European Journal of Cancer 52 (2016) 77–84

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Clinical Trial

Induction chemotherapy with docetaxel/cisplatin/5-fluorouracil followed by randomization to two cisplatin-based concomitant chemoradiotherapy schedules in patients with locally advanced head and neck cancer (CONDOR study) (Dutch Head and Neck Society 08-01): A randomized phase II study

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Received 22 May 2015; received in revised form 24 September 2015; accepted 24 September 2015
Available online 1 December 2015

KEYWORDS
Head and neck cancer;
Chemoradiotherapy;

Abstract ***Purpose:*** To study the feasibility of induction chemotherapy added to concomitant cisplatin-based chemoradiotherapy (CRT) in patients with locally advanced head and neck cancer (LAHNC).

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http://dx.doi.org/10.1016/j.ejca.2015.09.024

Induction chemotherapy; TPF

Patients and methods: LAHNC patients were treated with 4 courses of docetaxel/cisplatin/5-fluorouracil (TPF) followed by randomization to either cisplatin 100 mg/m^2 with conventional radiotherapy (cis100 + RT) or cisplatin 40 mg/m^2 weekly with accelerated radiotherapy (cis40 + ART). Primary endpoint was feasibility, defined as receiving ≥90% of the scheduled total radiation dose. Based on power analysis 70 patients were needed.

Results: 65 patients were enrolled. The data safety monitoring board advised to prematurely terminate the study, because only 22% and 41% (32% in total) of the patients treated with cis100 + RT (n = 27) and cis40 + ART (n = 29) could receive the planned dose cisplatin during CRT, respectively, even though the primary endpoint was reached. Most common grade 3–4 toxicity was febrile neutropenia (18%) during TPF and dehydration (26% vs 14%), dysphagia (26% vs 24%) and mucositis (22% vs 57%) during cis100 + RT and cis40 + ART, respectively. For the patients treated with cis100 + RT and cis40 + ART, two years progression free survival and overall survival were 70% and 78% versus 72% and 79%, respectively.

Conclusion: After TPF induction chemotherapy, cisplatin-containing CRT is not feasible in LAHNC patients, because the total planned cisplatin dose could only be administered in 32% of the patients due to toxicity. However, all but 2 patients received more than 90% of the planned radiotherapy.

Clinical Trials Information: NCT00774319.

1. Introduction

Most locally advanced head and neck cancer (LAHNC) patients are treated with concomitant chemoradiotherapy, since it has been shown that 5-years survival increased with 6–8% as compared to radiotherapy alone [1]. The most common used schedule is the RTOG schedule with cisplatin 100 mg/m^2 on days 1, 22 and 43 combined with conventional radiotherapy [2].Alternatively cisplatin 40 mg/m^2 combined with conventional or accelerated radiotherapy is applied [3–5]. A direct comparison of these two schedules with respect to toxicity, feasibility, or efficacy has not been performed yet.

Induction chemotherapy (IC) may improve the prognosis of LAHNC. Docetaxel, cisplatin and fluorouracil (TPF) has been proven superior to cisplatin and fluorouracil (PF) as induction chemotherapy in LAHNC with regard to efficacy and toxicity in two phase III studies, followed by radiotherapy alone, or by radiotherapy and concurrent carboplatin [6,7]. The main criticism on these phase III studies is their omission to use standard concomitant cisplatin-based chemoradiotherapy after TPF. Before the start of our study, no data were available on the feasibility of cisplatin-containing TPF followed by cisplatin-based concomitant chemoradiotherapy. We conducted a randomized phase II study in which all LAHNC patients received TPF followed by randomization to either concomitant chemoradiotherapy with cisplatin 100 mg/m^2 once every 3 weeks with conventional radiotherapy (cis100 + RT) or chemoradiotherapy with weekly cisplatin 40 mg/m^2 and accelerated radiotherapy (cis40 + ART). The aim of this CONDOR study was to evaluate the feasibility of these schedules.

2. Patients and methods

2.1. Patients eligibility

Patients with pathologically proven non-metastatic, previously untreated, locally advanced squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx or larynx, stage III or IV, were eligible. Patients were between 18 and 65 years of age, had a WHO performance status of 0–1, adequate bone marrow, hepatic and renal function. Exclusion criteria were active alcohol addiction, admission for chronic obstructive pulmonary disease during the last 12 months, weight loss of more than 10% during the last 3 months prior to study entry.

The ethics committee of the participating centers approved the protocol and the study was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent.

2.2. Treatment

The TPF regimen was the same regimen as used in the EORTC 24971/TAX 323 study [7]. TPF was administered via a central venous catheter on an inpatient basis for the first two days. Thereafter the patients received the last 3 days of 5-FU using a medication cassette reservoir at home. After two cycles, radiological evaluation according to RECIST version 1.0 was performed. In case of complete response (CR), partial response (PR)