

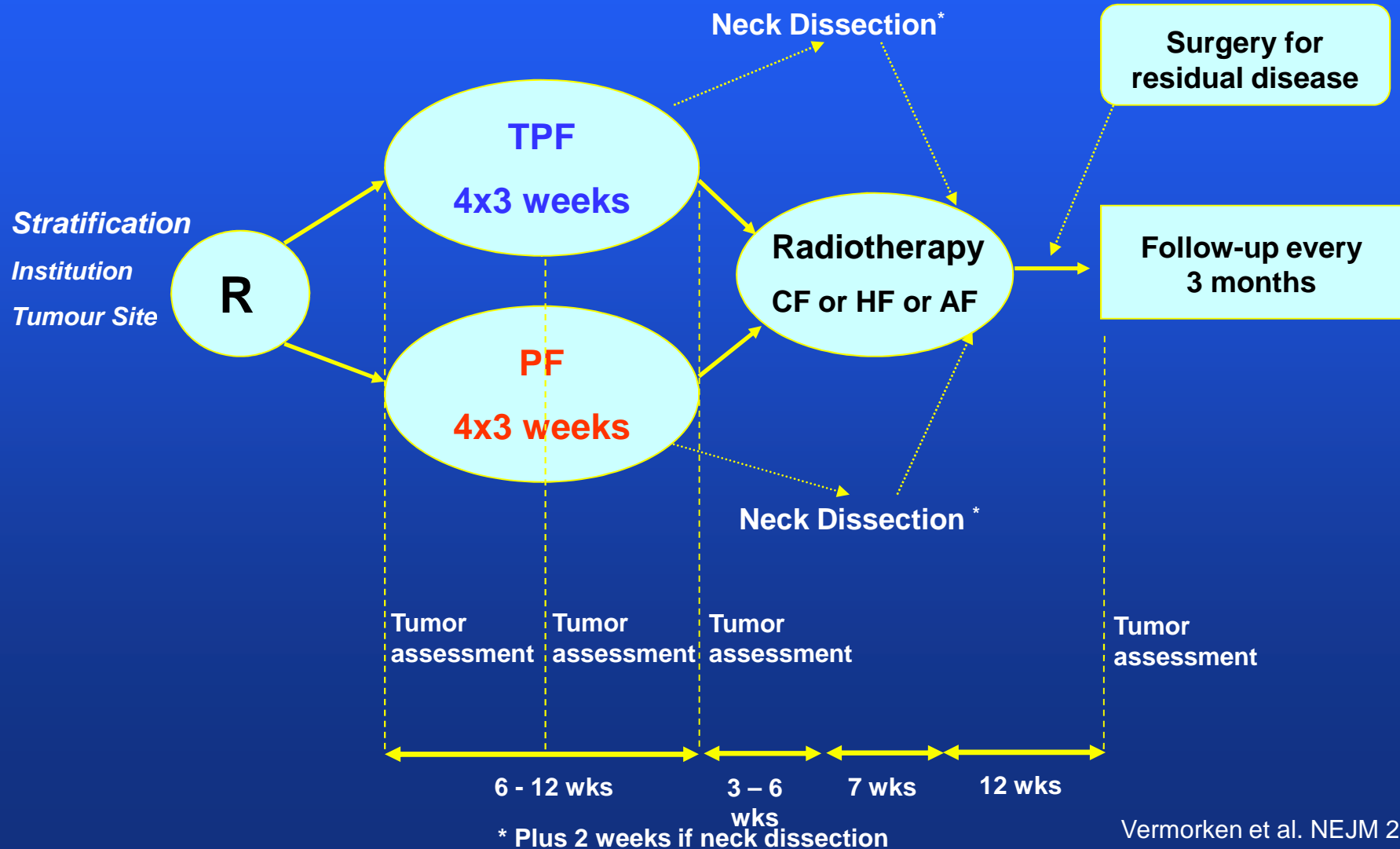
**Short-term health-related quality of life and  
symptom control with docetaxel, cisplatin, 5-  
fluorouracil (TPF) and cisplatin 5-fluorouracil  
(PF) for induction in unresectable  
locoregionally  
advanced head and neck cancer patients  
(EORTC 24971/TAX 323)**

**EGAM, 1<sup>st</sup> March 2011**

- **Concurrent chemoradiation now standard therapy for LAHNC**
- **Induction chemotherapy (cisplatin based) has been associated with OS gain**
- **Most active Cisplatin with 5-FU (standard arm) (PF)**
- **In phase II studies TPF maybe more active than PF**
- **Phase III study comparing TPF with PF (EORTC 24971/TAX323)**

- **Open-label, randomized, phase III**
- **37 institutions, 15 countries**
- **18-70 years**
- **St III or IV and no distant metastases LAHNC**
- **Previously untreated and locoregional advanced disease**
- **Considered unresectable**
- **No nasopharynx or (para)nasal cavities**

# Study design



# Patient characteristics

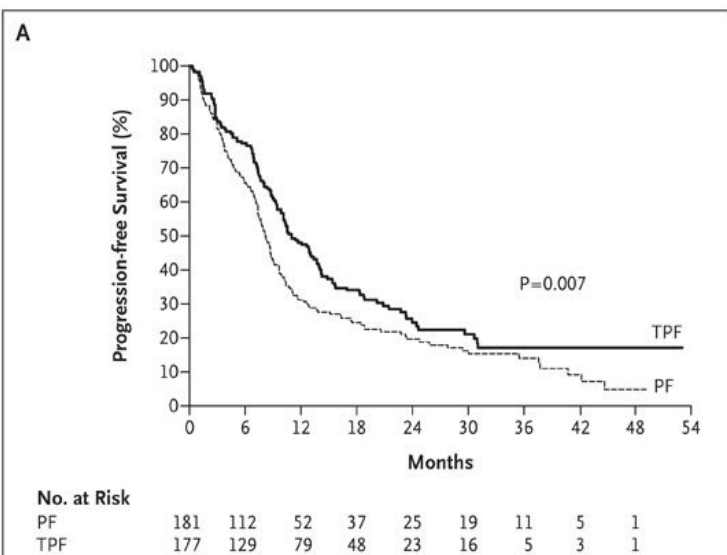
**Table 1. Baseline Characteristics of the Patients (Intention-to-Treat Population).\***

