

# Best of 2015: head and neck cancer

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Department of medical oncology



**INSTITUT  
ROI ALBERT II**  
CANCÉROLOGIE ET HÉMATOLOGIE  
Cliniques universitaires SAINT-LUC | UCL Bruxelles

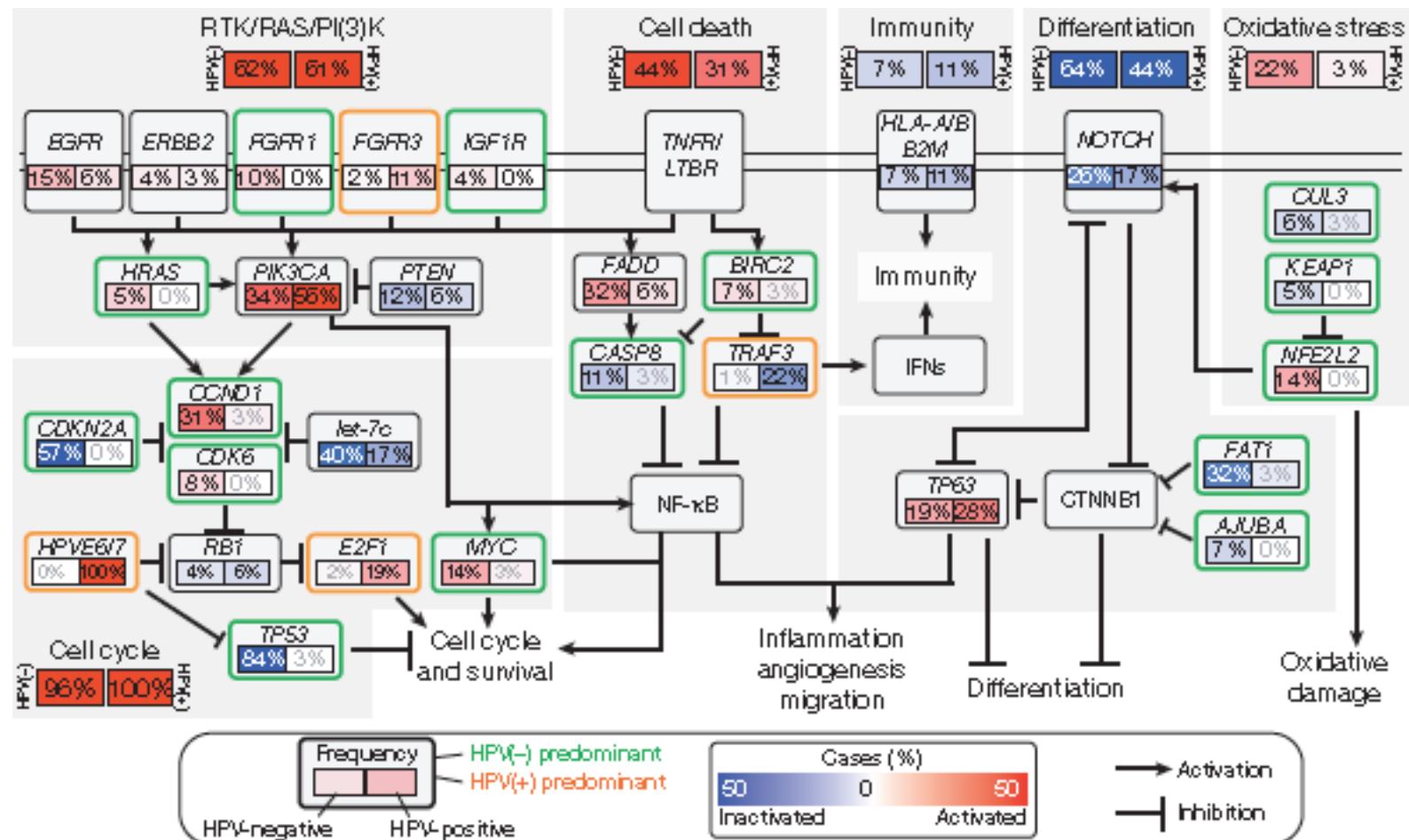


# Disclosure slide

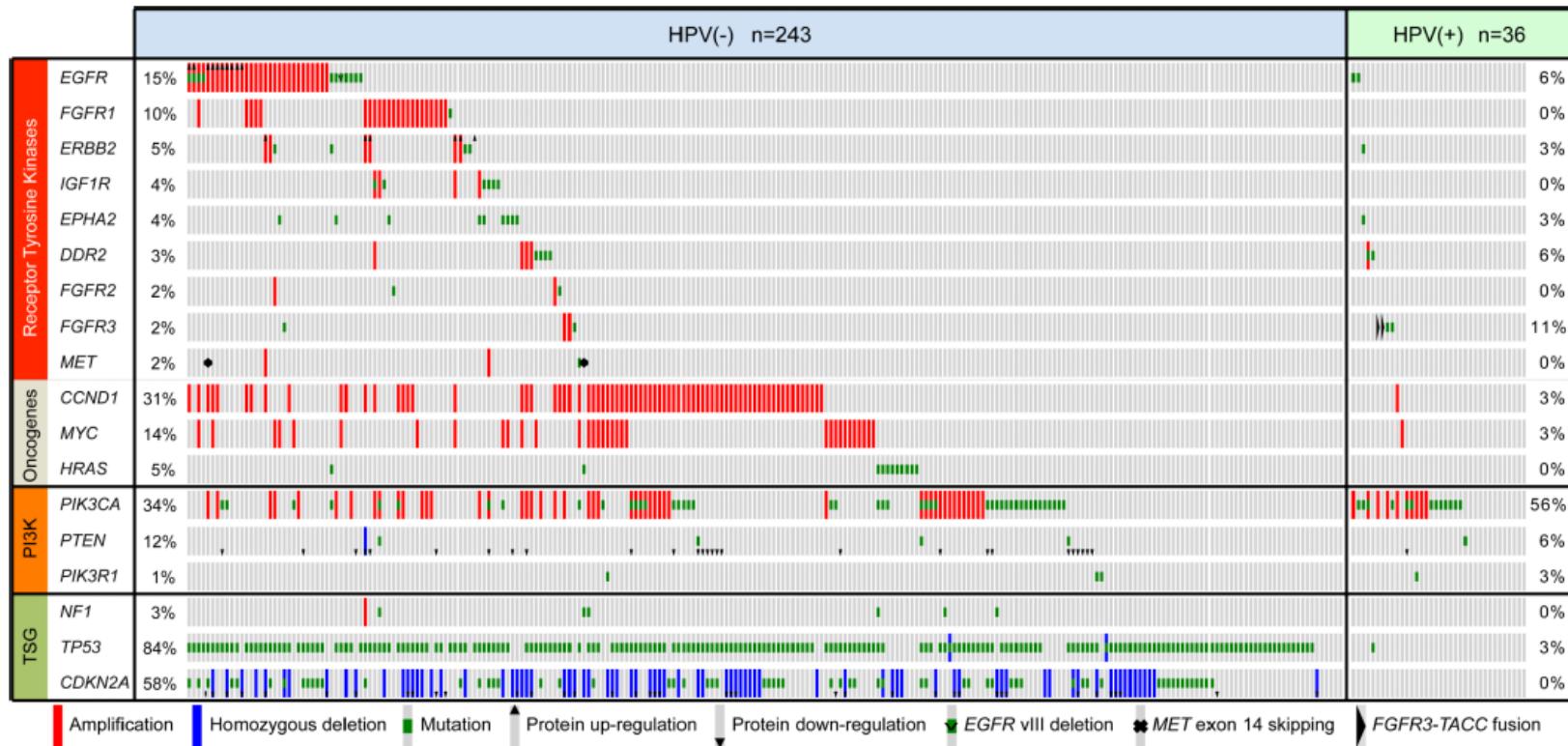
- Advisory board: Boehringer-Ingelheim, MSD, Debio
- Research grants: Novartis, Bayer, Janssen

