



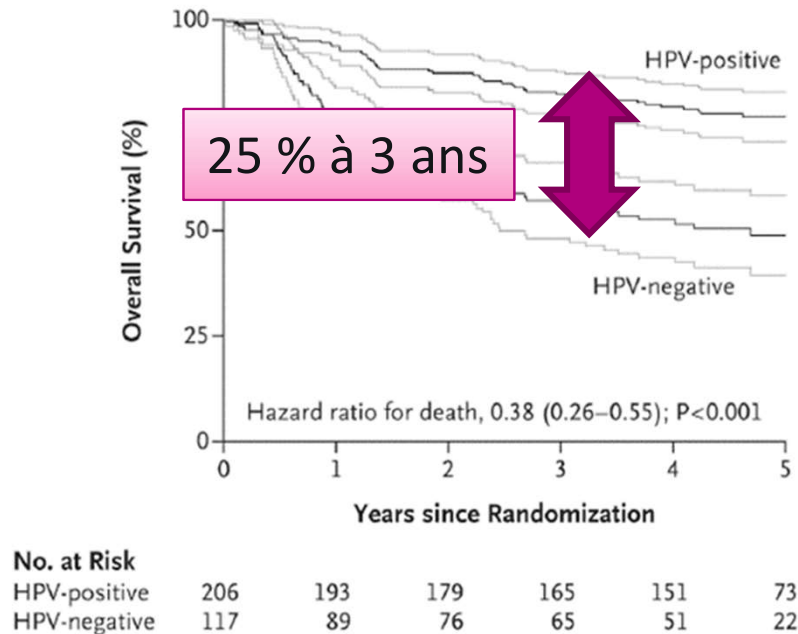
## ORATOR 2

Quelle désescalade en 2022 ?

