Phase II study with conventional radiotherapy (RT) + cetuximab in patients with advanced larynx cancer who responded to induction chemotherapy (IC). An organ preservation TTCC study.


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**Background**

Induction Chemotherapy with docetaxel/cisplatin/furocarb (TPF) is superior to cisplatin/furocarb (PF) in organ preservation: 3-year actuarial larynx preservation rate was 70.3% with TPF vs 57.5% with PF (p = 0.03).

Bioradiotherapy (BRT) is superior to RT alone in the loco-regional control of locally advanced head and neck tumors (2).

The 3-year larynx preservation rates were 87% in the cetuximab plus radiotherapy (BRT) group versus 77% in the radiotherapy alone group in the subanalysis of larynx preservation in the Bonner trial (3).

The aim of our study was to evaluate the efficacy and safety of IC followed by BRT for functional larynx preservation.

**Objective and study**

Phase II, open-label, multicenter study in patients with stage III-IVA laryngeal carcinoma candidates to total laryngectomy. The primary endpoint is to evaluate survival with functional larynx in patients with local tumor response to induction chemotherapy (IC) followed by BRT and then treated with Radiotherapy + Cetuximab (Bioradiotherapy).

- **Consider acceptable 3-yr survival: 50%**
- **Consider quite acceptable 3-yr survival: 65%**
- **Recruitment time: 24 months**
- **Minimum follow-up: 36 months**
- **Declaring the experimental arm as active if the true rate is ≤ 50% of a 0.05 (a, one-tailed test), and with a probability of rejecting the experimental arm if the true rate is compatible with 65% of a 0.1 (b), the size is 74 patients, undergoing TPF and with response were required.**

**Induction scheme**

- **Cisplatin (P):** 70 mg/m² on day 1, 14, 21, 28
- **Docetaxel (T):** 75 mg/m² on day 1
- **Cetuximab (C):** 400 mg/m² on day 1, then 250 mg/m² on day 15 (6 cycles)

**Study design and methods**

**Baseline characteristics**

- **Total laryngectomies: 3**
- **Conventional RT:**
  - 69.3% of median
  - 35.9% of patients

**Efficacy**

- **Complete response:** 37 (40%)
- **Partial response:** 34 (37%)
- **Stable Disease:** 8 (9%)
- **Progression:** 2 (2%)
- **Not evaluated:** 12 (13%)

**Induction Chemotherapy with TPF**

**Radiotherapy**

**Treatment sequence is ready to be concomitant RT + Cisplatin, sequential treatment with TPF + RT alone or with Cisplatin.**

**SAEs: Incidence related to TPF**

- **Total SAEs:** 17 (18%): Fascial neuropathy: 4 (4%)
- **Mucositis:** 3 (3%)
- **Pneumonia:** 1 (1%)
- **Necrosis:** 1 (1%)

**Toxicity during RT + cetuximab phase (after TPF)**

**Overall Survival with functional larynx, ITT population**

**Overall Survival according to TPF response**

**Conclusions**

- **Survival with fucctional larynx at 3 years (89.5%): rates was higher than the calculated critical value (59%), so we consider it is a positive study.**
- **The sequence induction CT with TPF follow by BioRT is safe and have an acceptable tolerance**
- **Complete response to TPF seems to be critical in order to achieve the best rate of survival with functional larynx**
- **Overall survival of patients without complete response to IC are not compromised**
- **This treatment sequence is ready to be compared in a phase III trial with what is considered standard treatment: concomitant RT + Cisplatin, sequential treatment with TPF + RT alone or with Cisplatin.**

**Table of Statistics**

- **Mean:** 42.1177
- **Median:** *
- **IQ:** R *

**Figures**

- **Survival with functional larynx, ITT population**
- **Survival with functional larynx according to TPF response**
- **Overall Survival, ITT population**
- **Overall Survival according to TPF response**