# Presentation outline

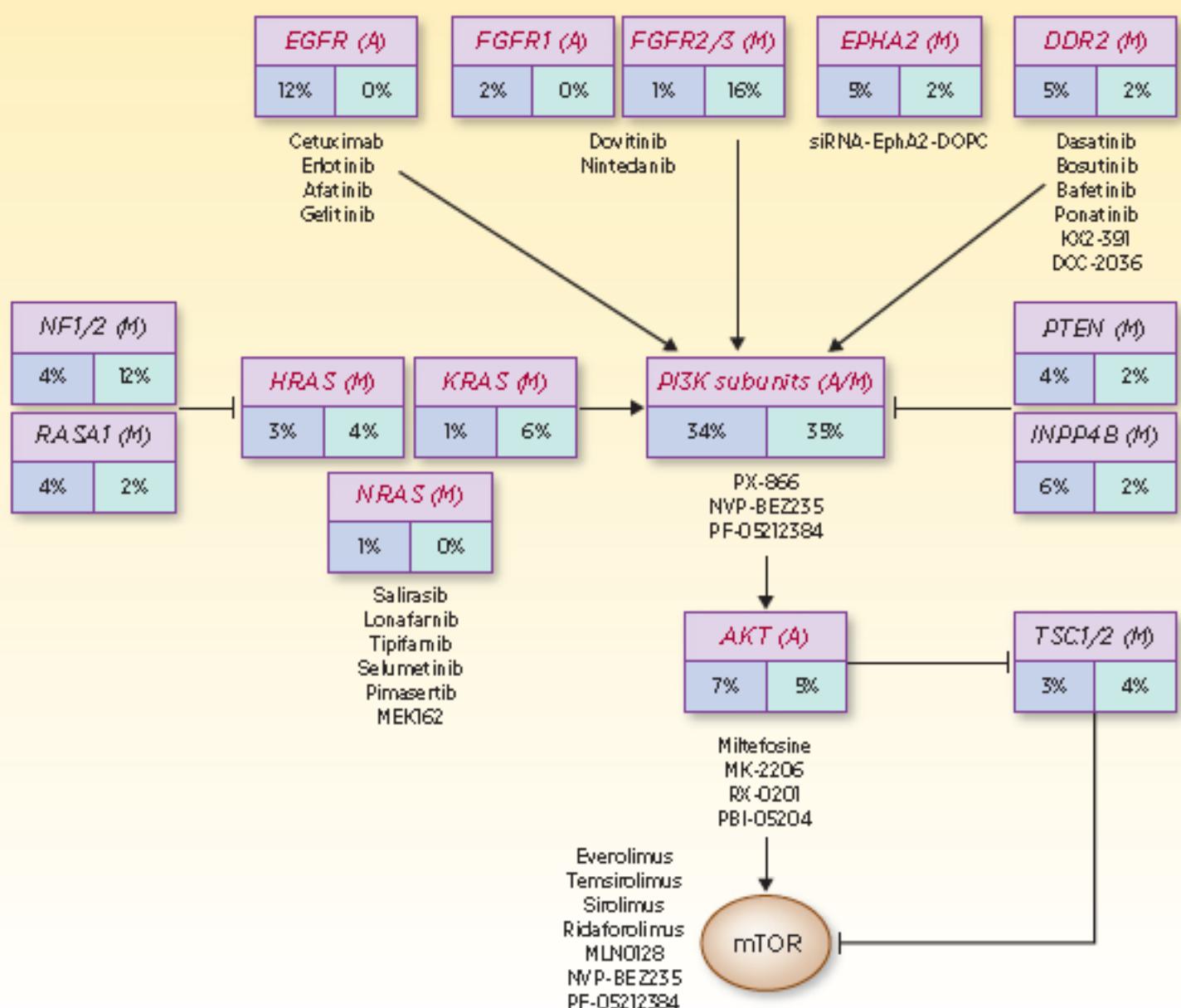
- The Cancer Genome Atlas project
- Anti-EGFR mAb with radiotherapy and HPV
- Nasopharyngeal cancer
- Oral cavity : elective neck dissection
- Recurrent/metastatic disease: immunotherapy



# Candidate therapeutic targets



Candidate therapeutic targets and driver oncogenic events. Alteration events for key genes are displayed by sample (n = 279). TSG, tumor suppressor gene.



