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Editorial

Chemotherapy for Advanced Non-Small Cell Lung Cancer: Quest for the Best Continues

Approximately one third of all cancer-related deaths are due to lung cancer, which accounts for more deaths each year than breast, prostate, and colon cancer combined. The median survival of patients with untreated metastatic non–small-cell lung cancer (NSCLC) is only four to five months and one year survival rate is about 10 percent.[1]

Chemotherapy for advanced NSCLC cancer is often considered ineffective or excessively toxic. However, meta-analysis has demonstrated that compared to supportive care, chemotherapy provides improvement in survival in patients with advanced non–small-cell lung cancer.[2] In addition, randomized studies comparing chemotherapy with the “best supportive care” have shown that chemotherapy reduces symptoms and improves the quality of life.[3]

Till 1990s, advanced NSCLC patients were mostly treated with cisplatinum based doublet where the second agent used to be one of the etoposide, mitomycin or vinka alkaloids. The last decade has seen the introduction of several new chemotherapeutic agents including the taxanes, gemcitabine, and vinorelbine, that produce single-agent response rates of more than 20% in previously untreated patients with advanced tumors. Results of several phase I-II trials have shown that the agents can be combined safely with cisplatin or carboplatin and that most combinations result in response rates of 35% to 40% or more .[4]

In an effort to ascertain the supremacy of one chemotherapy regimen comprising of a newer drug along with platinum agents, ECOG performed a clinical trial. The primary objective of this study was to compare overall survival in patients treated with cisplatin and gemcitabine, cisplatin and docetaxel, carboplatin and paclitaxel, or cisplatin and paclitaxel. The study concluded that though third-generation chemotherapy regimens in patients with NSCLC with good performance status moderately improved survival at one and two years (33% and 11%, respectively), there was no significant difference in survival among four commonly used regimens. The gemcitabin/cisplatinum combination, however, was associated with statistically significant longer median time to the progression of disease.[5]

In the current issue of the Journal, Lavrenkov et al[6] have retrospectively analyzed their experience with two cisplatin based regimens as first line chemotherapy for advanced NSCLC. The regimens included gemcitabin/cisplatin (GP) and vinorelbine/cisplatin (VP). In this report of 60 NSCLC patients treated with either of the two regimens at their center between 1998-2001, efficacy was compared in terms of response rates, survival and toxicity profile of the two groups.

VP arm was associated with grade III/IV neutropenia in 68% cases which was significantly more (p=0.007) compared with 29% incidence in GP arm. Besides, GP arm was associated with better survival rates (progression free, over all and one year). However, since the difference in the survival did not reach statistical significance, probably due to small sample size, definite recommendations can not be made based on this. Nevertheless the study does provide ground for further research on this issue.

Overall, the response rates to chemotherapy in advanced NSCLC with current chemotherapy protocols continue to be less than 30-40% and median survival less than an year. This study as also the other recently published

studies raise the question whether the chemotherapy has reached a plateau.[4] Hence clinical investigations utilizing novel treatment strategies are mandatory.

Expanding understanding of cell signaling and other biological pathways involved in tumorigenesis have helped in identifying new molecular targets and have opened up new era of targeted therapies. Several targeted agents have been evaluated in clinical trials in NSCLC and some studies have already produced definitive results. One such new agent, Gefitinib targeting epidermal growth factor receptor is being extensively assessed in NSCLC and it does offer promise of improved outcome .[7]

These novel agents have renewed our hopes about cancer therapies. The challenge is to match the treatment strategies with the biology of lung cancer and continue our quest for the best till we find a clear answer for the management of advanced NSCLC.

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