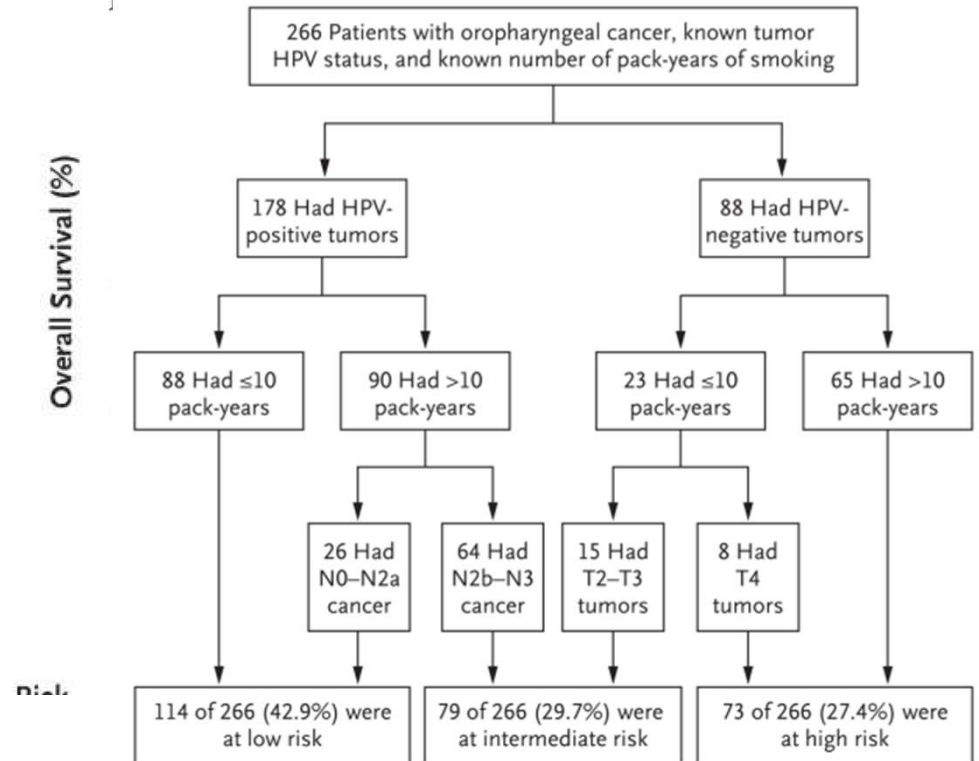
# De l'intérêt des résultats négatifs

- 2010 : analyse rétrospective de RTOG 0129

A Overall Survival According to Tumor HPV Status



A



# Echecs ?

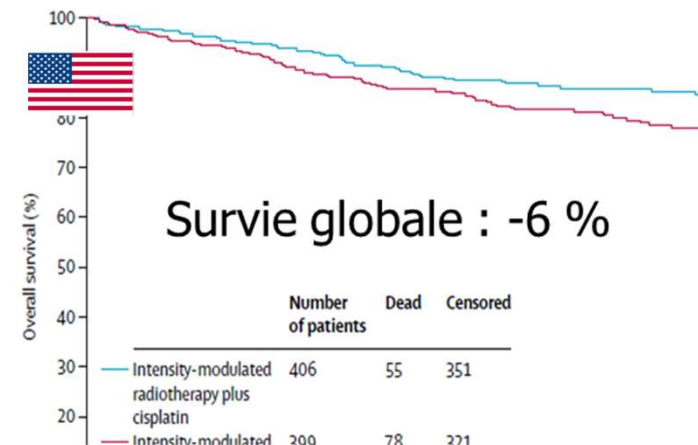
- RTOG 1016, De-Escalate, TROG 10.12




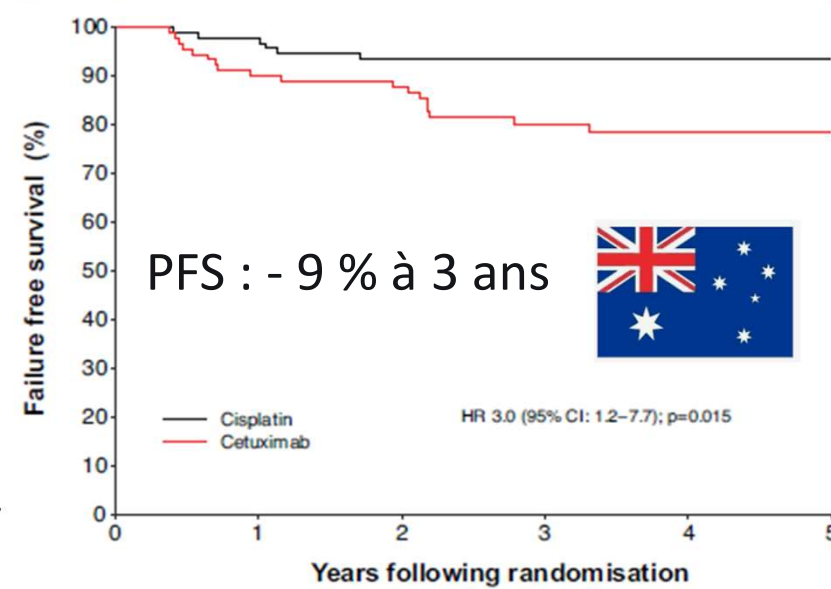
R

IMRT + CDDP

IMRT + Cetux

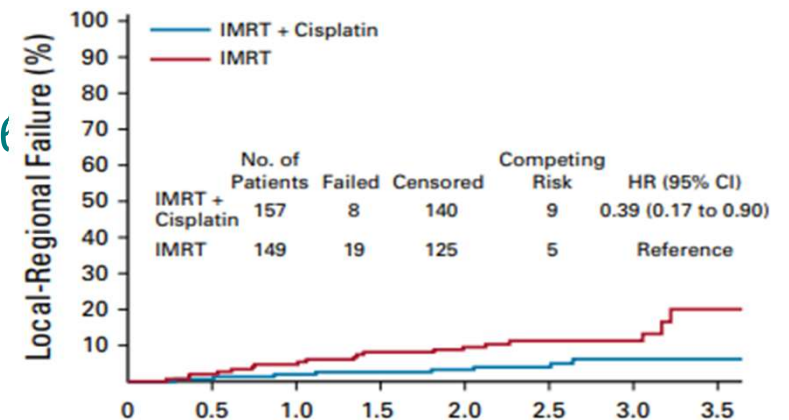
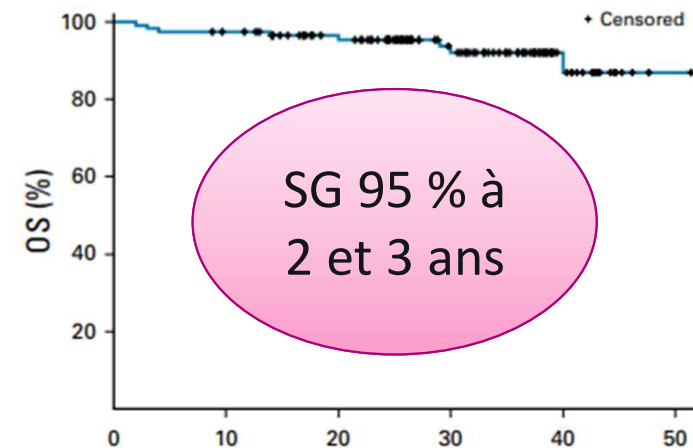


