporting home care.
Conclusion

Considering the QOL of patients with advanced lung cancer and the cost of medical care, it is rational to perform chemotherapy on an outpatient basis, as is the case in Western countries. Recent use of non-platinum antineoplastic agents and the drugs to prevent side effects has facilitated the practice of outpatient chemotherapy. A system for supporting home care, revision of medical fees, and improvement of the preparedness of hospitals for outpatient care are desired.

REFERENCES

7) Kearns, C.M. and Egorin, M.: Considerations regarding the less-than-expected thrombocytopenia encountered with combination paclitaxel/carboplatin chemotherapy. Semin Oncol 1997; 24(suppl 2): s2.91–s2.96.