MINIMALLY INVASIVE ESOPHAGECTOMY AFTER A NEOADJUVANT PROTOCOL WITH INDUCTION CHEMOTHERAPY AND CHEMORADIATION

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BACKGROUND

Esophageal cancer is the 8th most common cancer in the world. It is an extremely lethal disease, responsible for almost 400.000 deaths/year. Surgical resection alone was considered the gold standard in esophageal cancer treatment during the last century, with a global 15-40% cure rate. Since the publication of the CROSS trial in 2012, a dutch randomized multicenter phase III trial, neoadjuvant chemoradiation became the standard of care in many countries and also in our instituition, but the overall survival rates are still worse than the observed in other gastrointestinal malignancies. The optimal neoadjuvant approach is still matter of debate and the contribution of induction chemotherapy (IC) before preoperative chemorradiation is not known. The IC may allow for upfront systemic therapy to better adress the risk of distant disease and potentially contibute to cytoreduce the primary tumor, enhancing local control. Based on this considerations, we started a single center phase II trial to investigate the efficacy, feasibility and safety of preoperative IC followed by chemoradiation and minimally invasive surgery in patients with carcinoma of the esophagus and the EGJ The aim of this study is to evaluate the surgical and oncological outcomes, and quality of life of patients enrolled in the QUIMERA study.

METHODS

Inclusion criteria and evaluation:

Patients with histologically confirmed squamous cell or adenocarcinoma of the thoracic esophagus or GEJ (Siewert type I or II), aged 18-75 years, with a PS 0-2, clinical stage cT1b-3 cN0-2, will be eligible. Pretreatment staging will consist of medical history, physical examination, upper endoscopy with biopsy, broncoscopy, computed tomography (CT) scans of the neck, chest and abdomen and positron emission tomography (PET-CT).

Treatment plan (Figure 1)

Preoperative treatment will consist of two cycles of IC with carboplatin (175 mg/m2) and paclitaxel (AUC=5) on days 1 and 22, followed by radiotherapy of 45 Gys (25 x 1.8 Gys) and concurrent chemotherapy comprising carboplatin (AUC=2) and paclitaxel (50 mg/m2) weekely for five weeks. On day 14, patients will have another PET-CT to evaluate the early metabolic response. Four weeks after the ending of the neoadjuvant regimen, the patients will be re-staged with CT, endoscopy and PET-CT. To proceed to surgery, patients will be required to have no newly detected stage M1 disease and/or inoperable T4 disease.

Surgical Procedures (Figures 2 and 3)

The surgery will be scheduled 8-12 weeks after the completion of chemoradiation. All surgical procedures will be done the same surgeon.

The standard procededure is a minimally invasive esophagectomy with a thoraco-abdomino-cervical approach. The thoracoscopic phase is performed in the prone position. A complete two-field lymphadenectomy is mandatory and the reconstruction will be done preferably by a gastric conduit with a manual termino-terminal anastomosis with the cervical esophagus. A jejunostomy is performed during the laparoscopic phase for posoperative early nutrition and chest tubes are inserted for posoperative monitoring.

Data concerning the surgical and oncological results (procedure duration, blood loss, convertion and histopatogical data) will prospectivaly collected in electronic database. The mobidity and moratlity will be classified and graded following the Esophagectomy Complications Consensus Group recomendations.

QoL

The Quality of life evaluation will be performed using two standard forms: The EORTC developed QLQ-C30 and the esophageal cancer specific QLQ-EOS18, and EQ-5D-5. QoL will be measured in three points during the protocol: during the screening before the IC initiation; during the restaging, after the IC + CR and 8 to 10 weeks after the surgical procedure. The results calculated using the EORTC and EuroQuol procedures manual. (Figure 1).

PARCIAL RESULTS

From March 2017 to July 2018, 42 patients signed the informed consent form and were enroled. Of these, 26 were excluded because of M1 disease and 16 started the protocol. So far, 9 patients underwent surgery and 3 completed the neoadjuvant regimen and are waiting for the surgical procedure (Table 1).