	Cisplatin plus radiotherapy (95% CI)	Cetuximab plus radiotherapy (95% CI)	p value
<b>Primary outcome</b>			



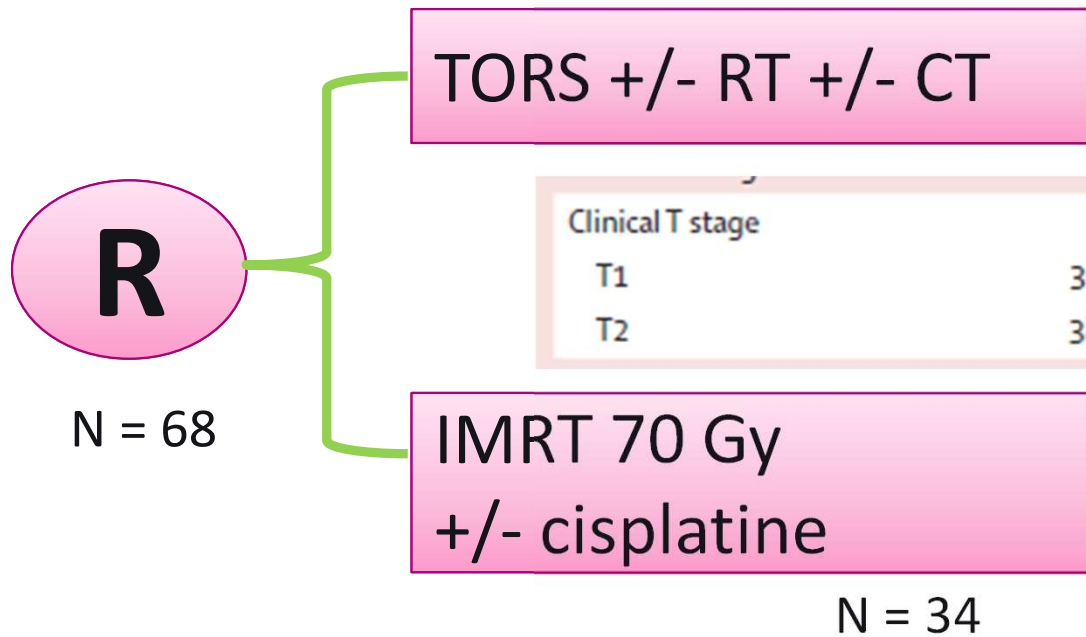
# Succès ?

- Décroissance de la dose de RT
  - 60 Gy + CDDP hebdo 30 mg / m<sup>2</sup>
  - 114 OPC stade 3 tabac < 10 PA
- NRG HN002
  - Phase 2 randomisée
  - IMRT accélérée 60 Gy 5 semaines VS RTCT (



# ORATOR 1 : cT1-2 N0-2 OPC

- Essai RANDOMISE entre CHIRURGIE et RADIOTHERAPIE !

