Original Research

Quality of life and swallowing with standard chemoradiotherapy versus accelerated radiotherapy and panitumumab in locoregionally advanced carcinoma of the head and neck: A phase III randomised trial from the Canadian Cancer Trials Group (HN.6)

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Abstract  Aim: To compare quality of life (QOL) between standard (SFX) chemoradiotherapy (arm A) and altered fractionation radiotherapy (AFX) with panitumumab (PMab; arm B).

Methods: Patients with T any N + M0 or T3-4N0M0 squamous cell head-neck carcinoma were randomised to SFX (70 Gy/35/7 wks) plus cisplatin (100 mg/m² IV × 3) versus AFX (70 Gy/35/6 wks) plus PMab (9 mg/kg IV × 3). QOL was collected at baseline, end of radiation therapy (RT) and 2, 4, 6, 12, 24 and 36 months post-RT using the Functional Assessment of Cancer Therapy Head and Neck (FACT-H&N), MD Anderson Dysphagia Index (MDADI) and SWAL-QOL. We hypothesised a 6-point more favourable change in FACT-H&N score from baseline to 1 year in arm B over arm A.

Results: Among 320 patients, median follow-up was 46 (range: 0.1–64.3) months, median age 56, 84% male, Eastern Cooperative Oncology Group PS 0 (71%), 1 (29%). Primary site was oropharynx in 81% (p16+ 68%, p16− 16%, missing 16%). Baseline scores did not differ by arm (A/B): FACT-H&N 116.5/115, MDADI Global 83/77, SWAL-QOL General 67/68. At 1 year, no difference was seen between arms in FACT-H&N change from baseline: A −1.70, B −4.81, p = 0.194. Subscale change scores by arm were (A/B): last week RT, FACT-Physical (−11.6, −10, p = 0.049), MDADI Physical (−40.4, −33.9, p = 0.045), and SWAL-QOL. Eating Duration (−61.2, −51.2, p = 0.02), Eating Desire (−53.3, −43.9, p = 0.031) and Mental Health (−42, −32.6, p = 0.009); 4 months, HN subscale (−7.7, −10, p = 0.014). No clinically important differences by arm were seen post-treatment.

Conclusions: PMab with AFX did not durably improve QOL or swallowing as compared with SFX with cisplatin.

Trial registration: ClinicalTrials.gov: NCT00820248.

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1. Introduction

Disease control for locoregionally advanced squamous cell carcinoma of the head and neck (LA-SCCHN) is improving, particularly in human papillomavirus (HPV)—related oropharyngeal cancers (OPC). Accepted treatment strategies produce significant long-term functional impact [1]. Current trials focus on developing equi-effective approaches with improved function relative to the standard, concurrent cisplatin with radiation therapy (RT) [2–7].

Improvements in survival for LA-SCCHN by the addition of chemotherapy or accelerated fractionation are at the expense of quality of life (QOL) [8]. Although studied with increasing frequency [9], QOL has been reported in few head and neck cancer randomised trials. The QOL effect of combining the epidermal growth factor receptor—inhibitor panitumumab (PMab) with accelerated fractionation RT (AFX) is unknown.

Concomitant epidermal growth factor receptor—inhibitor cetuximab, with RT, compared with RT alone, improved survival without worsening QOL in LA-SCCHN in the IMCL-9815 study [10,11]. Consequently, the HN.6 randomised phase III trial comparing progression-free survival (PFS) in patients with LA-SCCHN treated with standard fractionation (SFX) plus high-dose cisplatin (CIS) versus AFX plus PMab was designed with multiple secondary patient-reported outcomes (PROs). The standard arm was based on the Radiation Therapy Oncology Group 0129 trial, which showed no statistically significant difference in efficacy, acute or late toxicity, between 3 cycles of high-dose CIS with SFX versus 2 cycles with AFX. Since subgroup analysis of the IMCL-9815 study favoured AFX with biotherapy, AFX was chosen for the experimental arm.

PROs were measured as secondary end-points, however with a per-protocol primary QOL hypothesis: the median change in overall FACT-H&N score from baseline to 1 year would be 6 units higher in arm B (PMab/AFX) as compared with arm A (CIS/SFX). Although a previous study of AFX alone showed a median improvement of 8 units over 1 year, with systemic therapy in both arms, it was anticipated that overall QOL may decrease from baseline [12].

2. Patients and methods

Details of the HN.6 design and efficacy analysis have been published [13]. In brief, this multi-centre, open-label, randomised-controlled phase III Canadian Cancer Trials Group (CCTG) trial accrued fit patients with LA-SCCHN of the oral cavity, oropharynx, larynx or hypopharynx defined as T (any), N+, M0 or T3-4, N0, M0.

From December 2008 to November 2011, eligible patients stratified by T-category and N-category, intensity-modulated RT versus 3-dimensional conformal RT and anatomic location were randomised 1:1.
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