Clinical trials for HNSCC opened at Instituto Roffo

4-6 October 2017 - Buenos Aires, Argentina
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Instituto de Oncología Ángel H. Roffo
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The faculty has provided no information regarding significant relationship with commercial supporters and/or discussion of investigational or non-EMEA/FDA approved (offlabel) uses of drugs as of 25 September 2017.
RESEARCH AT INSTITUTO ANGEL H. ROFFO.
Clinical oncology
International Trials

- Phase III randomized study (V322) comparing PF vs. cisplatin+docetaxel in recurrent and/or metastatic SCCHN.

- Phase III randomized study (V324) comparing neoadjuvant chemotherapy with PTF vs. PF followed by simultaneous chemoradiotherapy for stage III and IV SCCHN.

- Phase III randomized study comparing methotrexate vs. Gefitinib 250 mg or 500 mg for recurrent and/or metastatic SCCHN. (IMEX)

- Phase III randomized study comparing cisplatin vs cisplatin + pemetrexed for recurrent and/or metastatic SCCHN.
  - (Spinnaker).

- Phase II study of Cetuximab + radiotherapy for T2 N0-1 Larynx cancer.
Afatinib vs MTX (LUX HN 1)
Second line – Cisplatin refractory patients

Patients with incurable R/M HNSCC progressing on/after first-line platinum-based therapy (N=474)

Randomisation (2:1)
Stratified by: ECOG PS (0 vs 1) and prior use of EGFR mAb therapy (Yes/No)

Afatinib
40 mg orally once daily (n=316)

Methotrexate
40 mg/m² IV weekly (n=158)

Primary endpoint: PFS
Key secondary endpoint: OS
Secondary endpoints: ORR, patient-reported outcomes, safety
Afatinib vs MTX (LUX HN 1)
Second line – Cisplatin refractory patients

*Odds ratio: 1.9 (0.88–4.14); p-value = 0.101
†Odds ratio: 1.5 (1.03–2.26); p-value = 0.035
‡Disease control rate (DCR): includes objective response and stable disease
Afatinib vs MTX (LUX HN 1)
Second line – Cisplatin refractory patients

- **PFS event, n (%):** Afatinib (n=322) 275 (85.4) vs MTX (n=161) 135 (83.9)
- **Median PFS (months):** Afatinib 2.6 vs MTX 1.7
- **HR (95% CI):** Afatinib 0.80 (0.65–0.98) vs MTX
- **Log-rank test p-value:** 0.030
Afatinib vs MTX (LUX HN 1)
Second line – Cisplatin refractory patients
LUX-Head & Neck 2: Randomized, double-blind, placebo-controlled, Phase III trial of afatinib as adjuvant therapy after chemoradiation in patients with primary unresected, high/intermediate-risk, squamous cell cancer of the head and neck

Barbara Burtness, Robert Haddad, José Dinis, José Manuel Trigo, Tomoya Yokota, Luciano de Souza Viana, Ilya Romanov, Jan Vermorken, Jean Bourhis, Makoto Tahara, José Getulio Martins Segalla, Amanda Psyrri, Irina Vasilevskaya, Chaitali Singh Nangia, Manuel Chaves-Conde, Bushi Wang, Neil Gibson, Eva Ehrnrooth, Kevin Harrington*, Ezra E. W. Cohen*

on behalf of the LUX-Head & Neck 2 investigators

*Contributed equally

Presented By Barbara Burtness at 2017 ASCO Annual Meeting
LUX-Head & Neck 2: study design

- Primary unresected, stage III-IVb HNSCC
- Prior curative CRT
- NED after CRT
- Oropharynx cancer patients eligible with >10 pk yrs smoking history

Adjuvant afatinib 40 mg/day orally

Randomization (2:1)
Stratified by:
- ECOG PS (0 vs 1)
- Nodal status (N0–N2a vs N2b–N3)

Matching placebo

Treatment for 18 mos or until recurrence/SPT or unacceptable AEs

- Primary endpoint: DFS (investigator assessed)
- Secondary endpoints: DFS rate at 2 years, OS, HRQoL