Characteristic	PF (N = 181)	TPF (N = 177)	Total (N = 358)	P Value
Male sex — no. (%)	162 (89.5)	159 (89.8)	321 (89.7)	0.87
Age — yr				0.77
Median	53	53	53	
Range	30–71	31–70	30–71	
Age — no. (%)				
<35 yr	4 (2.2)	2 (1.1)	6 (1.7)	
35–49 yr	58 (32.0)	53 (29.9)	111 (31.0)	
50–64 yr	101 (55.8)	104 (58.8)	205 (57.3)	
65–75 yr	18 (9.9)	18 (10.2)	36 (10.1)	
WHO performance status — no. (%) †				0.96
0	91 (50.3)	90 (50.8)	181 (50.6)	
1	90 (49.7)	86 (48.6)	176 (49.2)	
2	0	1 (0.6)	1 (0.3)	
Cancer site — no. (%)				0.99
Hypopharynx	52 (28.7)	53 (29.9)	105 (29.3)	
Larynx	13 (7.2)	12 (6.8)	25 (7.0)	
Oral cavity	32 (17.7)	31 (17.5)	63 (17.6)	
Oropharynx	84 (46.4)	81 (45.8)	165 (46.1)	
Tumor status — no. (%)				0.50
T1	1 (0.6)	3 (1.7)	4 (1.1)	
T2	15 (8.3)	10 (5.6)	25 (7.0)	
T3	36 (19.9)	41 (23.2)	77 (21.5)	
T4	129 (71.3)	123 (69.5)	252 (70.4)	
Node status — no. (%)				0.09
N0	26 (14.4)	16 (9.0)	42 (11.7)	
N1	29 (16.0)	27 (15.3)	56 (15.6)	
N2	103 (56.9)	102 (57.6)	205 (57.3)	
N3	20 (11.0)	32 (18.1)	52 (14.5)	
Unknown	3 (1.7)	0	3 (0.8)	
Disease sites in head and neck — no. (%)				0.77
1	25 (13.8)	19 (10.7)	44 (12.3)	
2	140 (77.3)	150 (84.7)	290 (81.0)	
≥3	13 (7.2)	7 (4.0)	20 (5.6)	
No tumor assessment at baseline — no. (%)	3 (1.7)	1 (0.6)	4 (1.1)	

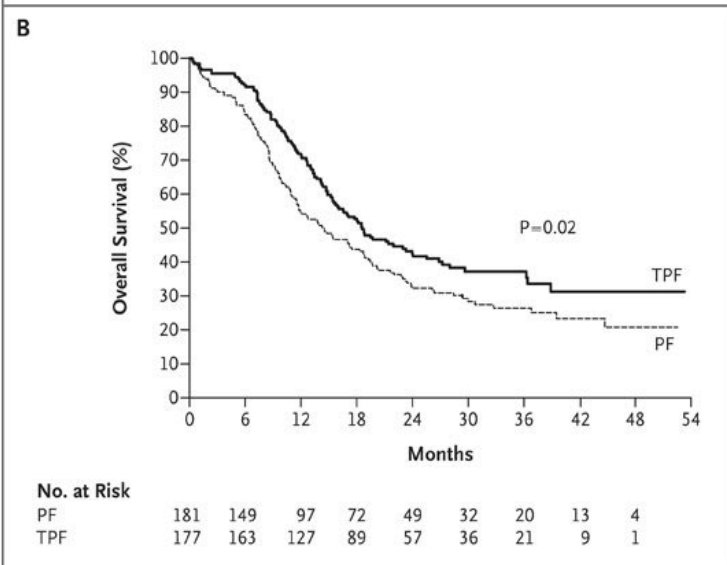
\* PF denotes cisplatin–fluorouracil, TPF docetaxel–cisplatin–fluorouracil, and WHO World Health Organization. Percentages may not total 100 because of rounding.

† A performance status of 0 denotes asymptomatic, 1 symptomatic and fully ambulatory, and 2 symptomatic and in bed less than 50% of the day.

# PFS and OS



	<b>PF</b>	<b>TPF</b>
<b>PFS median</b>	<b>8.2</b>	<b>11.0</b>
<b>HR</b>	<b>0.72 (0.57-0.91)</b>	



	<b>PF</b>	<b>TPF</b>
<b>OS median</b>	<b>14.5</b>	<b>18.8</b>
<b>HR</b>	<b>0.73 (0.56-0.94)</b>	

# Response to treatment

**Table 2. Response to Treatment and Survival.\***

Variable	PF (N=181)	TPF (N=177)	Hazard Ratio (95% CI)	P Value
<b>Progression-free survival</b>				
Median duration — mo	8.2	11.0	0.72 (0.57–0.91)	0.007†
Rate — %				
At 1 yr	31	48		
At 2 yr	20	25		
At 3 yr	14	17		
<b>Overall survival</b>				
Median duration — mo	14.5	18.8	0.73 (0.56–0.94)	0.02†
Rate — %				
At 1 yr	55	72		
At 2 yr	32	43		
At 3 yr	26	37		
<b>Response to chemotherapy</b>				
Overall — %	54	68		0.006‡
Complete — no. (%)	12 (6.6)	15 (8.5)		
Partial — no. (%)	85 (47.0)	105 (59.3)		
<b>Response to chemotherapy and radiotherapy</b>				
Overall — %	59	72		0.006‡
Complete — no. (%)	36 (19.9)	59 (33.3)		0.004‡
Partial — no. (%)	70 (38.7)	69 (39.0)		
Duration of response — mo	11.6	15.4	0.74 (0.53–1.03)	0.08§
Time to treatment failure — mo	7.8	10.5	0.70 (0.55–0.89)	0.003†

\* PF denotes cisplatin–fluorouracil, and TPF docetaxel–cisplatin–fluorouracil.

