Current Role of Irinotecan in the Treatment of Non-Small-Cell Lung Cancer

By F. Anthony Greco, MD

Dr. Kelly has provided a complete, well-written review of the current status and evolving role of irinotecan (CPT-11, Camptosar) as a cytotoxic agent for patients with non-small-cell lung cancer (NSCLC). Her review clearly demonstrates the value of irinotecan in this patient population and further supports the continued development of this agent in concert with other chemotherapeutic agents, biologically targeted agents, surgery, and/or radiotherapy.

Phase III Data Needed

Only a few prospective randomized phase III studies have investigated the possible advantage of irinotecan over other agents in the treatment of patients with advanced NSCLC. Certainly, the median survival times reported in individual studies appear promising, but there are inherent problems in comparing one study to another, and further confidence in the potential superiority of irinotecan over several other agents alone or in combination therapy will require additional phase III trials. Although Dr. Kelly did not specifically mention the incorporation of irinotecan-based therapy into neoadjuvant or adjuvant studies in patients with earlier-stage tumors (stages IB, II, resectable IIIA), data presented in her review suggest that this is also a reasonable approach.

If irinotecan/cisplatin becomes an accepted therapy for patients with advanced NSCLC or first-line therapy for patients with extensive-stage small-cell lung cancer (SCLC),[1] it is likely that many oncologists will substitute carboplatin (Paraplatin) for cisplatin in this regimen. Dr. Kelly discusses the available data on the combination of irinotecan and carboplatin, but they are from early studies with small numbers of patients. Further data on this doublet are clearly needed.

Phase II Doses

Dr. Kelly and associates are conducting a phase I trial of irinotecan and carboplatin at the University of Colorado. We are completing a phase I/II trial of the combination at the Sarah Cannon Cancer Center. Although these data from our study are preliminary, it appears that the recommended phase II doses will be irinotecan at 60 mg/m² on days 1, 8, and 15, and carboplatin at an area under the concentration-time curve (AUC) of 4 on day 1 only, with treatment cycles repeated every 28 days.

Other investigators, as described by Dr. Kelly, have concluded that the phase II doses are irinotecan at 50 mg/m² on days 1, 8, and 15, and carboplatin at AUC 5 on day 1, with cycles repeated every 28 days.[2,3] In addition, Fukuda et al[4] used irinotecan doses of 40 to 60 mg/m² on days 1, 8, and 15, and carboplatin at AUC 5 on day 1, repeated every 28 days in a phase I study. It is notable that 11 (85%) of 13 patients with SCLC and 7 (35%) of 20 patients with NSCLC responded in this phase I trial. These investigators also recommended irinotecan doses of 50 mg/m² and carboplatin at AUC 5 for phase II studies.

The doses determined in our phase I study were similar, but we concluded that more irinotecan (60 mg/m²) and less carboplatin (AUC 4) were appropriate phase II doses. The results of other trials (including Dr. Kelly’s study) utilizing a day 1 and 8 schedule every 21 days are awaited.

Conclusions

Our knowledge of the best available cytotoxic agents for patients with lung cancer needs further refinement, as does the incorporation of these drugs with promising biologically targeted agents. These studies remain an important priority for the future.
References:


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