DFS, disease-free survival; HRQoL, health-related quality of life; NED, no evidence of disease; OS, overall survival; pk yrs, pack years; SPT, second primary tumor

Presented By Barbara Burtness at 2017 ASCO Annual Meeting
Patient disposition

799 patients screened

617 patients randomized

411 to afatinib

606 to placebo

Not randomized: n=182
- Did not meet eligibility criteria: n=136
- Withdrew consent: n=30
- AEs before enrollment: n=3
- Lost to follow-up: n=1
- Other reasons: n=12

Stopped treatment: n=287
- Tumor recurrence/death: n=53
- SPT: n=4
- AEs: n=63
- Refusal to continue: n=52
- Other reasons*: n=4
- Discontinued when trial was stopped by the DMC: n=111

Stopped treatment: n=119
- Tumor recurrence/death: n=32
- SPT: n=3
- AEs: n=9
- Refusal to continue: n=13
- Other reasons*: n=2
- Discontinued when trial was stopped by the DMC: n=60

124 completed 18 months treatment

87 completed 18 months treatment

*Non-compliance with protocol/lost to follow-up
Primary endpoint: DFS (investigator assessed)

- Median treatment duration: 300.0 days with afatinib; 455.5 days with placebo
- 40% of planned events had occurred by the time of the futility analysis by the DMC

NE, not evaluable
Conclusions

• LUX-Head & Neck 2 was closed due to pre-planned futility analysis because the DMC concluded:
  - Study unlikely to demonstrate a significant efficacy advantage with afatinib
  - Adjuvant afatinib does not improve DFS versus placebo

• Afatinib can be tolerated for up to 18 months post-CRT, with appropriate dose adjustments and management of AEs

• Correlative analyses suggest p16 expression and loss of PTEN expression are markers of resistance to afatinib
Larynx preservation


- In spite of enhancing the complete response rate with more cycles of neoadjuvant chemotherapy only an early complete response correlates with a better disease free survival for larynx preservation. Proceedings ASCO 23:497, 2004.

- Larynx preservation (LP) with concurrent chemotherapy (CT) and hyperfractionated radiotherapy (RT) 3th IFHNOS Congress, 2006.

The experience of the Institute of Oncology Angel H. Roffo for larynx preservation

Dr. Raúl Eduardo Giglio
Multidisciplinary treatment of head and neck tumors
First protocol

1989-1995
TREATMENT PLAN
CHEMOTHERAPY: every 21 days.
CISPLATIN 100 mg/m² day 1
5-FLUOURACILO 1000 mg/m² continuous infusion day 1-5
HYPERFRACTIONATED RADIOTHERAPY:
Source: Co60
fractions: 2 fractions of 1.2 Gy separated by an interval of 6 hours.
TOTAL dose: 75-Gy.
TREATMENT DURATION: 6.5 WEEKS.
LARYNX PRESERVATION WITH CHEMOTHERAPY + SEQUENTIAL HYPERFRACTIONATED RADIOTHERAPY

- Admitted patients: 92 patients
- With RP or RC to 2 cycles of NACT: 67 (73%).
- Laryngectomy of rescue offered to 24 patients (one lost control).
- Response after the third cycle of chemotherapy complete response: 18/67 (27%)
- Partial response 42/67 (63%)
- Progression: 4/67 (6%)
- Lost control: 3/67 (4%)
- Sixty patients completed the combined treatment
Complete response 49/60 (81.7%)
Complete response in larynx + RND 3/60 (5%)
Overall complete response 52/60 (86.6%)
Partial response in larynx 6/60 (10%)
Progressive disease 2/60 (3%)
LARYNX PRESERVATION WITH CHEMOTHERAPY + SEQUENTIAL HYPERFRACTIONATED RADIOTHERAPY

Patients alive 31/60 (52%)

Patients disease free 29/60 (48%)

Patients with larynx preservation 27/60 (45%)
LARYNX PRESERVATION WITH CHEMOTHERAPY + SEQUENTIAL HYPERFRACTIONATED RADIOTHERAPY

Overall survival

Disease free survival

OS according to response to NACT

DFS according to response to NACT

SUPREVIVENCIA MEDIA: 66 m

SUPERVIVENCIA MEDIA: 40 MESES

P = 0.02557

P = 0.03311

RC

RP

RC

RP
1. Response rate complete after combined treatment of chemotherapy + radiotherapy + lymph node draining was 87% for eligible patients.

