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Clinical Trial Results

nab-Paclitaxel in Combination With Weekly Carboplatin With Concurrent Radiotherapy in Stage III Non-Small Cell Lung Cancer

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Author Summary

Lessons Learned

- The concomitant use of weekly *nab*-paclitaxel and carboplatin with concurrent radiotherapy was demonstrated to be a safe therapeutic approach in this phase I trial of 10 evaluable patients with stage III NSCLC.
- Despite the lack of systemic glucocorticoids, there were no reported infusion reactions or cases of peripheral neuropathy in this trial, both of which are known to occur with the use of paclitaxel.

Abstract

Background. Unresectable stage III non-small cell lung cancer (NSCLC) has a 5-year survival rate of 20%, and concurrent chemoradiotherapy results in significant toxicity with the use of current chemotherapeutic agents. *nab*-Paclitaxel was approved by the U.S. Food and Drug Administration in October 2012 for use along with carboplatin in advanced NSCLC. This study was undertaken to determine the maximum tolerated dose and dose-limiting toxicities (DLTs) of weekly *nab*-paclitaxel given in combination with carboplatin and concurrent radiotherapy in patients with unresectable stage III NSCLC.

Methods. Escalating doses of once-weekly *nab*-paclitaxel were given along with once-weekly carboplatin area under the plasma concentration time curve (AUC) of 2 and concurrent

Table 1. Individual patient outcomes

Patient	Dose level	Histology	Radiation	Response	DLT	OS (days)
1-01	0	ADC	3D	SD	None	372
1-02	0	SCC	3D	PR	None	1,427[a]
1-03	0	NSCLC NOS	3D	PR	None	1,273[a]
2-04	1	LCC	3D	PR	Esophagitis	601
2-05	1	ADC	3D	PR	None	1,289[a]
2-06	1	SCC	3D	PR	None	766[a]
2-07	1	ADC	3D	PR	Radiation dermatitis	325
1-08	0	ADC	3D	PR	None	330
1-09	0	SCC	IMRT	PR	None	551
1-10	0	ADC	IMRT	PR	None	258

[a]Patient was alive at last visit.

Abbreviations: 3D, three-dimensional conformal radiation; ADC, adenocarcinoma; DLT, dose-limiting toxicity; IMRT, intensity-modulated radiation therapy; LCC, large cell carcinoma; NSCLC NOS, non-small cell lung cancer, not otherwise specified; OS, overall survival; PR, partial response; SCC, squamous cell carcinoma; SD, stable disease.

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radiotherapy 66 Gy in 33 fractions, followed by 2 cycles of carboplatin and *nab*-paclitaxel consolidation chemotherapy.

Results. Eleven patients were enrolled and received treatment per protocol, with 10 evaluable for efficacy and toxicity. At dose level 1 (*nab*-paclitaxel 60 mg/m^2), 2 DLTs were observed: esophagitis and radiation dermatitis. Six patients were enrolled at dose level 0 (*nab*-paclitaxel 40 mg/m^2) with no DLTs. Nine of 10 evaluable patients had a partial response.

Conclusion. Concurrent chemoradiotherapy with *nab*-paclitaxel 40 mg/m^2 and carboplatin AUC 2 is a safe and well-tolerated therapeutic regimen in patients with stage III NSCLC. A separate phase I/II study to evaluate the efficacy of this regimen is under way. ***The Oncologist*** 2015;20:491–492

Discussion

In this phase I trial with 10 evaluable patients with stage III NSCLC, the concomitant use of weekly *nab*-paclitaxel and carboplatin with concurrent radiotherapy was demonstrated to be a safe therapeutic approach (Table 1). The maximum tolerated dose was *nab*-paclitaxel 40 mg/m^2 with carboplatin AUC 2 along with daily radiotherapy to a dose of 66 Gy in 33 fractions. There was no DLT at this dose level. Adverse events (AEs) were common but expected, given this modality of therapy and stage of disease. In fact, the range and grade of AEs were similar to previous trials using concurrent chemoradiotherapy for stage III disease [1, 2].

Because of the nature of a phase I trial and the small number of patients enrolled, it is not appropriate to draw meaningful conclusions concerning overall response rate (ORR) or survival. In this trial, however, 30% of the patients were alive ~3 years after enrollment, a result similar to the acknowledged survival pattern for patients with stage III NSCLC [1, 2]. In addition, the ORR in this small phase I trial was 90%, with 9 patients experiencing a partial response by RECIST. Phase III trials of combination chemoradiotherapy in stage III disease have reported ORRs between 50% and 80% [5–7].

There is significant room for improvement in the treatment of stage III NSCLC. To that end, numerous cytotoxic agents and novel therapies have been tested or are being evaluated in this cohort of patients. Its effectiveness in this population will require further investigation, and a phase I/II trial is ongoing comparing radiotherapy given concurrently with either carboplatin plus *nab*-paclitaxel or carboplatin plus paclitaxel (ClinicalTrials.gov identifier NCT01757288).

Author disclosures and references available online.

For Further Reading:

Eva Branden, Gunnar Hillerdal, Karl Kolbeck et al. Pemetrexed and Gemcitabine Versus Carboplatin and Gemcitabine in Non-Small Cell Lung Cancer: A Randomized Noninferiority Phase II Study in One Center. ***The Oncologist*** 2015;20:365.

Abstract

Background. The standard treatment for non-small cell lung cancer (NSCLC) stages IIIb and IV is a platinum compound combined with a third-generation cytotoxic agent. We decided to conduct a phase II study to assess whether the platinum compound could be replaced with pemetrexed with similar results and without an increase in side effects.

Methods. Consecutive eligible patients were randomized to either the standard arm of gemcitabine plus carboplatin (GC) or the experimental arm of gemcitabine plus pemetrexed (GP).

Results. Fifty evaluable patients were enrolled in the GC arm, and 44 received GP. There were 10 partial responses in the GC arm and 16 in the GP arm. With GC, mean survival was 9 months compared with 15 months with GP. The side effects were similar in both groups.

Conclusion. Pemetrexed can replace platinum compounds in the first-line treatment of stage IIIb and IV NSCLC without increasing the side effects. A trend toward better survival was observed in the patients receiving pemetrexed instead of a platinum compound, and this should be studied further.