Ecole d'été SSORL
Sommerschule SGORL

groupe de travail de chirurgie cervico-faciale
Arbeitsgruppe Hals- und Gesichtschirurgie

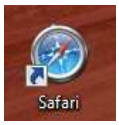
31.08.2012
01.09.2012

Bettlach, 31.08.2012

Chemo/immunotherapy for the treatment of SCCHN in 25 minutes !

"The Legend"

No conflict of interest



1. *Exclusive Radiotherapy concomitant with*
   - *1.1 CT (chemotherapy)*
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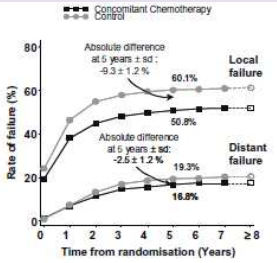
2. Induction
3. Larynx preservation
4. Customizing treatment
5. Metastatic or recurrent
6. Take home message

1.1 Exclusive RT-CT



Absolute benefit = 6.5 %

*Overall, the meta-analysis included 93 trials with chemotherapy in 17346 patients.

Pignon Radiother Oncol 2009

1.1 Exclusive RT-CT

Type of RT	HR	
Postoperative RT	0.79	
Conventional RT	0.83	P = 0.19
Altered fractionated RT	0.73	

Type of CHT	HR	
Poly-CT		
5-FU & Platin	0.75	
5-FU or Platin	0.83	P = 0.41
Neither 5-FU nor Platin	0.73	
Mono-CT		
Mono Platin	0.74	P = 0.006
Mono other	0.89	

Pignon Radiother Oncol 2009

1.1 Exclusive RT-CT : analysis by tumor site

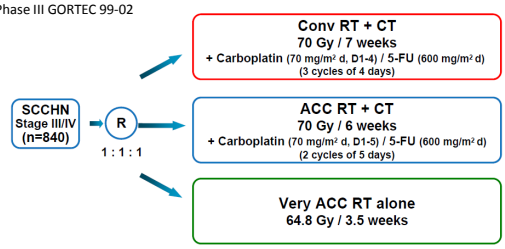
Timing of CT 5y abs. benefit	Adjuvant HR	Neoadjuvant HR	Cct HR	P
Oral cavity	0.94 + 0.4 %	0.93 + 2.2 %	0.80 + 8.9 %	0.15
Oropharynx	1.15 - 0.4 %	1.00 + 1.4 %	0.78 + 8.1 %	< 0.0001
Larynx	1.05 + 0.1 %	1.00 + 3.8 %	0.80 + 5.4 %	0.05
Hypopharynx	1.06 - 2.3 %	0.88 + 5.3 %	0.85 + 4 %	0.31

Total benefit HR 0.87 (benefit consistent in all tumor locations)
Higher benefit for CCT only for oropharyngeal and laryngeal tumors

Blanchard Radiother Oncol 2011

1.1 Exclusive RT-CT : more intense ?

Phase III GORTEC 99-02

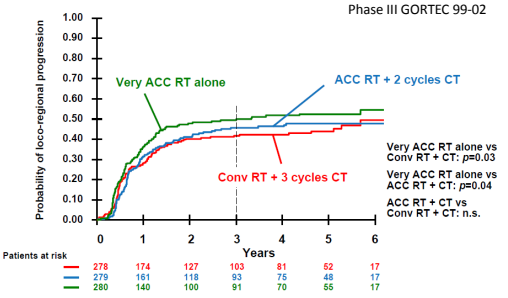


Conv, conventional; ACC, accelerated; RT, radiotherapy; CT, chemotherapy;

Bourhis Lancet Oncol 2012
(courtesy of J. Bourhis)

1.1 Exclusive RT-CT : more intense ?

Phase III GORTEC 99-02



Bourhis Lancet Oncol 2012
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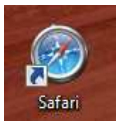