† The P value was calculated with the use of an adjusted Cox proportional-hazards model.

‡ The P value was calculated with the use of an unadjusted chi-square test.

§ The P value was calculated with the use of an unadjusted log-rank test.

**Table 3. Grade 3 or 4 Hematologic and Nonhematologic Adverse Events during Chemotherapy (Safety Population).\***

Event	PF (N=179) <i>no. of patients (%)</i>	TPF (N=173) <i>no. of patients (%)</i>
<b>Hematologic†</b>		
Neutropenia	94 (52.5)	133 (76.9)
Anemia	23 (12.8)	16 (9.2)
Thrombocytopenia	32 (17.9)	9 (5.2)
Leukopenia	41 (22.9)	72 (41.6)
<b>Nonhematologic‡</b>		
Alopecia	0	20 (11.6)
Nausea	12 (6.7)	1 (0.6)
Stomatitis	20 (11.2)	8 (4.6)
Lethargy	3 (1.7)	5 (2.9)
Diarrhea	6 (3.4)	5 (2.9)
Vomiting	8 (4.5)	1 (0.6)
Neurotoxicity	1 (0.6)	1 (0.6)
Anorexia	6 (3.4)	1 (0.6)
Infection	11 (6.1)	12 (6.9)
Febrile neutropenia	5 (2.8)	9 (5.2)
Weight loss	1 (0.6)	0
Local toxic effect	1 (0.6)	1 (0.6)
Constipation	1 (0.6)	0
Hearing loss	5 (2.8)	0
Esophagitis, dysphagia, or odynophagia	0	1 (0.6)
Gastrointestinal pain	1 (0.6)	0

\* PF denotes cisplatin–fluorouracil, and TPF docetaxel–cisplatin–fluorouracil.

† Hematologic toxic effects are listed regardless of whether there was a relationship with a study drug.

‡ Nonhematologic toxic effects were related to treatment.

- QoL collected through
  - EORTC QLQ-C30 (version 3.0)
  - EORTC QLQ H&N35
- QoL was assessed
  - at baseline (prior randomization)
  - at end of cycle 2, and 4
  - at 6 and 9 months after completion of radiotherapy
- PSS-HN, assessed by the clinician
  - Pain thermometer (visual analogue scale)

**Global QoL**

**Pain**

**Swallowing**

**Speech**

**Coughing**

**Hypotheses:**

- The TPF arm will be superior to the PF arm in lowering symptom levels.
- Due to the expected higher toxicity of the experimental arm, no significant difference in global QoL is anticipated

## QoL windows

Assessment	Lower bound	Upper bound
Baseline	14 days before randomization	14 days after randomization but ≤ start of chemotherapy
At end of cycle 2	3 weeks before but > start of cycle 2	3 weeks after but ≤ start of cycle 3 or start of radiotherapy
At end of cycle 4	3 weeks before but > start of cycle 3	3 weeks after but ≤ start of radiotherapy
At 6 months after radiotherapy**	3 months* before	1.5 month after
At 9 months after radiotherapy**	1.5 month before	1.5 months after

\*1 month=365.25/12 days=30.4375 days

\*\*6 months and 9 months after the end of radiotherapy

# QoL compliance

	<i>Forms expected</i>	<i>Forms received</i>	<i>Percentage</i>	<i>Difference</i>
<b>Baseline</b>	<b>358</b>	<b>346</b>	<b>97</b>	<b>0.225</b>
<i>C-5FU-DOC</i>	<i>177</i>	<i>169</i>	<i>95.5</i>	
<i>C-5FU</i>	<i>181</i>	<i>177</i>	<i>97.8</i>	
<b>End of cycle 2</b>	<b>328</b>	<b>282</b>	<b>86</b>	<b>0.340</b>
<i>C-5FU-DOC</i>	<i>164</i>	<i>144</i>	<i>87.8</i>	
<i>C-5FU</i>	<i>164</i>	<i>138</i>	<i>84.2</i>	
<b>End of cycle 4</b>	<b>255</b>	<b>193</b>	<b>76</b>	<b>0.545</b>
<i>C-5FU-DOC</i>	<i>136</i>	<i>105</i>	<i>77.2</i>	
<i>C-5FU</i>	<i>119</i>	<i>88</i>	<i>74.0</i>	
<b>At 6 months after RT</b>	<b>198</b>	<b>108</b>	<b>55</b>	<b>0.794</b>
<i>C-5FU-DOC</i>	<i>112</i>	<i>62</i>	<i>55.4</i>	
<i>C-5FU</i>	<i>86</i>	<i>46</i>	<i>53.5</i>	
<b>At 9 months after RT</b>	<b>170</b>	<b>76</b>	<b>45</b>	<b>0.443</b>
<i>C-5FU-DOC</i>	<i>95</i>	<i>40</i>	<i>42.1</i>	
<i>C-5FU</i>	<i>75</i>	<i>36</i>	<i>48.0</i>	