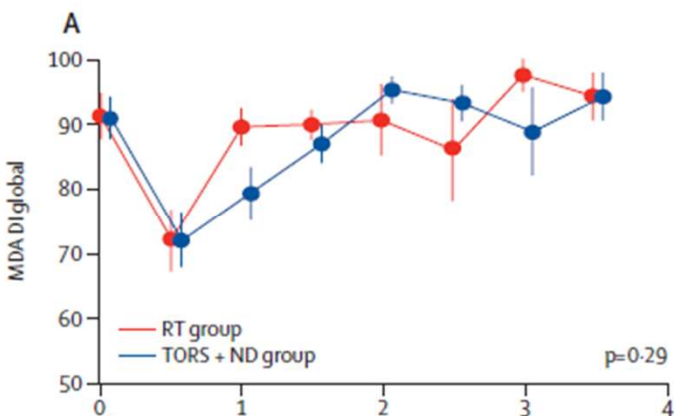


	All patients (n=68)	RT group (n=34)	TORS + ND group (n=34)
Age, median (IQR)	58.5 (52.9-65.2)	60.0 (53.2-65.2)	58.1 (52.6-64.5)
Sex			
Male	59 (87%)	31 (91%)	28 (82%)
Female	9 (13%)	3 (9%)	6 (18%)
Smoking history	49 (72%)	28 (82%)	21 (62%)
>21 drinks per week	7/40 (18%)	1/18 (6%)	6/22 (27%)
Primary site			
Tonsil or tonsillar foss	50 (74%)	26 (76%)	24 (71%)
Base of tongue	18 (26%)	8 (24%)	10 (29%)
Clinical T stage			
T1	30 (44%)	13 (38%)	17 (50%)
T2	38 (56%)	21 (62%)	17 (50%)
0	60 (88%)	30 (88%)	30 (88%)
1	8 (12%)	4 (12%)	4 (12%)
Baseline scan			
CT head, neck, and chest	40 (59%)	22 (65%)	18 (53%)
CT chest and MRI head and neck	6 (9%)	2 (6%)	4 (12%)
CT neck and chest	9 (13%)	4 (12%)	5 (15%)
PET and CT neck and chest	13 (19%)	6 (18%)	7 (21%)
p16 positive	60 (88%)	30 (88%)	30 (88%)
Radiotherapy	56 (82%)	32 (94%)	24 (71%)
Chemotherapy	31 (46%)	23 (68%)	8 (24%)
Chemotherapy regimen			
Cisplatin	24/31 (77%)	19/23 (83%)	5/8 (63%)
Carboplatin	6/31 (19%)	3/23 (13%)	3/8 (38%)
Cetuximab	1/31 (3%)	1/23 (4%)	0
Chemotherapy cycles, median (IQR)	3 (3-6)	3 (2-6)	6 (4-5-6)

Data are presented as number (%) unless otherwise stated. RT=radiotherapy. TORS + ND=transoral robotic surgery and neck dissection. ECOG=Eastern Cooperative Oncology Group.

**Table 1: Baseline and treatment characteristics**

# ORATOR 1



	1 year				Clinically meaningful decline*		
	RT group	TORS + ND group	Effect estimate (95% CI)	p value†	RT group	TORS + ND group	p value
Total (primary endpoint)	86.9 (11.4)	80.1 (13.0)	6.7 (0.2 to 13.2)	0.042	7/27 (26%)	11/27 (41%)	0.25
Global	89.6 (15.1)	79.3 (22.6)	10.3 (0.2 to 20.4)	0.046	6/27 (22%)	14/27 (52%)	0.024
Emotional	88.8 (12.0)	81.3 (12.5)	7.4 (0.9 to 14.0)	0.027	5/27 (19%)	13/27 (48%)	0.021
Functional	89.9 (11.5)	86.5 (12.0)	3.4 (-2.9 to 9.6)	0.28	7/27 (26%)	9/26 (35%)	0.49
Physical	83.1 (14.1)	75.3 (16.5)	7.9 (-0.3 to 16.0)	0.058	12/27 (44%)	16/27 (59%)	0.28
Composite (total score excluding global score)	86.7 (11.4)	80.2 (13.1)	6.5 (0.0 to 13.1)	0.049	6/27 (22%)	11/27 (41%)	0.14

Data are presented as mean (SD) unless otherwise stated. RT=radiotherapy. TORS + ND= transoral robotic surgery and neck dissection. \*Defined as a decrease of at least 10 points. †p values adjusted for stratification by p16 status (post-hoc analysis): total (p=0.054), global (p=0.071), emotional (p=0.040), functional (p=0.29), physical (p=0.064), and composite (p=0.062).