2. The rate of laryngeal preservation was 45% for the same group (27/60 patients).

3. The rate of recurrence after reaching the full response was 48% (25/52 patients) with an average time of 13.2 months (range 3-72 months).
Second Protocol

1995-2001
OBJECTIVES

• Primary: Increase response complete rate by increasing the number of cycles of neoadjuvant chemotherapy.

• Secondary:
  1. Increase the rate of laryngeal preservation.
  2. Increase the survival rate with preserved larynx.
Treatment strategy

- 2 cycles of PF
  - Response
    - 1, 2 or 3 additional cycles of PF
    - CR or PR with 5 cycles
      - hyperfractionated RT
        - CR: control
        - PR: surgical rescue
  - No response
    - surgery + Radiotherapy
RESPONSE to NACT in the LARYNX (n = 68)

Responders: 56 (82.3%) (63.2%) *

Complete response: 41 (60.3%) (19%) *

Partial response: 15 (22.3%)

Non-responders: 12 (17.7%) *

*(previous trial)
Results after chemotherapy + radiotherapy in responding patients (n = 51) (5 pts lost to follow up)

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>46/51 (90.2%)</td>
</tr>
<tr>
<td>CR POST NACT</td>
<td>36/38 (94.7%)</td>
</tr>
<tr>
<td>PR POST NACT</td>
<td>10/13 (76.9%)</td>
</tr>
<tr>
<td>PR</td>
<td></td>
</tr>
<tr>
<td>(PP POST NACT)</td>
<td>2/51 (3.9%)</td>
</tr>
<tr>
<td>PD</td>
<td>3/51 (5.8%)</td>
</tr>
<tr>
<td>(CR POST NACT)</td>
<td>2/51 (3.9%)</td>
</tr>
<tr>
<td>(PR POST NACT)</td>
<td>1/51 (1.9%)</td>
</tr>
</tbody>
</table>
Current status (n = 62) (patients who completed treatment).

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients alive</td>
<td>39/62</td>
<td>62.9%</td>
</tr>
<tr>
<td>Patients alive and disease free</td>
<td>35/62</td>
<td>56.5%</td>
</tr>
<tr>
<td>Patients with larynx preservation</td>
<td>23/62</td>
<td>37%</td>
</tr>
<tr>
<td>Patients alive with larynx preservation</td>
<td>23/35</td>
<td>65%</td>
</tr>
</tbody>
</table>
**Overall survival**

**OS AT 60 M : 58%**

**Disease free survival**

**DFS AT 60 M : 40%**
**OS according to response to NACT**

P = 0.28486

**DFS according to response to NACT**

P = 0.60240
DFS according to velocity of response to NACT

P = 0.02858

3 CICLOs

4/5 CICLOS
CONCLUSIONS

1. There was a significant increase in the CR after 4/5 cycles (36.7% vs. 60.7%) \((p = 0.0368)\) but this did not influence the PL or SV.

2. Patients with CR and patients with PR and NR had the same OS and DFS possibly because of early rescue with surgery.

3. The patient with early CR (ECR) (3 cycles) had a better DFS than patients with late CR (LCR) (4/5 cycles).
CONCLUSIONS

1. Patients with ECR had better OS and DFS than patients with RP or NR.

2. The LP rate was similar to our earlier study (37% vs. 28.7%)(p=0.3835).

3. In this experience, the ECR rate is the best indicator for the PL and SV.
Third protocol

2005-2009
Larynx preservation CT+RT
Objectives

Enhance the overall survival and larynx preservation rate in previously selected patients as responders to 1 or 2 cycles of PF with SCC of the larynx stages II bulky, III and IV that required a total laryngectomy using CTRT.
Larynx preservation with CTRT demographics