**QoL analysis restricted to data up to 6 months after RT**

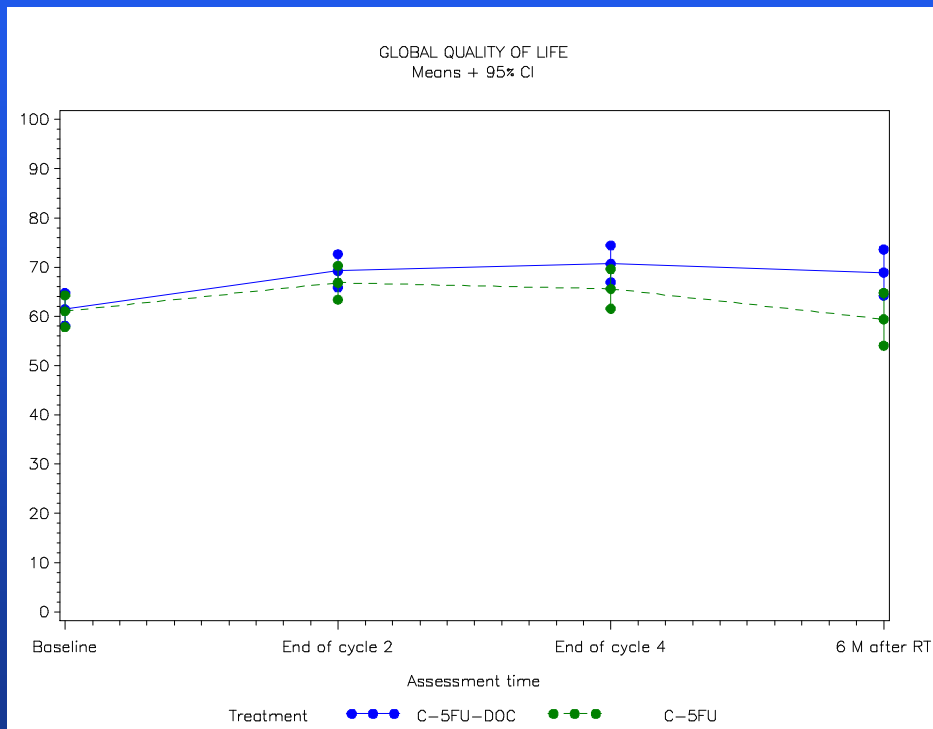
**Note: 1/3 data less for the H&N35 module due to the non availability of translated questionnaires (Slovak Republic, Serbia and Hungary)**

## Interpretation:

- Level of statistical significance of 0.01 for the primary QoL scales
- Minimum clinically meaningful change in QoL of 10 points
- Other QoL scales examined on an exploratory basis

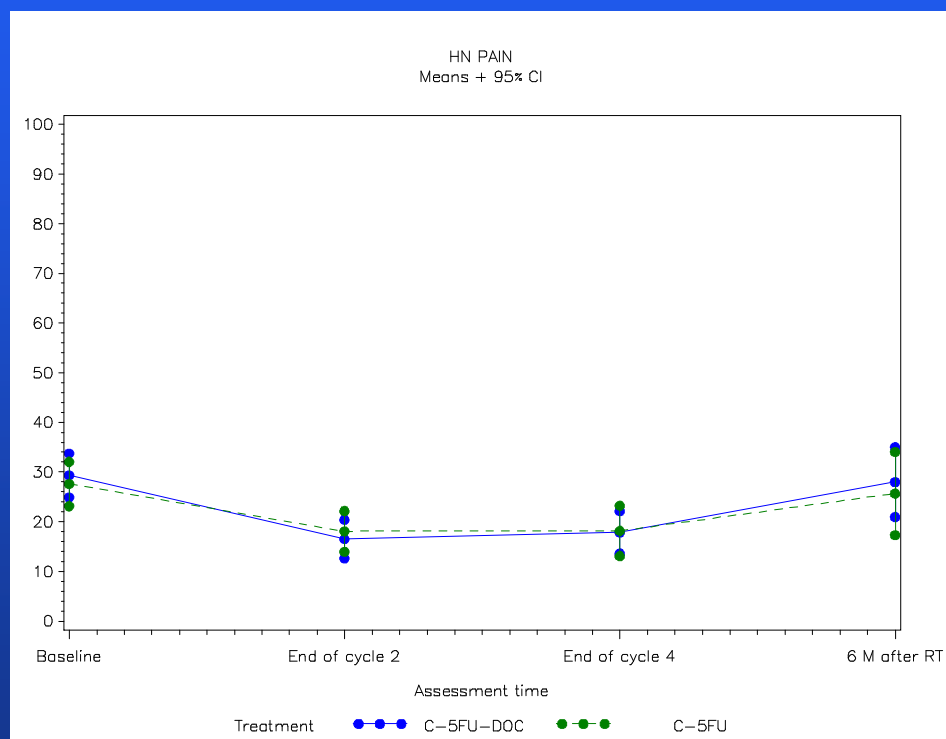
Method of analysis: a mixed-model with an undefined covariance structure was fitted to longitudinal QoL data to test for differences between the two treatment arms

