# Noeadjuvant chemoradiotherapy with 5-fluorouracil-cisplatin combined with cetuximab in patients with resectable locally advanced esophageal carcinoma: A prospective phase I/II trial (FFCD-PRODIGE 3)—Preliminary phase II results - Abstract #4091

Laetitia Dahan, Christophe Mariette, Marc Ychou, Tan Dat Nguyen, Rosine Guimbaud, Thomas Aparicio, Veronique Vendrely, Xavier d'Journo, Fabien Subtil, Franck Bonnetain, Antoine Adenis, Jean Francois Seitz
FFCD, France

## Background

❖Chemoradiotherapy (CRT) for locally advanced esophageal cancer is based on 5FU combined with cisplatin.
❖The anti-EGFR antibody cetuximab increases the efficacy of RT-based regimen for patients (pts) with cancer of the head and neck.
❖This phase I/II trial was evaluating MTD (data presented of the phase I), safety and pathologic complete response (pCR) rate of the combination of cetuximab with platinum-based CRT in esophageal cancer.

## Methods

**ELIGIBILITY**

- Squamous cell or adenocarcinoma of the oesophagus or gastroesophageal junctions siewert I
- Resectable tumor
- Us T1N+, T2N0 or N+, T3N0 or N+
- WHO Performance Status 0-1 / Age 18-75 years
- Weight loss <15% in the last 6 months
- No hepatopathy

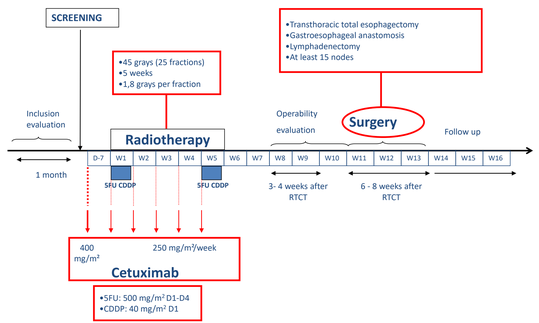
**STATISTICS**

- Multicenter phase I/II study
- One step Flemming design
- Primary endpoint: pathologic complete response (Mandard criteria) > 20%
- Secondary endpoints
  - surgical complications
  - mortality
  - R0 resection rate
  - Overall survival, Relapse free survival, toxicity

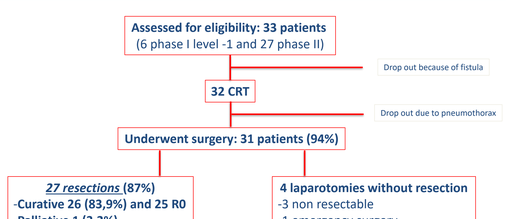
**ASSESSMENTS**

- Clinical examination
- Endoscopy + biopsy
- Endoscopic ultrasonography (EUS)
- CT scan of the chest and abdomen
- Bronchoscopy

## Schema




## Diagram




## Patient characteristics

| | Patient characteristics n = 33 |
|---|---|
| Age (year) | 60 [41-76] |
| Sex - Male | 28 (84,9%) |
| - Female | 5 (15,1%) |
| Performance status: - 0 | 21 (63,6%) |
| - 1 | 12 (36,4%) |
| Weight loss - <15% | 31 (94%) |
| - >15% | 1 (3%) |
| Histology - Squamous | 20 (60,6%) |
| - Adenocarcinoma | 13 (39,4%) |
| Classification - Stage IIa | 4 (12,1%) |
| - Stage IIb | 4 (12,1%) |
| - Stage III | 25 (75,8%) |

## Treatment and CRT Toxicity

| | Level -1 (n = 32) |
|---|---|
| Chemotherapy | |
| -2 weeks of 5FU-CDDP | 30 (94%) |
| -1 week of 5FU-CDDP | 2 (6%) |
| Cetuximab | |
| -6 weeks of CTX | 28 (88%) |
| -5 weeks of CTX | 2 (6%) |
| -3 weeks of CTX | 1 (3%) |
| -1 week of CTX | 1 (3%) |
| Radiotherapy | |
| -25 fractions | 30 (94) |
| -28 fractions | 1 (3%) |
| -7 fractions | 1 (3%) |

| | Maximale toxicity n = 32 |
|---|---|
| Allergy | |
| Grade 1, 2 | 0 (0%) |
| Grade 3, 4 | 1 (3,1%) |
| Skin toxicity | |
| Grade 0 | 7 (21,9%) |
| Grade 1, 2 | 24 (75%) |
| Grade 3, 4 | 1 (3,1%) |
| Hematologic toxicity | |
| Grade 0, 1, 2 | 31 (96,9%) |
| Grade 3, 4 | 1 (3,1%) |
| Gastrointestinal toxicity | |
| *Mucositis, Nausea* | |
| Grade 0, 1, 2 | 31 (96,1%) |
| Grade 3, 4 | 1 (3,1%) |
| *Oesophagitis* | |
| Grade 0, 1, 2 | 28 (87,5%) |
| Grade 3, | 3 (9,4%) |
| Grade 4 | 1 (3,1%) |

## Postoperative complications

| | Surgery n = 31 |
|---|---|
| Postoperative complications | 15 (48,4%) |
| Surgical complications | 8 (25,8%) |
| Anastomotic leak | 3 (9,7%) |
| Anastomotic leak +l aryngeal paralysis | 1 (3,2%) |
| Chylothorax | 1 (3,2%) |
| Transplant necrosis + Re-operations | 1 (3,2%) |
| Pleural complication | 1 (3,2%) |
| Pleural complication + Gastroparesis | 1 (3,2%) |
| Medical complications | 13 (41,9%) |
| Acute respiratory distress syndrome (ARDS) | 8 (25,8%) |
| Postoperative deaths | 4 (12,9%) |
| Clavien Score | |
| -grade 4 | 4 (12,9%) |
| -grade 3 | 0 (0%) |
| -grade 2b | 4 (12,9%) |
| -grade 2a | 3 (9,7%) |
| -grade 1 | 4 (12,9%) |

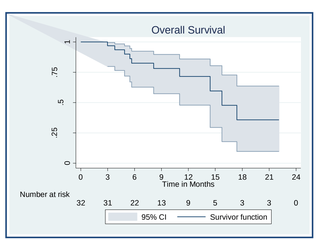
## Histopathologic response

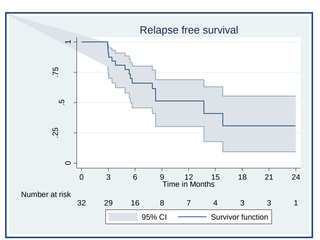
❖**GRT1*: 5 (18,5%)** complete tumor response
**- 3 ypT0N0 ; 11,1% pRC**
- 2 ypT0N+
❖**GRT2: 6 (22,2%)** residual cancer cells scattered through fibrosis
❖**GTR3: 8 (29,6%)** an increased number of residual cancer cells, with predominant fibrosis
❖**GRT4: 6 (22,2%)** residual cancer outgrowing fibrosis

*Tumor regression grade

## Survivals

| | Median (months) | [95% CI] |
|---|---|---|
| RFS | 13.7 | [5.47– .] |
| OS | 15.7 | [11.01– .] |




## Conclusion

❖**Adding cetuximab to preoperative chemoradiotherapy including 5FU and cisplatin did not increase pCR.**
❖**The recommended dose level of chemotherapy determined during phase I, which was dose level -1 and lower than expected, could explain those disappointing results.**
❖**We won't initiate a phase III trial.**