Clinical prognostic factors in advanced non-small cell lung cancer (NSCLC): Cox regression analysis based on 789 patients treated in three consecutive randomized trials

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ABSTRACT

Background: Treatment efficacy and toxicity of the three studies have been presented at ASCO (2006, Abstract No. 7035). Patients (pts) received gemcitabine or docetaxel either as single agents in different schedules and doses or as a platinum-doublet. Our retrospective analysis is to identify the clinical factors which would influence pts prognosis.

Methods: Pts' eligibility criteria included histologically confirmed stage IIIb or IV, performance status (PS) 0–2, and no prior chemotherapy. Overall survival (OS) was similar in all three studies. 819 pts were enrolled in 1998–2004, of whom 789 pts of them were evaluable for this analysis: 81% of pts had stage IIIb disease and PS1–2. Univariate and multivariate (stepwise) Cox regression analyses were performed to evaluate the impact of baseline characteristics and of quality of life (QoL) on OS.

Results: Factors which have a significant impact on OS are the laboratory parameters hemoglobin (Hgb) and LDH (p<0.0001), WHO PS (p=0.001) and the EORTC QOL measure for lung cancer LC13, (p=0.0006), respectively (see Table). Gender measured univariately also influences OS significantly (p=0.0085) but has less impact in the multivariate model (p=0.37). Age (<65 vs ≥65) (HR = 0.92, p=0.38), and histology (adenocarcinoma/other) (HR = 0.89, p=0.96) are not of prognostic value for OS. Other factors such as tumor stage (stage IIIb vs IV), presence of extra-thoracic metastases, number of co-morbidities, and surgical and radiologic pretreatment also have no prognostic influence on OS. Analysis for the effect of smoking on OS could not be performed since few pts had never smoked.

Conclusions: Our retrospective analysis confirms the prognostic value of serum Hgb and LDH, WHO PS, and QOL LC13 as clinical determinants for OS.

INTRODUCTION

Prognostic factors (PF) are pivotal in the treatment of patients with non-small cell lung cancer (NSCLC) for selecting appropriate treatment, defining eligibility criteria for new clinical trials, providing insights into the disease process and therapeutic response, and in aiding the stratification of patients by risk subgroup. Of particular interest are analyses of PF based on clinical and laboratory data from recent clinical studies. Statistical methods

- Univariate testing was performed.
- Cox regression analysis was performed to evaluate the significance of different factors in predicting OS.
- Factors included in the analysis were: hemoglobin (Hgb); lactate dehydrogenase (LDH); gender; age; performance status (PS); quality of life (QoL); histology; tumor stage; presence of extra-thoracic metastases; number of comorbidities; prior surgery or radiotherapy; and smoking history.
- Regression analysis of survival data was performed based on the Cox proportional hazards model and using the conditional log-rank regression with the SAS PHREG procedure.
- Stepwise forward selection and backward elimination methods were used.
- Two-sided statistical significance was set at 0.05.

METHODS

Patient characteristics

- Between February 17, 1998 and December 2, 2004, 819 patients were enrolled at 34 centers in Germany and Western Europe; 789 patients were evaluable and baseline characteristics were well balanced between the treatment arms in the three studies (Table 1).

- Assessments

  - In the prospective analyses, OS was defined as the time from randomization to death or censoring. As previously reported, OS was similar in the three studies and the study populations were pooled for the present analysis.
  - Retrospective analysis of the effect of baseline demographic and clinical factors on OS was performed as described in the statistical methods below.
  - Time-to-event data were described using Kaplan–Meier curves.

- Conclusions: Our retrospective analysis confirms the prognostic value of serum Hgb and LDH, WHO PS, and QOL LC13 as clinical determinants for OS.

- Non-surgical approaches are unable to tolerate more toxic regimens. To define the optimum treatment regimen for NSCLC, it is important to identify clinical factors which influence patient outcome.

- Overall survival (OS) was similar in all three studies. 819 pts were enrolled in 1998–2004, of whom 789 pts of them were evaluable for this analysis: 81% of pts had stage IIIb disease and PS1–2. Univariate and multivariate (stepwise) Cox regression analyses were performed to evaluate the impact of baseline characteristics and quality of life (QoL) on OS.

- Factors which have a significant impact on OS are the laboratory parameters hemoglobin (Hgb) and LDH (p<0.0001), WHO PS (p=0.001) and the EORTC QOL measure for lung cancer LC13, (p=0.0006), respectively (see Table). Gender measured univariately also influences OS significantly (p=0.0085) but has less impact in the multivariate model (p=0.37). Age (<65 vs ≥65) (HR = 0.92, p=0.38), and histology (adenocarcinoma/other) (HR = 0.89, p=0.96) are not of prognostic value for OS. Other factors such as tumor stage (stage IIIb vs IV), presence of extra-thoracic metastases, number of co-morbidities, and surgical and radiologic pretreatment also have no prognostic influence on OS. Analysis for the effect of smoking on OS could not be performed since few pts had never smoked.

- Conclusion: Our retrospective analysis confirms the prognostic value of serum Hgb and LDH, WHO PS, and QOL LC13 as clinical determinants for OS.

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