The mean surgical time was 429 min (360-540) and mean hospital stay was 17 days (7-56). There were no conversions to open surgery. There was no mortality and 3 patients had major complications. The mean node count in the surgical specimen was 24 (13-48). A complete pathological response was observed in 4 cases.

TABLE 1 – Patient and Tumor Characteristics

Age (years)	58.5 (43 – 71)
Male	6
Female	3
Tobacco use	9
Alcohol use	5
Histology	
SCC	5
AC	4
Tumor Location	
Upper third	0
Middle third	2
Lower third and EGJ	7
Serum Albumin (mean)	4.0 g/dl (3.2-4.4)
Clinical stage	
IA	0
IB	0
IIA	0
IIB	2
IIIA	4
IIIB	3
IIIC	0
IV	0
Time to surgery (mean)	11 weeks (9-13)

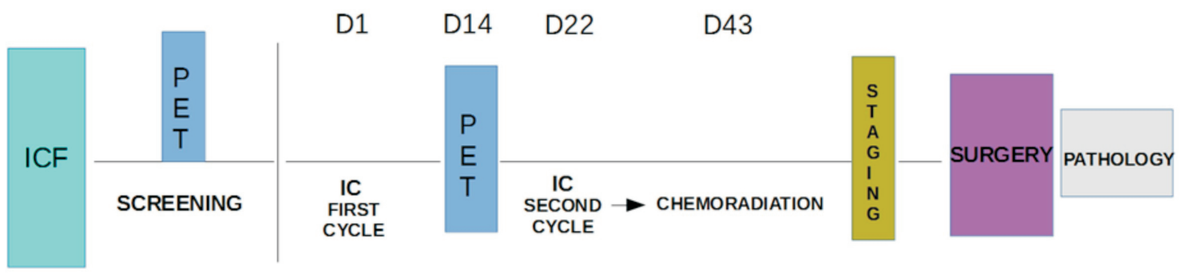

Figure 1. QUIMERA study protocol. *ICF*, informed consent form; *IC*, induction chemotherapy

Figure 2. Surgical Procedure. A. Patient positioning in prone position. B. Detail of thoracoscopic esophageal dissection.

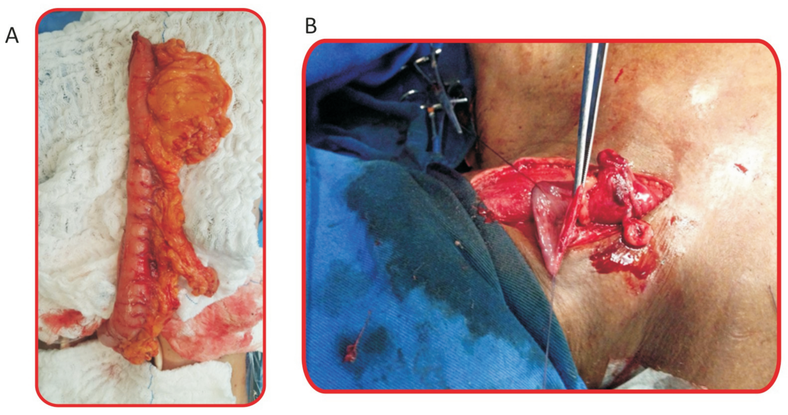

Figure 3. Surgical Procedure A- Gastric conduit .B- Cervical anastomosis

CONCLUSIONS

Our initial results are encouraging and suggests that IC followed by chemoradiation is a safe, feasible, active and well-tolerated regimen and that it may increase the PCR, especially for squamous cell carcinoma. The minimally invasive esophagectomy following the IC + CR was feasible, safe and had a adequate oncologic result. After the protocol completion there will be data available for a definitive evalutation of the procedure.

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