## QoL-C30 – Global quality of life



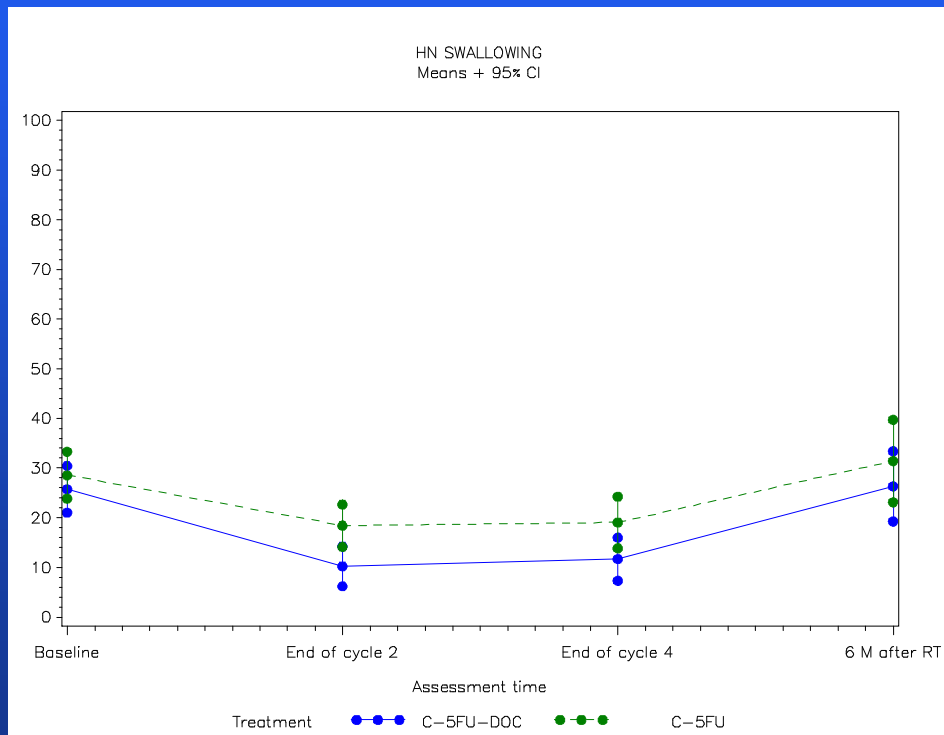
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.1873</b>
<b>Baseline</b>	<b>61.5 (SD=1.69)</b>	<b>61.1 (SD=1.64)</b>	<b>0.8646</b>
<b>End of cycle 2</b>	<b>69.3 (SD=1.73)</b>	<b>66.8 (SD=1.75)</b>	<b>0.3290</b>
<b>End of cycle 4</b>	<b>70.7 (SD=1.91)</b>	<b>65.6 (SD=2.05)</b>	<b>0.0695</b>
<b>6 M after RT</b>	<b>68.9 (SD=2.39)</b>	<b>59.4 (SD=2.73)</b>	<b>0.0092</b>

## H&N35 – Pain



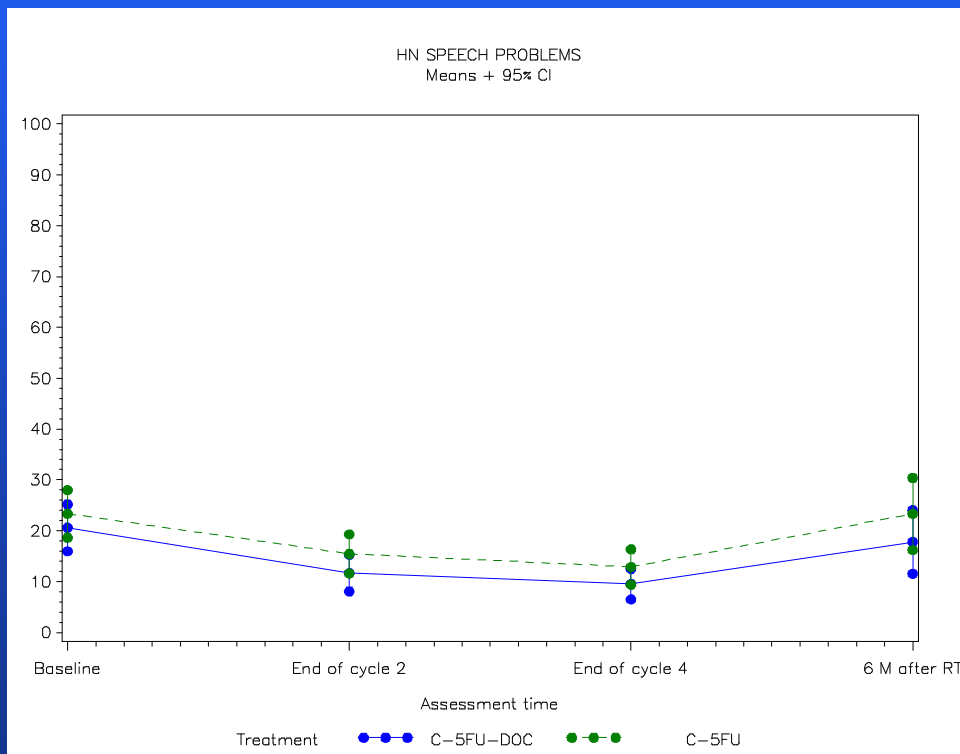
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.8578</b>
Baseline	29.3 (SD=2.26)	27.6 (SD=2.28)	0.5907
End of cycle 2	16.5 (SD=1.97)	18.1 (SD=2.09)	0.5931
End of cycle 4	17.9 (SD=2.17)	18.2 (SD=2.6)	0.9291
6 M after RT	28 (SD=3.59)	25.7 (SD=4.27)	0.6773

