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Original Research

A randomised phase II study of chemoradiotherapy with or without nimotuzumab in locally advanced oesophageal cancer: NICE trial☆

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Abstract ***Purpose:*** Chemoradiotherapy is the standard treatment for patients with inoperable locally advanced oesophageal cancer. We sought to assess the safety and efficacy of chemoradiation combined with nimotuzumab, a humanised antibody directed against epidermal growth factor receptor (EGFR).
Patients and methods: Untreated patients with inoperable locally advanced oesophageal cancer and no distant metastases were randomised to chemoradiotherapy (cisplatin and fluorouracil combined with external beam radiation) alone or in combination with nimotuzumab. The primary end-point was the endoscopic complete response (eCR) rate, and secondary end-points comprised quality of life (QoL) and safety. The combined eCR and pathologic complete response (cEPCR) and overall survival (OS) were also evaluated.
Results: We enrolled 107 patients with a mean age of 59 years, and 93% had squamous cell carcinoma. Toxicity was manageable in both arms with no important differences in adverse events (AEs). We performed post-treatment endoscopies in 67 patients, including 60 who had a biopsy. In the intent-to-treat population, the eCR rates with and without nimotuzumab were 47.2% and 33.3% ($P = 0.17$), respectively, and the cEPCR rates were 62.3% and 37.0% ($P = 0.02$), respectively. With a median follow-up of 14.7 months, the hazard ratio (HR) for OS was 0.68 (95% confidence interval (CI): 0.44–1.07; $P = 0.09$) with a median OS of 15.9 months for the nimotuzumab arm and 11.5 months for the control arm. Regarding QoL, a significant difference was observed for the physical subscale score ($P = 0.03$) with lower values for the control arm.
Conclusion: Combined chemoradiotherapy plus nimotuzumab is safe for patients with locally advanced oesophageal cancer, it appears to increase the cEPCR rate, and without compromising QoL.
Clinical trials: Identification number: EF024-201; Trial registry: NCT01249352.

1. Introduction

Oesophageal cancer is the eighth most commonly diagnosed cancer and sixth leading cause of cancer death in males; however, its incidence rate considerably varies worldwide [1]. In 2014, 18,170 new cases of the disease were estimated in the United States of America, and there were 10,780 in Brazil [2,3]. Squamous cell carcinoma (SCC) is the most common histology in areas with higher incidence of oesophageal cancer. Regardless of histology, approximately 50% of patients present with locally advanced disease, and fewer than 60% have a potentially resectable tumour. For operable patients, surgery alone confers 5-year overall survival (OS) rates of 15–20%, and a median OS of 18 months [4,5]. For patients who are not candidates for surgery, radiotherapy alone provides 5-year OS rates ranging from 0% to 15% [6,7].

The poor outcomes of patients with locally advanced oesophageal cancer have driven the evaluation of radiotherapy combined with concurrent cisplatin and fluorouracil in the landmark Radiation Therapy Oncology Group (RTOG) trial 85-01 [7]. The 5-year survival rate was 26% for the chemoradiotherapy group compared with 0% for the group that received radiotherapy alone. This positive result has made chemoradiotherapy a standard approach for inoperable oesophageal cancer [8]. However, even after chemoradiotherapy, locally recurrent or persistent disease is still a challenge.

No other chemotherapy regimen has been demonstrated to be superior to cisplatin-based chemotherapy when administered concurrently with radiotherapy. The addition of novel agents to chemoradiotherapy is then crucial for efforts attempting to improve clinical outcomes. The epidermal growth factor receptor (EGFR)