<table>
<thead>
<tr>
<th>M/F</th>
<th>52/8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>58 a</td>
</tr>
<tr>
<td>Suprag.</td>
<td>30 (50%)</td>
</tr>
<tr>
<td>Glottic</td>
<td>30 (50%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>T2</th>
<th>T3</th>
<th>T4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>3</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td>N1</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>N2</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>N3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Stage II bulky: 3  
Stage III: 42  
Stage IV: 15
Larynx preservation with CTRT

Treatment plan

1° QT → Dudosa → 2° QT

RC O RP → RT+CDDP
RC o RP → NR → CX + RT

NR
Larynx preservation with CTRT

**Doses**

**5-FU 1000 mg/m²/d x 5 d**

**INDUCTION:**

- CDDP 100 mg/m²/d d1
- 5-FU 1000 mg/m²/d x 5 d

**Hiperfracciniates Total dose**

- 1,2Gy 1,2Gy
- 1,2Gy 1,2Gy

**Total dose**

- 74.4 Gy

**CDDP 100 mg/m²**

- d 1
- d 21
- d 42

**6.5 weeks**

**6 hs**
Larynx preservation with CTRT
Response to NACT

<table>
<thead>
<tr>
<th>Response after 1 cycle of PF (n=60)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>1 pt</td>
</tr>
<tr>
<td>PR</td>
<td>36 pts</td>
</tr>
<tr>
<td>Doubtful</td>
<td>19 pts</td>
</tr>
<tr>
<td>Non response</td>
<td>4 pts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Response after 2 cycles of PF (n=19)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>4 pts</td>
</tr>
<tr>
<td>PR</td>
<td>12 pts</td>
</tr>
<tr>
<td>Non response</td>
<td>3 pts</td>
</tr>
</tbody>
</table>

Global response rate: 88.3% (53/60 pts)
<table>
<thead>
<tr>
<th>Response to CTRT (n=50)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>43 (71.6)</td>
</tr>
<tr>
<td>PR</td>
<td>5 (8.3)</td>
</tr>
<tr>
<td>NE</td>
<td>2 (3.3)</td>
</tr>
</tbody>
</table>

Larynx preservation with CTRT
Larynx preservation with CTRT
Recurrences (n=43 pts)

<table>
<thead>
<tr>
<th>Recurrences after CR</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>4</td>
</tr>
<tr>
<td>Local + LN</td>
<td>1</td>
</tr>
<tr>
<td>Local + distance</td>
<td>1</td>
</tr>
<tr>
<td>LN alone</td>
<td>3</td>
</tr>
<tr>
<td>LN + distance</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10 (23%)</td>
</tr>
</tbody>
</table>
Larynx preservation with CTRT
Last follow up

Pts alive
33/60 (55%)
(median follow up 31 m)

Specific survival
41/60 (68.3%)

Larynx preservation
31/60 (51.6%)
Larynx preservation with CTRT
Last follow up

Overall survival

DFS

SVG Global
Media: 51 m

TLP
Media: 57 m

LP survival

Specific sv

SV con Laringe
Media: 63 m

SV Específica
Media: 63 m
Larynx preservation with CTRT

Conclusions

CR rate was superior (71.6% vs 67.2% p=0.6).
Recurrence rate was inferior.
(23% vs 47.8% p=0.015).
Overall survival rate was similar.
(55% vs 62.9% P=0.37).
Larynx preservation rate was superior
(51.6% vs 36.7% p=0.048).
Treatment of T2 N0-1 larynx cancer with hyperfractioned (HRT) + Cetuximab
Study objectives

• Primary objective:
  – To increase the local control rate (CR) for T2 larynx cancer with the combination of HRT + cetuximab.