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# DKTK-ROG initiative

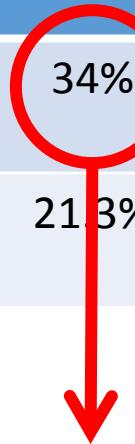
221 with oral cavity, hypopharynx, and oropharynx uniformly treated patients with surgery followed by chemoradiation

	p16 negative oropharynx Non-oropharynx cancer	p16 positive oropharynx	P value
Drivers mutations <i>PI3KCA, RAS</i>	11%	34%	0.001
Tumor suppressor gene mutations	72.9%	21.3%	< 0.001

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Lower survival

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**Lower survival**

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# Cetuximab improves overall survival

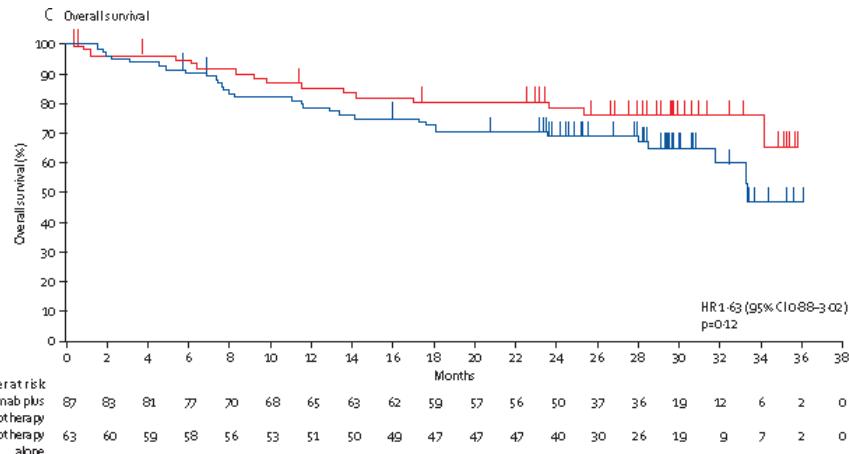
Stage III/IV: curative intention

Study	N	Regimens	3-y LRC	Median Survival
Bonner Lancet Oncol 2010	213  versus 211	Radiotherapy + Cetuximab  Radiotherapy	47%  34%	49 months  29 months

Benefit of cetuximab may be more pronounced in p16+ patients

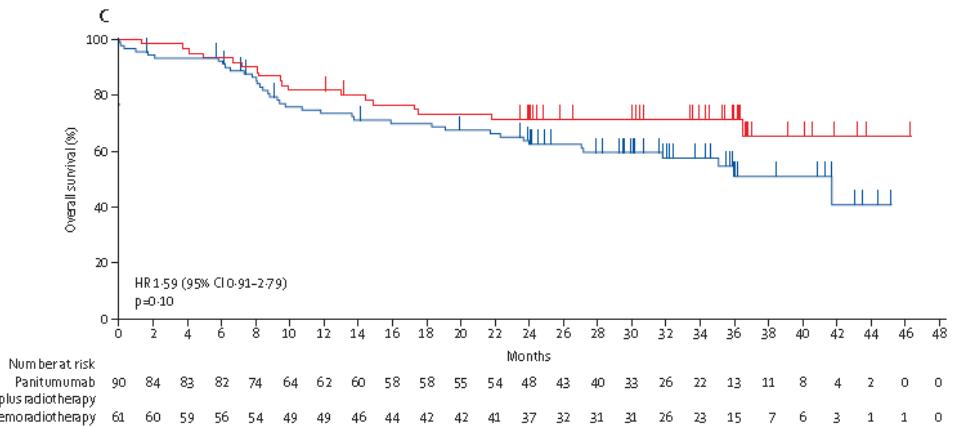
3-y Loco-regional control	p16+ oropharynx	p16- oropharynx
RT + Cetuximab	87% (HR:0.31)	32% (HR: 0.78)
RT	65%	20%

# Panitumumab and chemoradiation



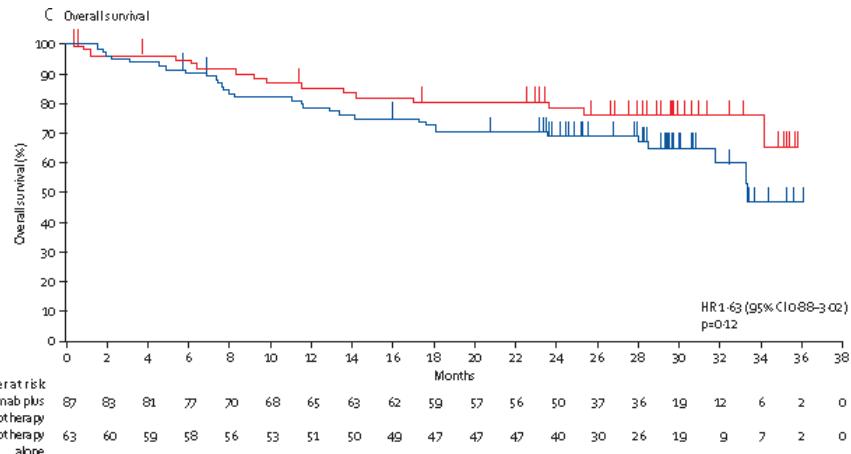
Concert 1: chemoradiation vs  
chemoradiation plus panitumumab

Concert 2: Chemoradiation vs  
radiotherapy plus panitumumab



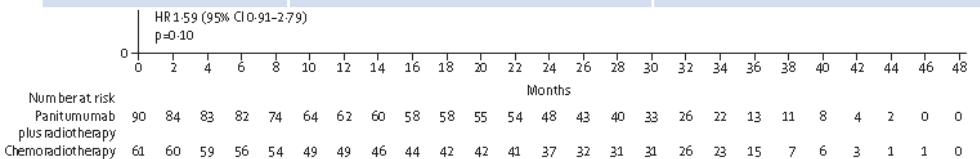
Mesia et al, Lancet Oncology 2015  
Giralt et al , Lancet Oncology 2015

# Panitumumab and chemoradiation



Concert 1: chemoradiation vs chemoradiation plus panitumumab

2-Y survival	Chemoradiation	RT+panitumumab
	71%	63%



Concert 2: Chemoradiation vs radiotherapy plus panitumumab

# Panitumumab + RT vs chemoradiation

NCIC CTG HN6  
Stage III/IV

Conventional Radiation (70 Gy in 7 weeks)