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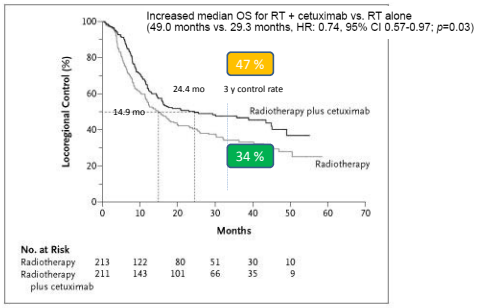
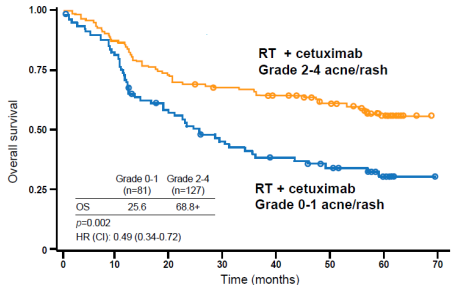
1.2 Immunotherapy (Cetuximab)

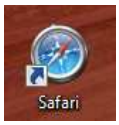


Bonner NEJM 2006

1.2 Immunotherapy (Cetuximab)



Bonner Lancet Oncol 2010



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1.3 RTCT vs RTCetuxi

Indirect comparison of the efficacy of cetuximab and cisplatin[=] inoma of the head and neck

CONCURRENT CISPL[CDDP/RT > CTX/RT] CETUXIMAB AND RADIATION FOR[CK CANCER

LAWRENCE KOUTCHER, M.D.[FURY, M.D., PH.D.,†

Conclusions: In this study of LAHNC patients, CDDP/RT achieved better locoregional control, FFS, and OS than C225/RT. Although the results were upheld on multivariate analysis, they must be interpreted cautiously because of the retrospective nature of the study and significant differences in patient selection. There was no statistically

Levy Curr Med res Opin 2011; Koutcher IJROBP 2011

1.3 RT-CT vs RTCT + CTX : RTOG 0522

Stage III & IV* SCC :
- Oropharynx
- Larynx
- Hypopharynx

Stratification :
- Lx *vs* Non-Lx
- N0 *vs* N1-2b *vs* N2c-3
- Zubrod PS
- 3-D *vs* IMRT
- PET (oui *vs* non)

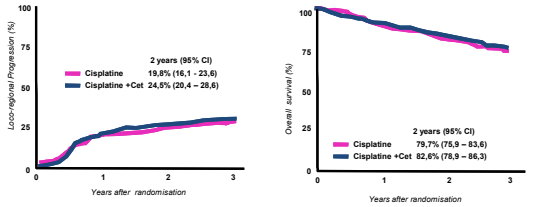
R

- AFX-CB: 72 Gy/42 F/6 sem + Cisplatine: 100 mg/m2, q3sem x2
- AFX-CB: 72 Gy/42 F/6 sem + Cisplatine: 100 mg/m2, q3sem x2 Cetuximab: 400 mg/m² x1, puis 250 mg/m²/sem

Exclus T1N+, T2N1

Ang, ASCO 2011

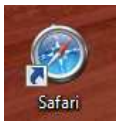
1.3 RT-CT vs RT-CT + CTX



Ang, ASCO 2011

1. Radiotherapy concomitant with… : Key messages

- Improved loco-regional control, (IA)
- Small benefit in survival
- Alternative RT-CTX
  - Toxicity profile
- RT-CT vs RT-CTX ?
- RT-CT vs RT-CT + CTX, **not yet**



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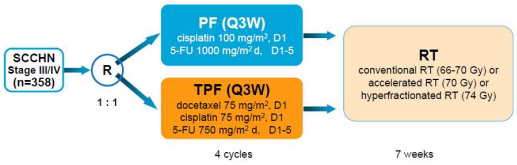
2. Induction : Tax 323 Vermorken

Tax 323, Vermorken

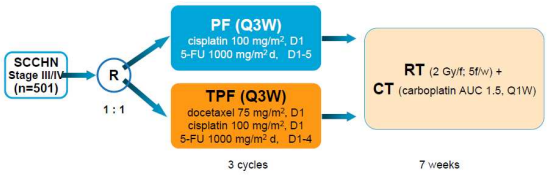


-↑ PFS 11 mo vs 8.2 mo (HR 0.72; p = 0.007)
- OS 18 mo vs 14.5 (p = 0.02)

Vermorken NEJM 2007
(courtesy of J. Bourhis)