• Secondary objectives:
  – To evaluate the time free of laryngectomy (rescue laryngectomy if PR, SD, PD, or relapse).
  – To evaluate response rate.
  – To evaluate toxicity.
Results: baseline characteristics

• Patients:
  – n=20 patients (19 M/1 F)
  – N1: 2/20 (10%)
  – Tumor site:
    • Glottic: 65%
    • Supraglottic: 35%
  – Median age: 65 years (range 53-72)
Results

• Compliance:
  – 18/20 patients completed treatment with HRT (90%).
  – Duration of treatment: Mean 8 weeks +/- 1.
  – Median HRT dose: 76.65 Gy.
  – Median duration of HRT: 7 weeks.
  – 17/20 patients (85%) received 8 doses of cetuximab.
Results: efficacy

20 patients

16 pts CR
- 12 pts NED with LX
- 4 pts recurred
  - Salvage surgery
    - 4 pts NED

3 pts PR
  - Salvage surgery
    - 2 pts NED
  - 1 pt Dead

1 pt dead not related to Treat.

CR: complete response  PR: partial response  NED: no evidence of disease (alive and disease free)  LX: larynx
Results

- Median follow up: 15 months (range 6.7-29 months+).
- 16/20 patients (80%) achieved a CR.
- 18/20 patients alive and disease free.
- 12/18 (66%) patients with local control and larynx preservation.
- Median time free of laryngectomy: 17 months (range 6.7-29 months+).
- Median time of recurrence after CR: 9 months.
Conclusions

• Eighty five percent of the patients received treatment according to protocol.
• Local control rate was higher than the historical rate at the Instituto Ángel Roffo (66% vs 61%)
• Median time free of laryngectomy was 17 months.
• Eighty percent of the patients are alive.
• This treatment was safe with moderate local toxicity.
Unresectable tumors


Oropharynx

• SUSTAINED HIGH COMPLETE RESPONSE RATE WITH AN INTENSIVE TREATMENT OF CONCURRENT CHEMORADIOTHERAPY FOR OROPHARYNX CANCER. Proceedings ASCO21:239a, 2002. (POSTER SESSION)

• NEOADJUVANT CHEMOTHERAPY (CT) FOLLOWED BY SIMULTANEOUS CHEMORADIOTHERAPY (CT+RT) FOR OROPHARYNX CANCER (OPC). 3th IFHNOS CONGRESS, 2006.
Oropharynx cancer
## Features at diagnosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Included</td>
<td>71</td>
</tr>
<tr>
<td>Non-evaluable patients</td>
<td>10*</td>
</tr>
<tr>
<td>Evaluable patients</td>
<td>61</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>9/52</td>
</tr>
<tr>
<td>Median age</td>
<td>56 (r 41-73)</td>
</tr>
<tr>
<td>TNM</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>18</td>
</tr>
<tr>
<td>N0</td>
<td>13</td>
</tr>
<tr>
<td>T3</td>
<td>24</td>
</tr>
<tr>
<td>N1</td>
<td>14</td>
</tr>
<tr>
<td>T4</td>
<td>19</td>
</tr>
<tr>
<td>N2</td>
<td>24</td>
</tr>
<tr>
<td>N3</td>
<td>10</td>
</tr>
</tbody>
</table>

* 5 pts due to toxicity

* 5 pts in which response could not be evaluated
Treatment plan

- **D1**
  - CDDP 100 mg/m² D1
  - 5FU 1000 mg/m² D1-5 CI

- **D21**
  - CDDP 30 mg/m² (MD: 50 mg/m²)
  - 5FU 300 mg/m² bolus

- **D28 - D60**
  - Hyperfractionated 2 fx of 150 cgy.
  - except days 35, 42, 49
  - y 56 when a unique dose of 200 cgy was administrated.