Cisplatin 100 mg/m<sup>2</sup> Day 1, 22, 43  
N=160

Primary endpoint = PFS

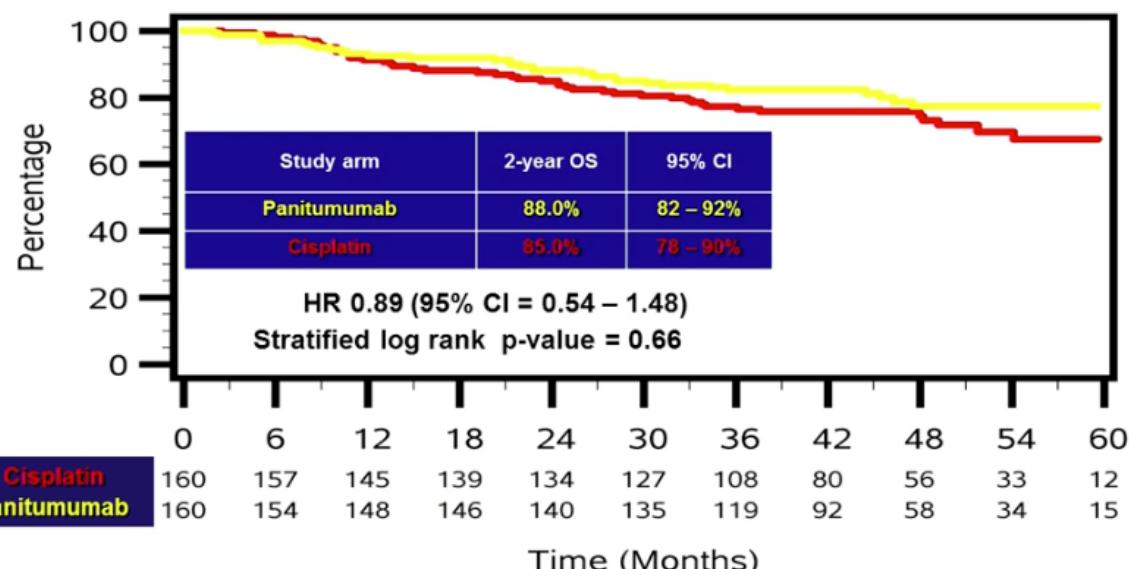
Accelerated Radiation (70 Gy in 6 weeks)

Panitumumab 9 mg/kg one week before RT  
and on days 15 and 36  
N=160

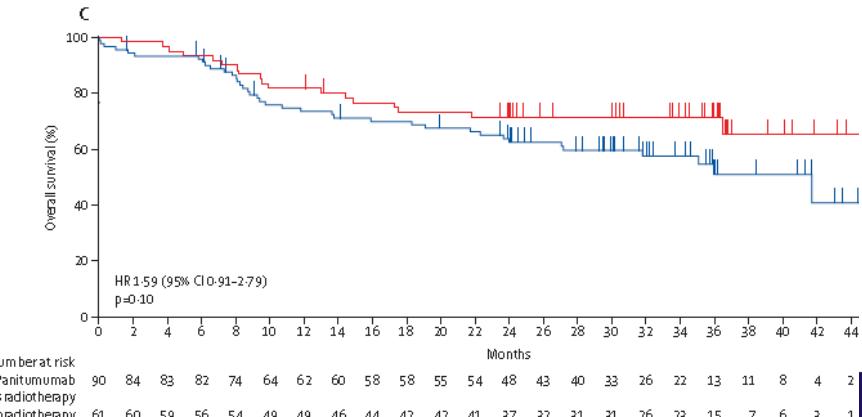
## Primary Endpoint: PFS



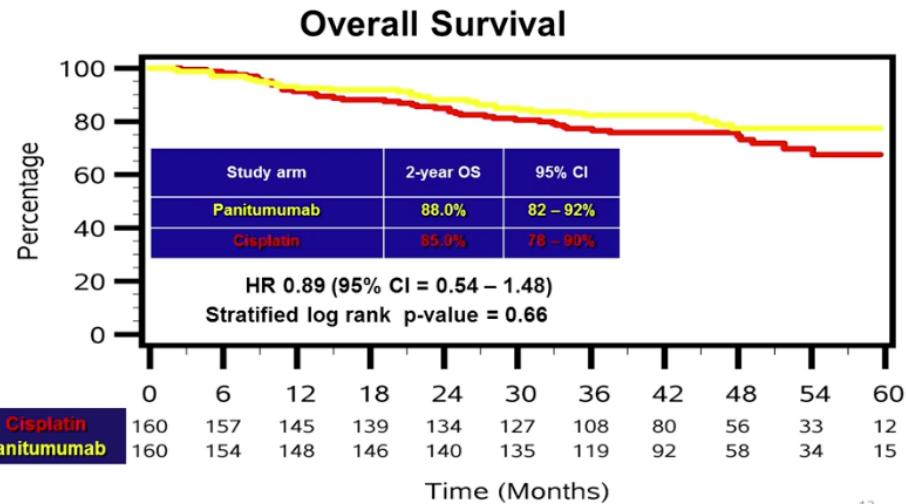
## Overall Survival



## CONCERT 2



## NCIC trial



p16+ = 20%

p16+ = 75%

This supports the investigation of treatment de-escalation in favorable HPV positive by replacing chemotherapy with anti-EGFR mAbs