## H&N35 – Swallowing



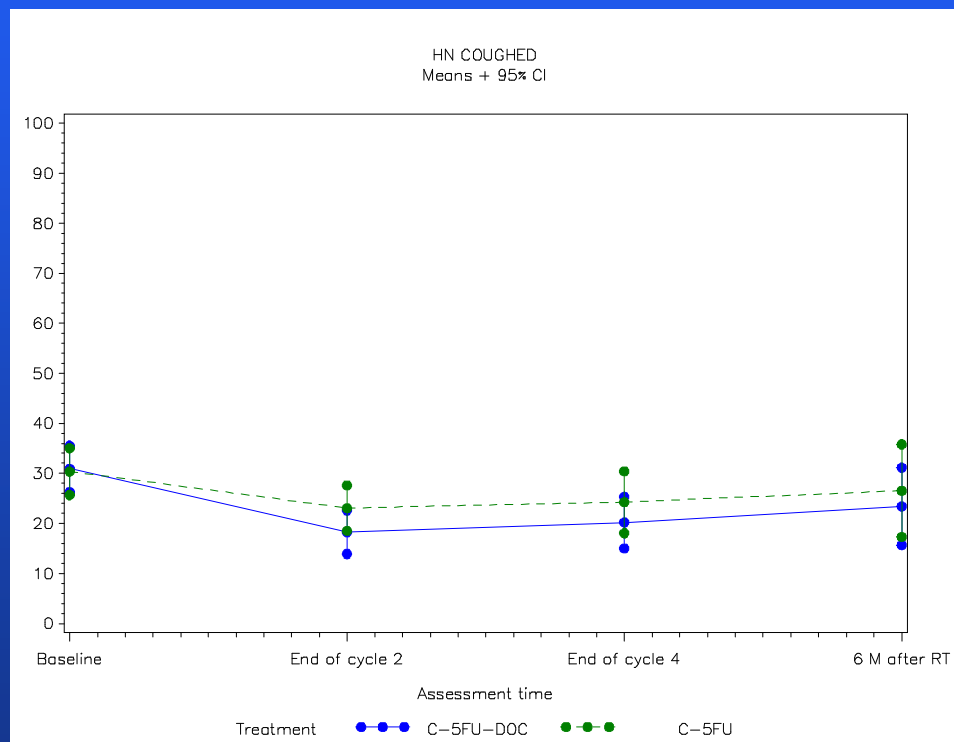
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.0163</b>
<b>Baseline</b>	25.7 (SD=2.41)	28.6 (SD=2.42)	<b>0.4079</b>
<b>End of cycle 2</b>	10.2 (SD=2.05)	18.4 (SD=2.18)	<b>0.0066</b>
<b>End of cycle 4</b>	11.7 (SD=2.22)	19.1 (SD=2.64)	<b>0.0335</b>
<b>6 M after RT</b>	26.3 (SD=3.61)	31.4 (SD=4.23)	<b>0.3611</b>

## H&N35 – Speech



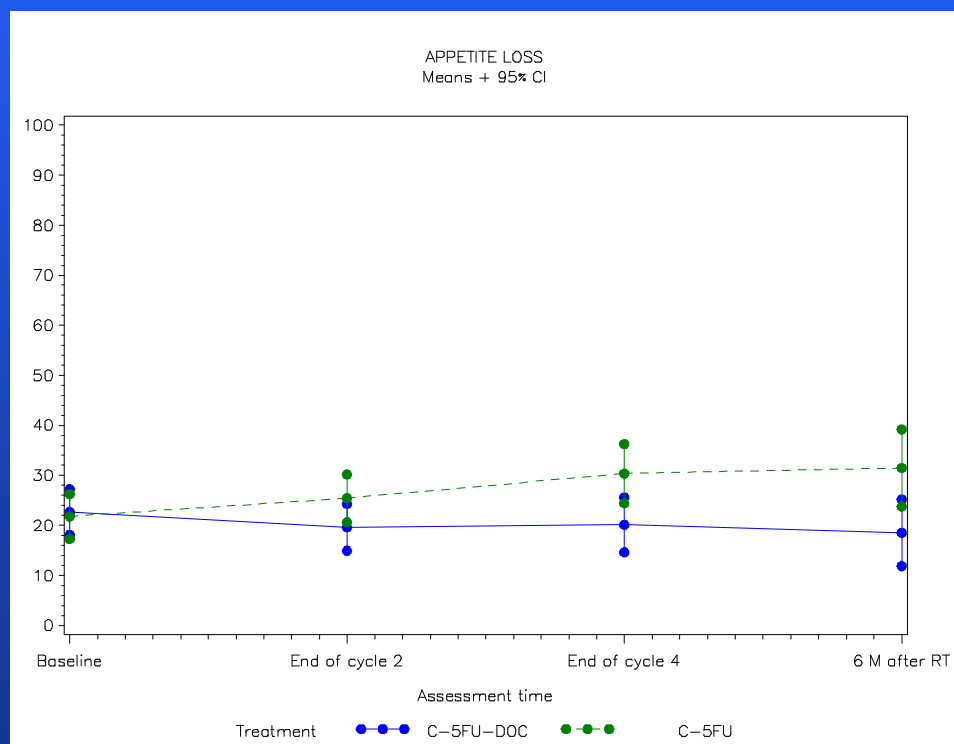
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.2940</b>
<b>Baseline</b>	20.6 (SD=2.37)	23.3 (SD=2.38)	<b>0.4149</b>
<b>End of cycle 2</b>	11.7 (SD=1.84)	15.5 (SD=1.96)	<b>0.1623</b>
<b>End of cycle 4</b>	9.5 (SD=1.54)	12.9 (SD=1.76)	<b>0.1520</b>
<b>6 M after RT</b>	17.8 (SD=3.19)	23.3 (SD=3.62)	<b>0.2541</b>