- **70 Gy**
## Results I

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with complete treatment</td>
<td>47/61 (77%)</td>
</tr>
<tr>
<td>Treatment duration media</td>
<td>77 d (r 56-119)</td>
</tr>
<tr>
<td>Radiotherapy duration media</td>
<td>42 d (r 25-77)</td>
</tr>
<tr>
<td>Average dose intensity</td>
<td>85.7%</td>
</tr>
</tbody>
</table>
## Results II

### Response to CT+RT

<table>
<thead>
<tr>
<th>Response Type</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>46/61 (75.4)</td>
</tr>
<tr>
<td>Partial response</td>
<td>10/61 (16.4)</td>
</tr>
<tr>
<td>No response</td>
<td>5/61 (8.2)</td>
</tr>
</tbody>
</table>

Salvage surgery  
Final complete response  
Response duration  

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Salvage surgery</td>
<td>5</td>
</tr>
<tr>
<td>Final complete response</td>
<td>51/61 (83.6)</td>
</tr>
<tr>
<td>Response duration</td>
<td>media:21 m (1-90+ m)</td>
</tr>
</tbody>
</table>
## Results III

<table>
<thead>
<tr>
<th>Status (01/2006)</th>
<th>Pts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive NED</td>
<td>29/61 (47.5)</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>2/61 (3.2)</td>
</tr>
<tr>
<td>Cancer deaths</td>
<td>25/61 (41)</td>
</tr>
<tr>
<td>Deaths due to other causes</td>
<td>5/61 (8.1)</td>
</tr>
<tr>
<td>Organ preservation</td>
<td>27/29 (93)</td>
</tr>
</tbody>
</table>
Results IV

Overall survival

Event free survival
Conclusions

• This treatment is very effective and feasible.
• The majority of the patients can complete it.
• Severe toxicities that cause the hospitalizations of patients occur when the treatment has already been completed.
• A high response rate and a low rate of recurrence in patients with oropharyngeal cancer were obtained.
• It allowed a high rate of preservation of organs.
Toxicity

- ALTERNATING CHEMOTHERAPY + RADIOTHERAPY WITH AMIFOSTINE PROTECTION FOR HEAD AND NECK CANCER. EARLY STOP OF A RANDOMIZED TRIAL. Proceedings ASCO16:384a, 1997. (PRESENTACIÓN ORAL)


- PROSPECTIVE FUNCTIONAL STUDY IN PATIENTS WITH HEAD AND NECK CANCER AFTER TREATMENT WITH CHEMOTHERAPY AND RADIOTHERAPY. 7th International Conference on Head and Neck Cancer., 2008.

- IMPACT OF DISPHAGIA ON QUALITY OF LIFE OF PATIENTS WITH SQUAMOS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN) AFTER CHEMORADIOTHERAPY. 8th International Conference on Head and Neck Cancer., 2012
Neck management

- FOLLOW UP FOR HEAD AND NECK CANCER PATIENTS WITH N 2-3 ACHIEVING A COMPLETE RESPONSE AFTER CHEMOTHERAPY + RADIOTHERAPY. 7th International Conference on Head and Neck Cancer., 2008.

Thyroid cancer

- USEFULNESS AND PITFALLS OF PET/CT IN PAPILLARY THYROID CANCER (PTC). 8th International Conference on Head and Neck Cancer., 2012
“Utility of swallowing fiber endoscopy (FEES) to detect dysphagia in patients with squamous cell carcinoma of the head and neck (SCCHN) treated with radiation (RT) alone or simultaneous chemotherapy and radiation (CTRT)"

Brotzman Gabriela, Giglio Raúl, Zund Santiago, Pereira David.

Institute of Oncology Ángel H. Roffo. Departaments: Speech Therapy, Oncology, Head and Neck Surgery and Radiotherapy.
Introduction:

Dysphagia is a symptom that can be caused by either structural or functional pathological processes. Safe oral food intake may be compromised either because of the disease or the treatments in patients with SCCHN. That is why an early intervention of the speech therapist to treat the dysphagia can be worthwhile.
Objetive

• To analyze the utility of FEES in a prospective trial for early detection of dysphagia and so install a quick treatment in patients with SCCHN treated with either RT or CTRT.
### Materials and Methods I

34 patients with SCCHN with dysphagia  
Median age: 58 years

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N ( %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (76)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (24)</td>
</tr>
<tr>
<td>Tumor site</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>15 (44.2)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>13 (38.2)</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Treatment for SCCHN</td>
<td></td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>31 (91.2)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3 (8.8)</td>
</tr>
</tbody>
</table>
## Materials and Methods II