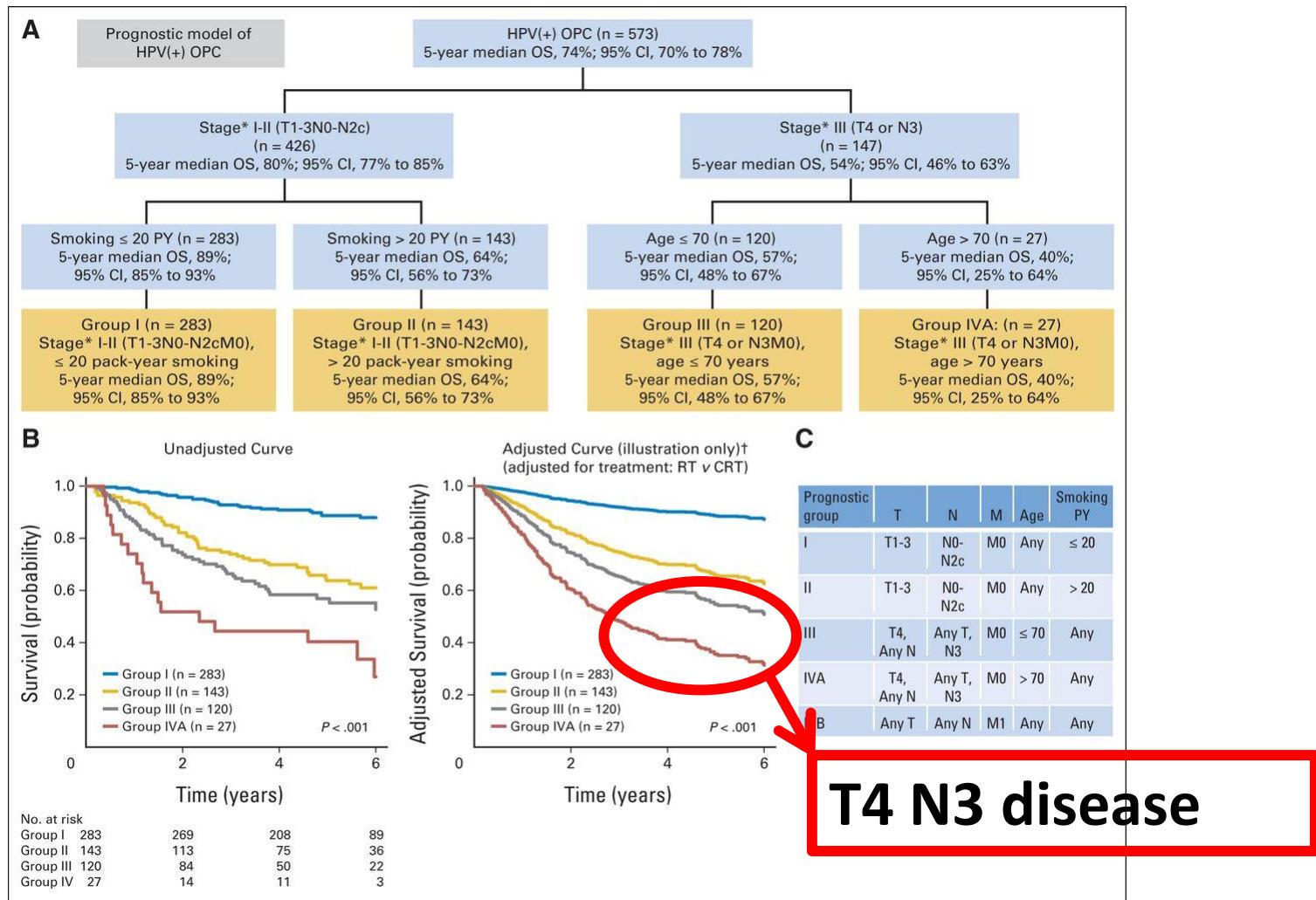
# De-intensification in HPV head and neck cancer ?

- De-intensification of systemic therapy
  - Cetuximab versus cisplatin (RTOG1016, TROG1201, De-escalate)
- De-intensification of radiation therapy
  - Surgery to select for de-intensification of radiation (ECOG331, ADEPT)
  - Induction chemotherapy to select for de-intensification of radiation (ECO1308, Quarterback study)

# HPV+ oropharynx: low-risk group

- T0-T3,N0-N2c, M0, HPV + or p16 +, less than 10 pack-years
- Radiotherapy 60 Gy + cisplatin 30 mg/m<sup>2</sup>/week
- Primary endpoint was pCR, N=49
- pCR = 86%, all the patients alive (median follow-up 15 months)

NOT A STANDARD OF CARE: we need randomized trials



Shao Hui Huang et al. JCO 2015;33:836-845

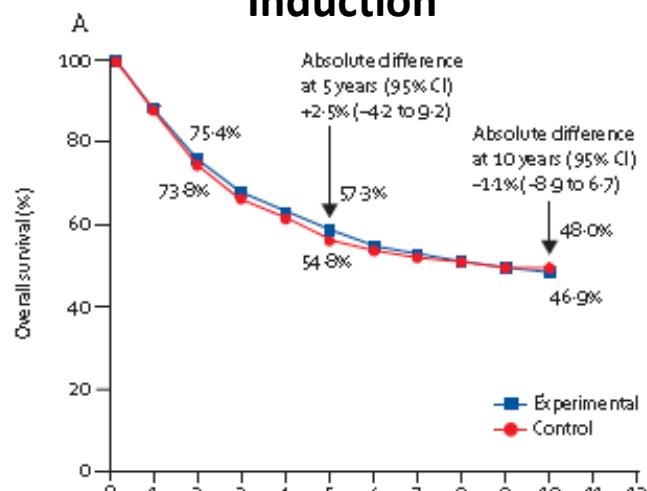
JOURNAL OF CLINICAL ONCOLOGY ASCO

Huang et al. J. Clin Oncol 2015

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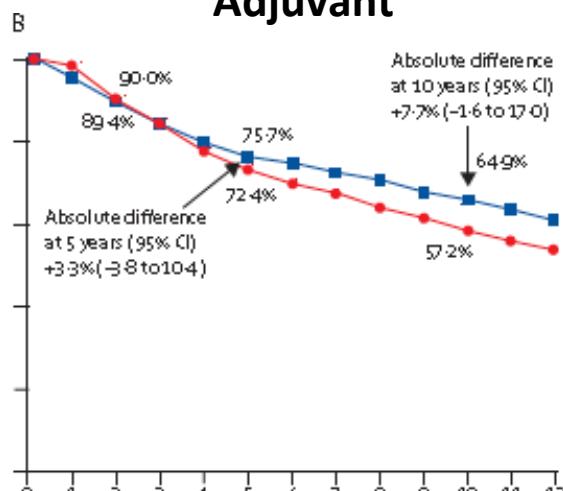
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## Induction