2. Induction : Tax 324 Posner

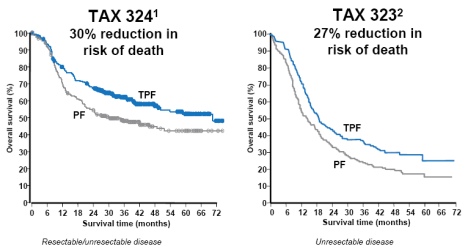
Tax 324, Posner



-↑ PFS 36 mo vs 13 mo (HR 0.71; p = 0.004)
- OS 71 mo vs 30 mo (HR 0.7 ; p = 0.006)

Posner NEJM 2007
(courtesy of J. Bourhis)

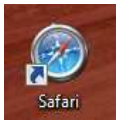
2. Induction



1. Posner NEJM 2007; 2. Vermorken NEJM 2007

2. Induction : key messages

- Induction with TPF before CT-RT ?
- Studies on going
- Not yet



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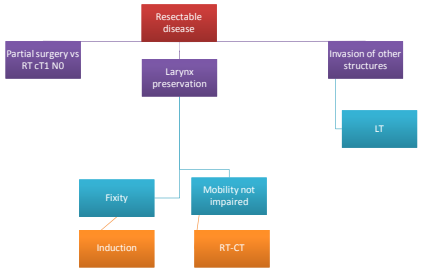
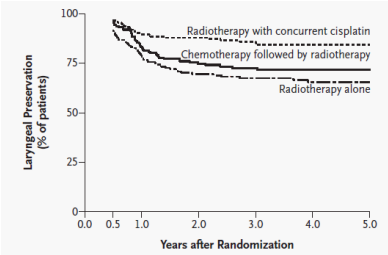
3. Larynx preservation



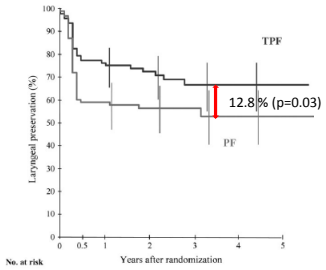
Pfister JCO 2006

3. Larynx preservation



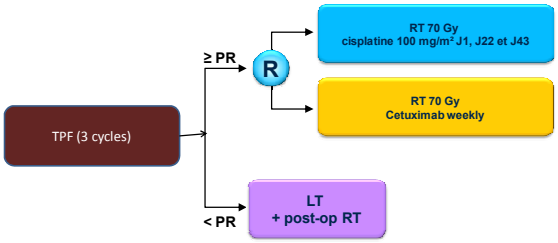
Forastiere NEJM 2003

3. Larynx preservation : GORTEC 2000-01



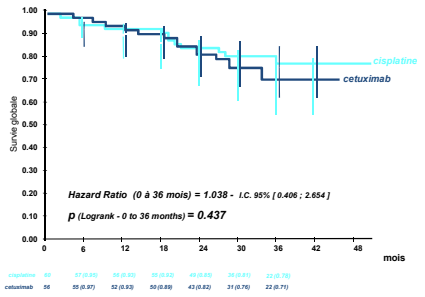
Pointreau J Natl Cancer Inst 2009

3. Larynx preservation



Lefebvre, ASCO 2009

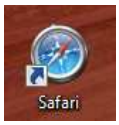
3. Larynx preservation



Lefebvre, ASCO 2009

3. Larynx preservation : key messages

- Yes whenever possible
- Induction ?
- CCRT : evidence IA



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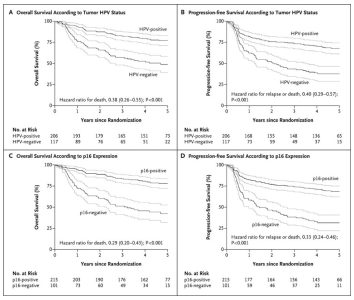
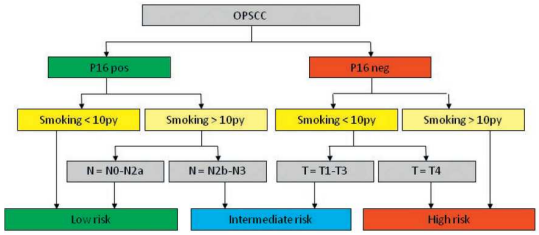
4.1 Customizing treatment : Oropharynx et HPV

3-y outcome	HPV +	HPV -
OS	83 %	57 %
PFS	74 %	43 %
Loco-regional failure	14 %	35 %
Metas	8.7 %	14.6 %
II. primary	5.9 %	14 %