**Table 2: Quality-of-life scores at 1 year for the MD Anderson Dysphagia Inventory**

Données manquantes : 16 %

- Groupe RT : 20 %
- Groupe chir : 12 %

Nombre limité de patients

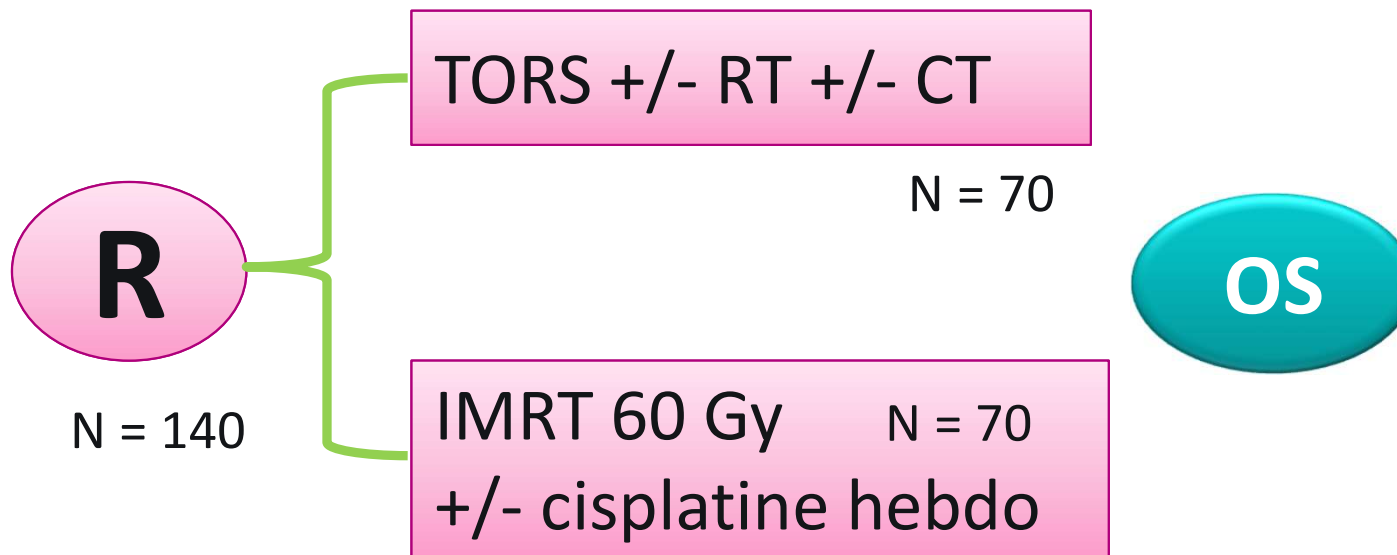
Comparaison avec RT 70 Gy

20 % patients T/OH

Seulement 30 % TORS unimodal



## ORATOR 2 : OPC BR cT1-2 N0-2 HPV +



The data safety monitoring committee met biannually to review toxic effect outcomes. An interim analysis had been planned to occur after the accrual of 70 total patients (35 per arm), with unacceptable toxic effects predefined as a grade 5 toxic effect rate of 5% or more in either arm (ie, 2 grade 5 toxic effects occurring for 35 patients)

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## ORATOR 2 : OPC BR cT1-2 N0-2 HPV +