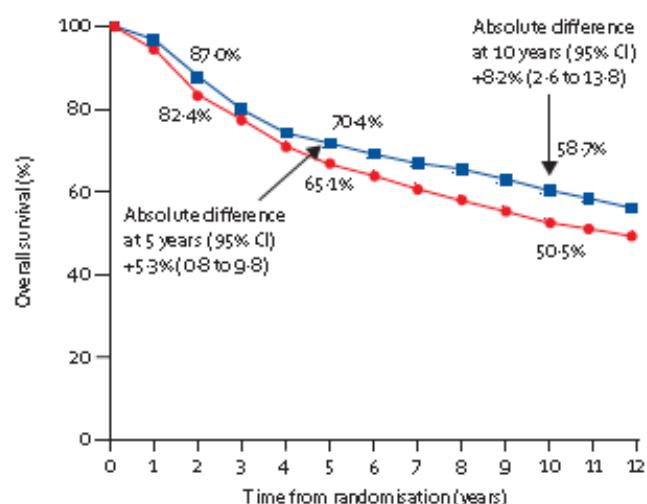
fdeaths/on-years	Years 0-2	Years 3-5	Years 6-10	Years >10
Experimental	119/856	77/822	25/537	0/36
Control	129/856	78/766	17/516	0/49

## Adjvant



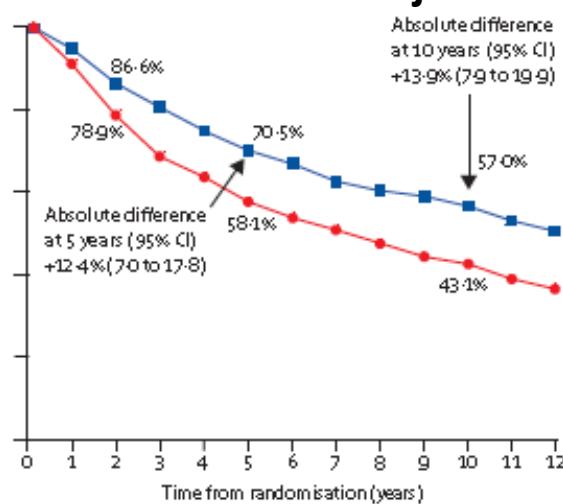
Years 0-2	Years 3-5	Years 6-10	Years >10
46/833	40/699	18/586	12/403
44/855	52/704	25/525	15/348

## Concomitant



fdeaths/on-years	Years 0-2	Years 3-5	Years 6-10	Years >10
Experimental	116/1214	144/1968	63/1290	27/662
Control	117/1654	145/1841	81/1592	20/513

## Concomitant + Adjuvant

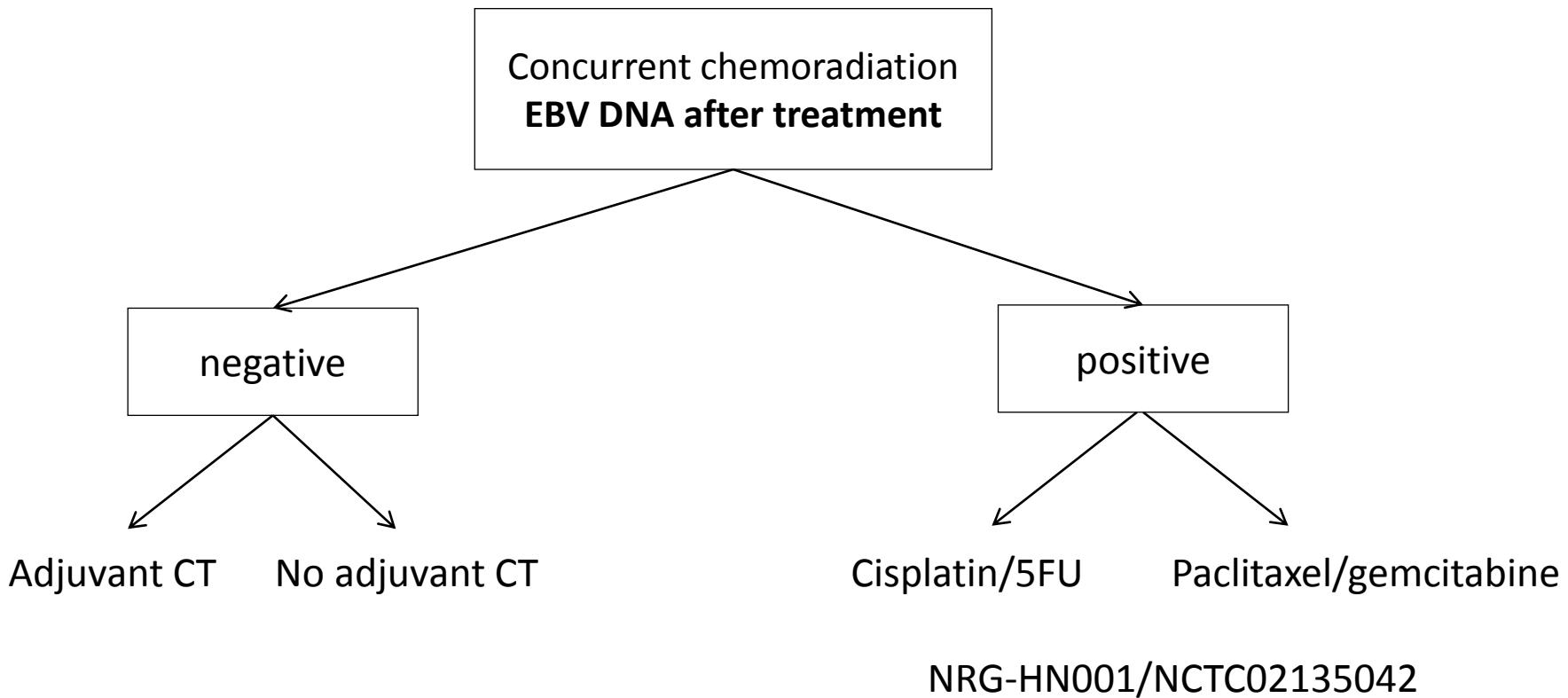


Years 0-2	Years 3-5	Years 6-10	Years >10
84/1188	102/1460	67/1477	24/420
135/1151	141/1421	81/1454	20/393

# Post-IMRT 8 weeks and 6 months undetectable plasma EBV DNA

N=289	Undetectable EBV DNA		Detectable EBV DNA	
	8 weeks	6 months	8 weeks	6 months
3-year Survival	95%	97%	81%	83%