## H&N35 – Coughing



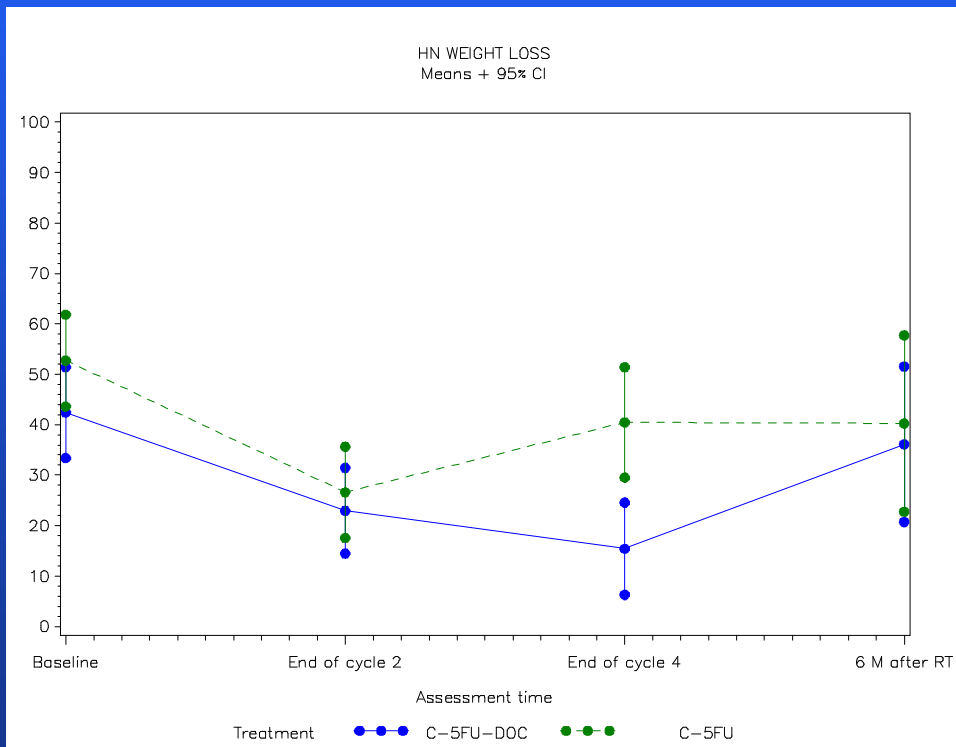
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.2934</b>
Baseline	30.9 (SD=2.36)	30.4 (SD=2.39)	0.8666
End of cycle 2	18.3 (SD=2.22)	23.1 (SD=2.32)	0.1357
End of cycle 4	20.2 (SD=2.63)	24.2 (SD=3.16)	0.3261
6 M after RT	23.4 (SD=3.96)	26.6 (SD=4.72)	0.6099

## QoL-C30 - Appetite loss



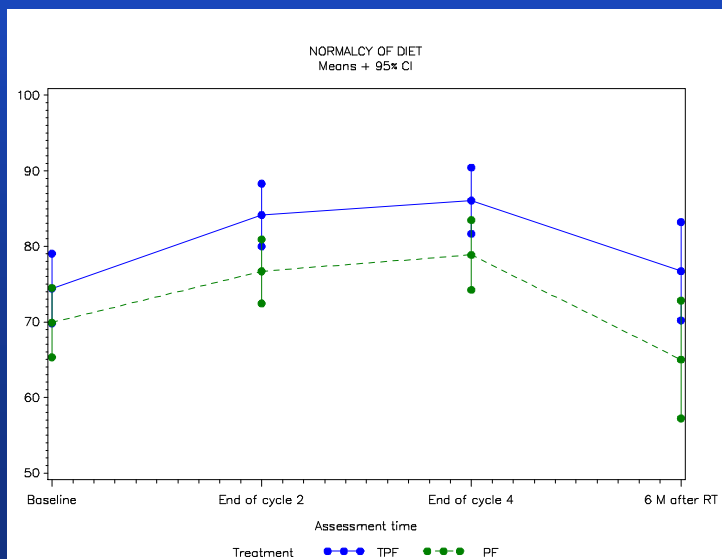
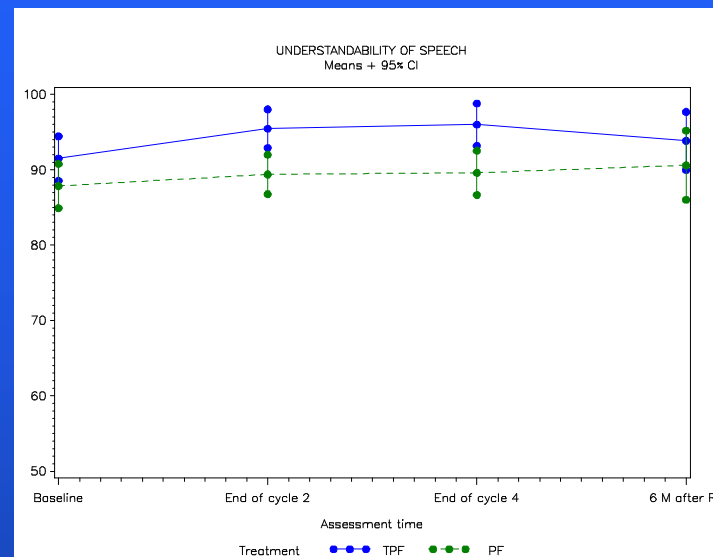
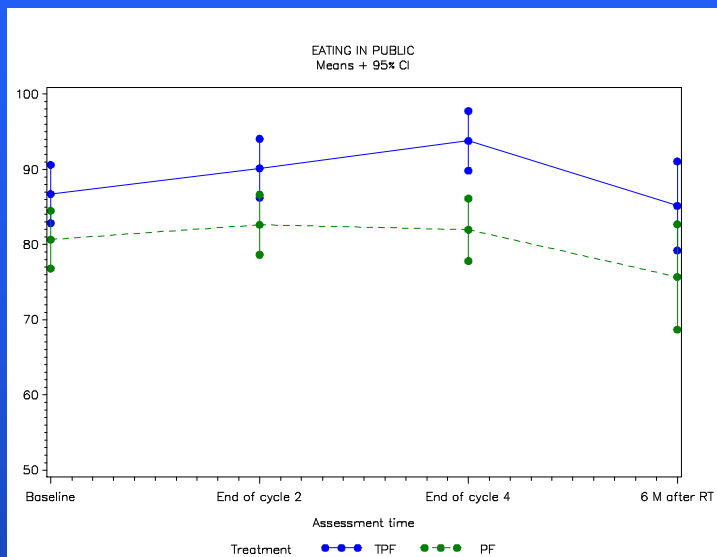
Assessment Time	TPF	PF	Treatment difference P-value
<b>Overall</b>			<b>0.0383</b>
<b>Baseline</b>	22.7 (SD=2.33)	21.8 (SD=2.29)	<b>0.7867</b>
<b>End of cycle 2</b>	19.6 (SD=2.39)	25.4 (SD=2.44)	<b>0.0907</b>
<b>End of cycle 4</b>	20.1 (SD=2.79)	30.4 (SD=3.02)	<b>0.0134</b>
<b>6 M after RT</b>	18.5 (SD=3.39)	31.5 (SD=3.93)	<b>0.0131</b>