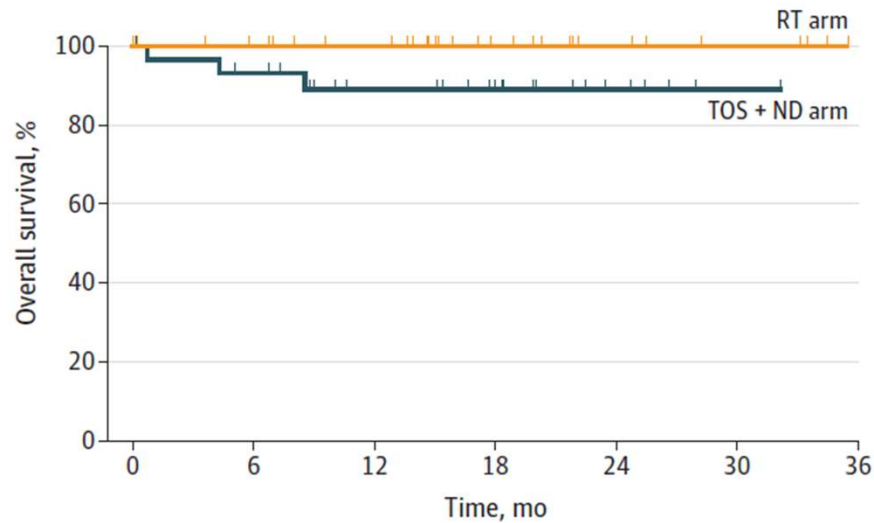
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## ORATOR 2 : OPC BR cT1-2 N0-2 HPV +

- 2 SAE de grade 5 dans le bras TORS
  - Hémorragie oropharyngée J4
    - Malgré trachéotomie et ligature de la carotide unilatérale
  - Spondylodiscite à J 110 post chirurgie
    - 1 mois après la fin de la radiothérapie post-opératoire
- Fermeture de l'essai pour risque de toxicité de grade 5 inacceptable à la moitié du recrutement.
  - Contexte de déflation thérapeutique où le risque de SAE G5 n'est pas acceptable

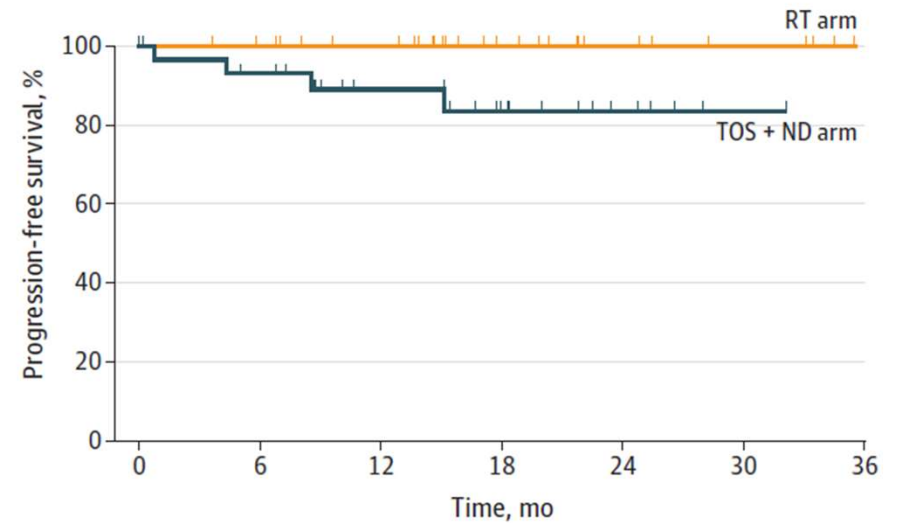
# ORATOR 2 : OPC BR cT1-2 N0-2 HPV +

**A** Overall survival stratified by treatment arm



No. at risk		0	6	12	18	24	30	36
RT arm	30	27	23	13	7	4		
TOS + ND arm	31	26	17	12	5	1		

**B** Progression-free survival stratified by treatment arm



No. at risk		0	6	12	18	24	30	36
RT arm	30	27	23	13	7	4		
TOS + ND arm	31	26	17	11	5	1		

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## Discussion : affaire pliée ?

- Marge de 1 cm demandées
  - Trop grandes ?
- Contexte de déflation thérapeutique
  - Ne pas risquer de conclure à tort
- Centres ayant une expérience importante
  - Courbes d'apprentissage déjà acquise

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# Futurs essais

- NRG HN005
  - Essai randomisé phase 2/3
  - RTCT standard vs RT-CT 60 Gy + CDDP weekly vs RT – nivolumab
  - Attendu pour 2025
- BEST OF
  - « meilleure IMRT vs meilleure chirurgie »
  - Standardisation ?
- PATHOS
  - TORS puis Rt à dose réduite