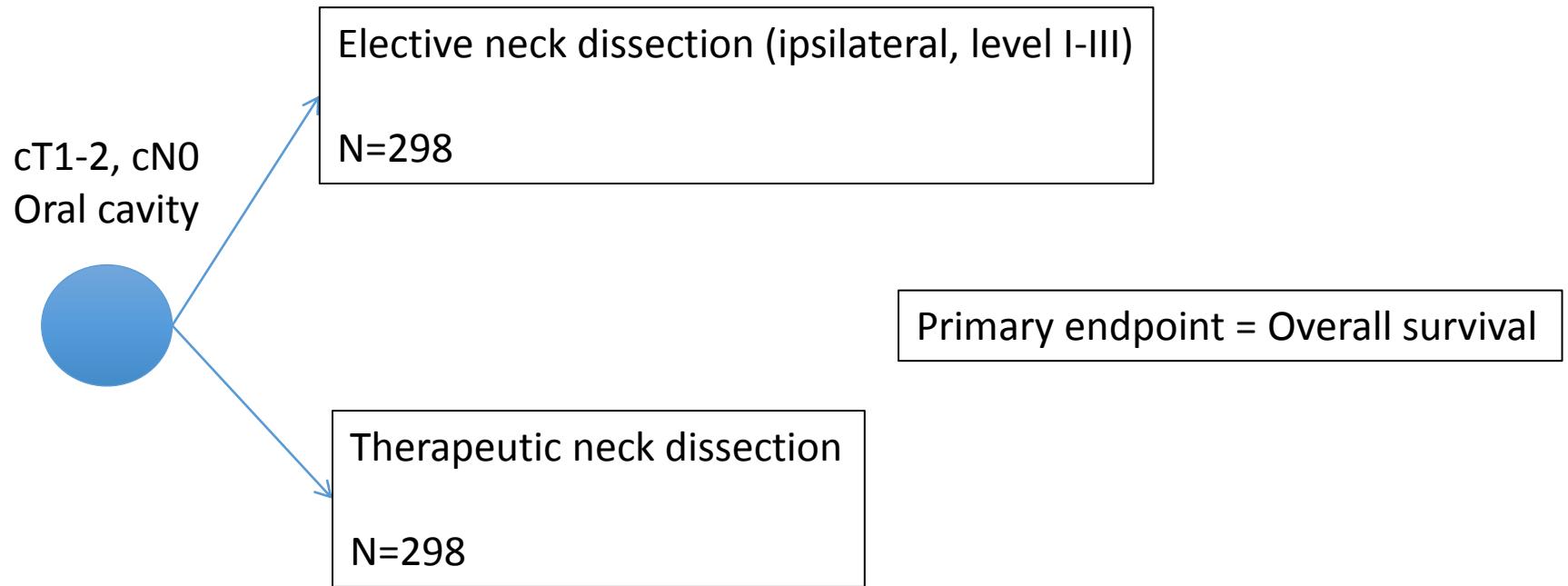
# Plasma EBV DNA



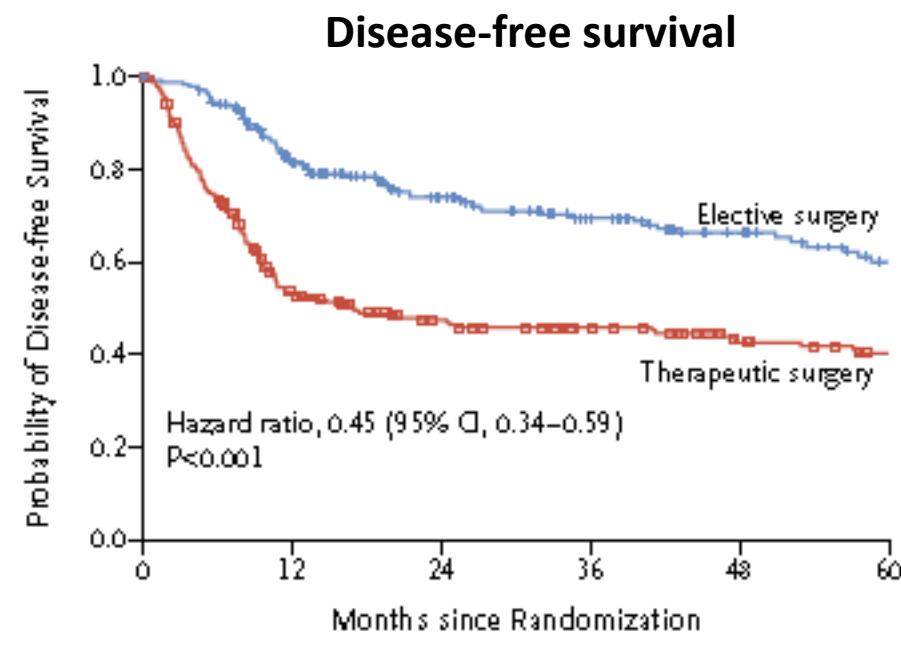
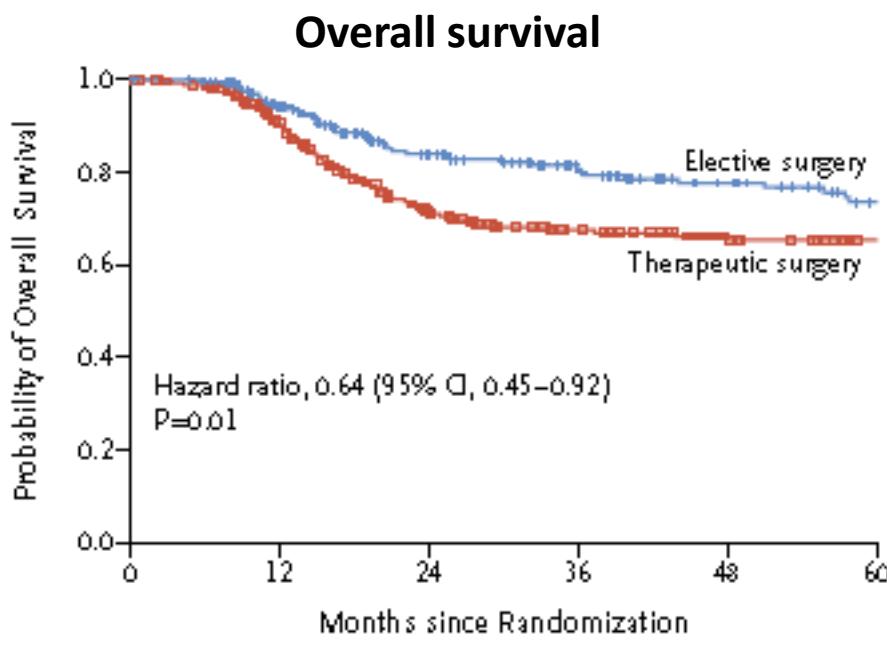
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# Elective versus therapeutic neck dissection in oral cavity