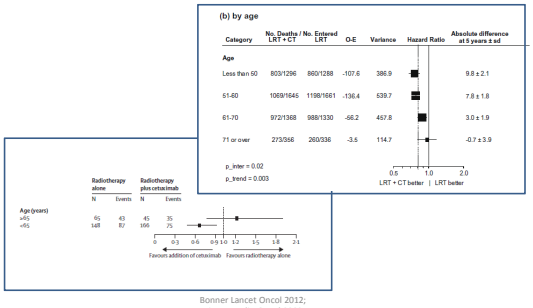
Ang NEJM 2010

4.1 Customizing treatment : Oropharynx et HPV



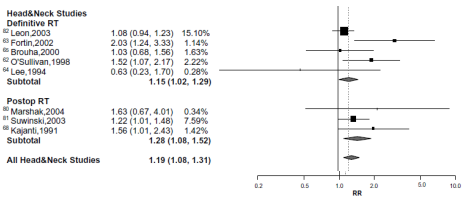
Broglie SMF 2012

4.2 Customizing treatment : age-related



Bonner Lancet Oncol 2012;
Pignon Radio Oncol 2009

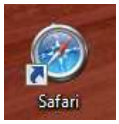
4.3 Customizing treatment : waiting time for radiotherapy



Exclusive RT : risk of local recurrence 3.7 %/month of delay

Adjuvant RT : risk of local recurrence 6.3 %/month of delay

Chen Radiother Oncol 2008



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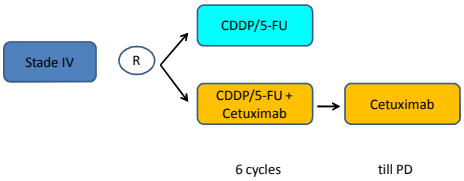
5. Recurrent or metastatic

	n	Regimen	ORR (%)	Median OS (months)	Significant OS benefit
Grose et al 1985[2]	100	Methotrexate Cisplatin	16 8	5.0 4.5	No
Forastiere et al 1992[3]	277	Cisplatin + 5-FU Carboplatin + 5-FU Methotrexate	32* 21 10	6.6 5.0 5.6	No
Clavel et al 1994[4]	382	CABO Cisplatin + 5-FU Cisplatin	34* 31* 15	7.3 7.3 7.3	No
Gibson et al 2005[5]	218	Cisplatin + 5-FU Cisplatin + paclitaxel	27 26	8.7 8.1	No
Vermorken et al 2008[6]	442	Platinum + 5-FU Platinum + 5-FU + cetuximab	20 36*	7.4 10.1*	Yes

CABO, cisplatin + methotrexate + bleomycin + vincristine
*significant

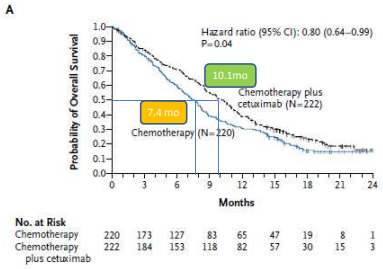
Groose Cancer Treat Rep 1985; Forastiere JCO 1992; Clavel Ann Oncol 1994; Gibson JCO 2005; Vermorken NEJM 2008 (courtesy of J. Vermorken)

5. Recurrent or metastatic



Vermorken NEJM 2008

5. Recurrent or metastatic



Vermorken NEJM 2008

5. Recurrent or metastatic : key message

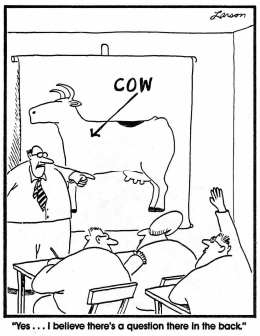
- Platinum-based doublet: ↑RR but not OS
- Benefit of OS with Platinum/5-FU + Cetuximab

6. Take home message

- CCRT : yes (CDDP vs Cetuximab)
- Induction : not yet
- Larynx preservation: whenever possible
- Customizing treatment : the future
- Recurrent or metastatic : discuss the goal

Acknowledgments

- Prof. J. Bourhis for some dias presented at the ESMO 2010
- Merck for some highlights



"Yes . . . I believe there's a question there in the back."