## H&N35 – Weight loss

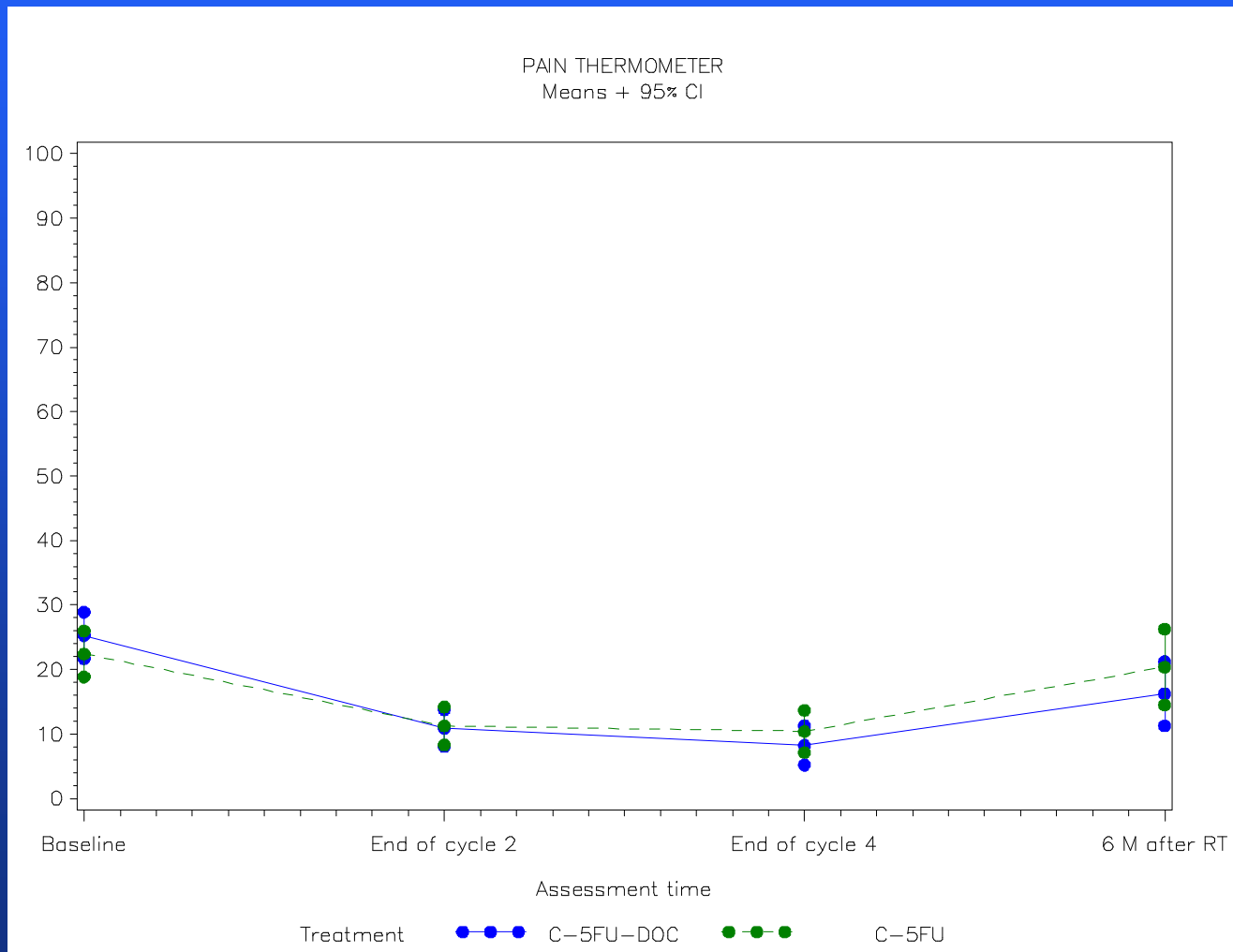


Assessment Time	C-5FU-DOC	C-5FU	Treatment difference P-value
<b>Overall</b>			<b>0.0030</b>
<b>Baseline</b>	42.4 (SD=4.6)	52.7 (SD=4.64)	<b>0.1164</b>
<b>End of cycle 2</b>	22.9 (SD=4.33)	26.6 (SD=4.62)	<b>0.5641</b>
<b>End of cycle 4</b>	15.4 (SD=4.67)	40.5 (SD=5.58)	<b>0.0007</b>
<b>6 M after RT</b>	36.1 (SD=7.86)	40.3 (SD=8.93)	<b>0.7293</b>

# Performance status scale for H&N



# Pain thermometer



## Conclusion

- **Global HRQOL increased during induction chemotherapy in both treatment arms in LAHNC while symptoms levels decreased**
- **Besides improvement of PFS and OS and reduction of toxicity, there was a trend towards improved global HRQOL during the treatment period. Six months after the end of radiotherapy, global HRQOL was higher in the TPF arm than in the PF arm (mean difference of 9.5 points,  $p=0.0092$ ).**

## Conclusion

- **However, the low compliance does not allow to draw definitive conclusions.**
- **Swallowing problems decreased more in the TPF arm than in the PF arm at the end of cycle 2 but to a limited extent**

- **EORTC headquarters:**

**ME Mauer, C Coens, A Bottomley**

- **Investigators:**

**R Mesia, M Degardin, S Jelic, R Mesia, M  
Degardin, S Jelic, J Betka, J Bernier, E  
Remenar, JS Stewart, JH Preiss, D van den  
Weyngaert, JB Vermorken**

- **on behalf of the EORTC Head and Neck Group**