### Swallowing fiber endoscopy (FEES)

<table>
<thead>
<tr>
<th>It evaluates</th>
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<tbody>
<tr>
<td>Anatomy and mobility of the pharynx and larynx</td>
</tr>
<tr>
<td>Retention of secretions</td>
</tr>
<tr>
<td>Penetration and/or aspiration</td>
</tr>
<tr>
<td>Deficits in bolus mis-direction</td>
</tr>
<tr>
<td>Compensatory Maneuvers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>It gives</th>
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</thead>
<tbody>
<tr>
<td>Airway protection as it relates to swallowing function</td>
</tr>
<tr>
<td>Biofeedback/teaching</td>
</tr>
<tr>
<td>Optimum delivery of bolus consistencies and sizes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Textures used</th>
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</thead>
<tbody>
<tr>
<td>Fluid liquid consistency</td>
</tr>
<tr>
<td>Nectar liquid consistency</td>
</tr>
<tr>
<td>Semisolid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
</tbody>
</table>
Scale of basal secretions of Langmore

GRADE 0. Normal (moist).

GRADE 1. Pooling outside of laryngeal vestibule anytime during observation.

GRADE 2. Pooling in laryngeal vestibule transiently, spills in over the observation period or patient clears them at some point.

GRADE 3. Pooling in laryngeal vestibule consistently, there continuously, and patient does not clear them.
**Penetration – Aspiration Scale of Rosenbek I**

**Level 1:** Material does not enter airway.

**Level 2:** Material enters the airway, remains above the vocal folds, and is ejected from the airway.

**Level 3:** Material enters the airway, remains above the vocal folds, and is not ejected from the airway.

**Level 4:** Material enters the airway, contacts the vocal folds, and is ejected from the airway.
Level 5: Material enters the airway, contacts the vocal folds, and is not ejected from the airway.

Level 6: Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway.

Level 7: Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort.

Level 8: Material enters the airway, passes below the vocal folds, and no effort is made to eject.
Fluoroscopic swallowing Test
Results: Swallowing safety

FESS was very well tolerated by all the patients and there were no complications due to the procedure which was fulfilled in an average time of 7 minutes.
Results: Treatments for dysphagia

- Postural techniques, therapeutic maneuvers to protect the airway and thickeners for the liquids: 21/34 (62.5%)
- Gastrostomy: 11/34 (32.3%)
- Not required: 2/34 (5.8%)
Results: Scale of basal secretions of Langmore

- Grade 0: 15/34 (44.1%)
- Grade 1: 13/34 (38.2%)
- Grade 2: 6/34 (17.7%)
Results: Penetration – Aspiration Scale of Rosenbek

- 21/34 (61.7%)
- 5/34 (14.7%)
- 4/34 (11.7%)
- 4/34 (11.7%)

Level 1
Level 4
Level 5
Level 6
Conclusions

The FEES is a reliable test that allows to detect dysphagia and to lead to a therapeutic solution. As it is performed by the head and neck surgeon and the speech therapist it can be done as soon as the treatment finishes for a more adequate management.
Current trials

• Larynx preservation stage III and bulky stage II (LX/HP):
  • 1 cycle PTF followed by CTRT in responders.

• Oropharynx cancer:
  • T1-3 N0N2b: CTRT CDDP+ RT
  • T4 or N2c-N3: 3 cycles PTF followed by CBDCA+ RT.

• Stage III and IVa Oral Cavity:
  • Surgery followed by RT or CTRT.
Currents trilas

- NPC stages III and IVa:
  - 3 cycles of PTF followed by CRTRT (CDDP).

- Unresectable tumors:
  - 3 cycles PTF followed by CBDCA+ RT.

- Rehabilitation:
  - Early intervention with exercises to prevent Dysphagia in patients treated with CTRT.
Epidemiology and biomarkers

• Study for head and neck cancer (HNC) in South America-INTERCHANGE (IARC-IOAR, CURIE y Tornu y 13 centers in Brasil and Uruguay)
Unidad funcional de tumores de cabeza y cuello

Thank You
Any questions?