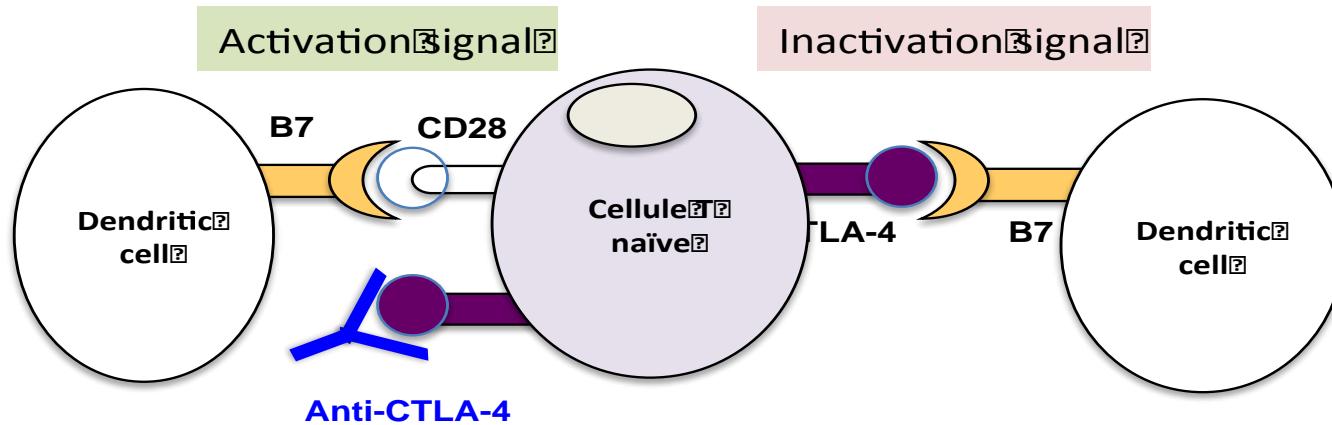
# Elective versus therapeutic neck dissection in oral cavity



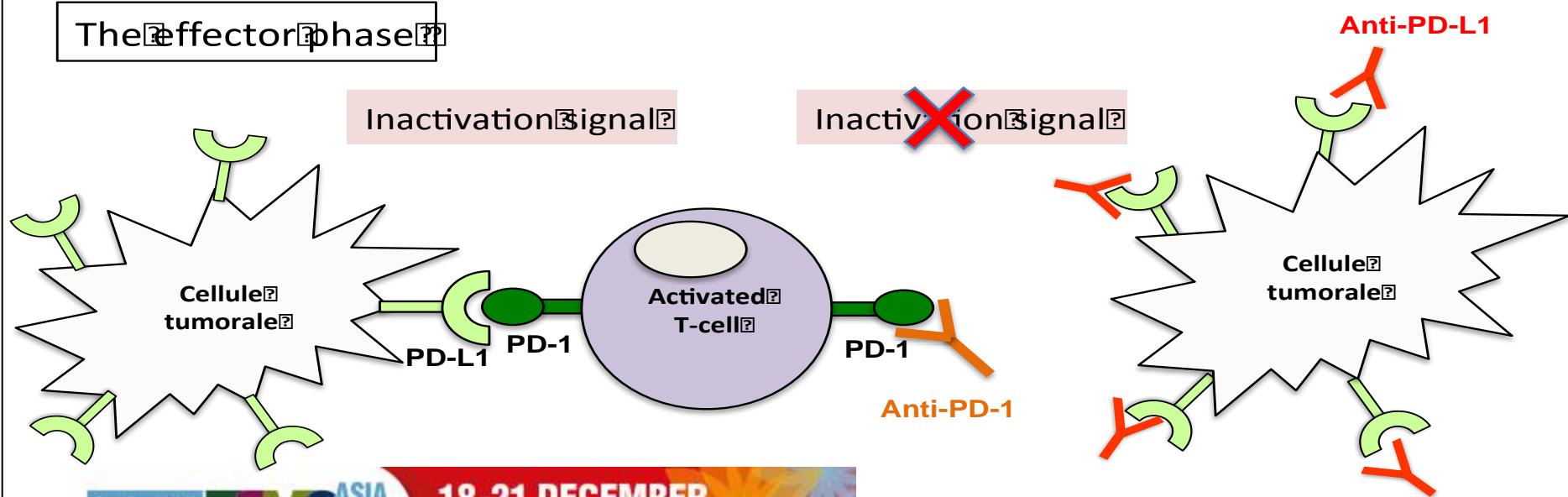
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## The Priming phase



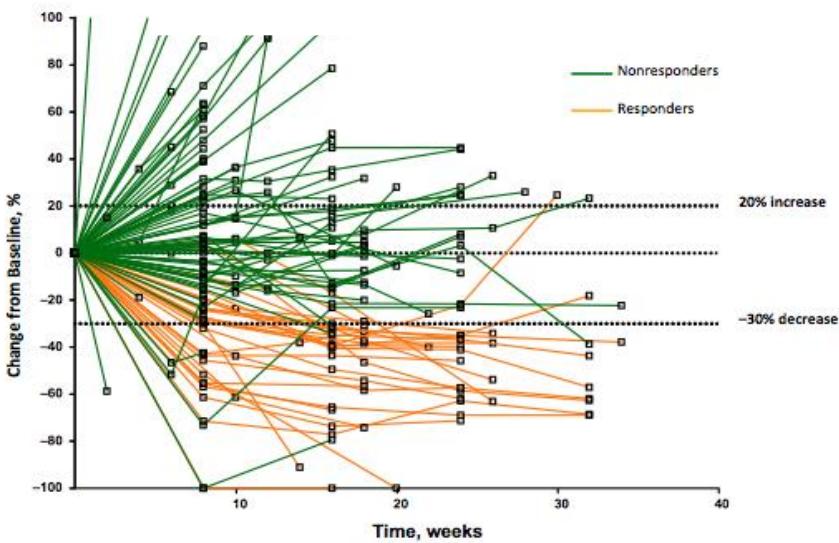
## The Effector phase



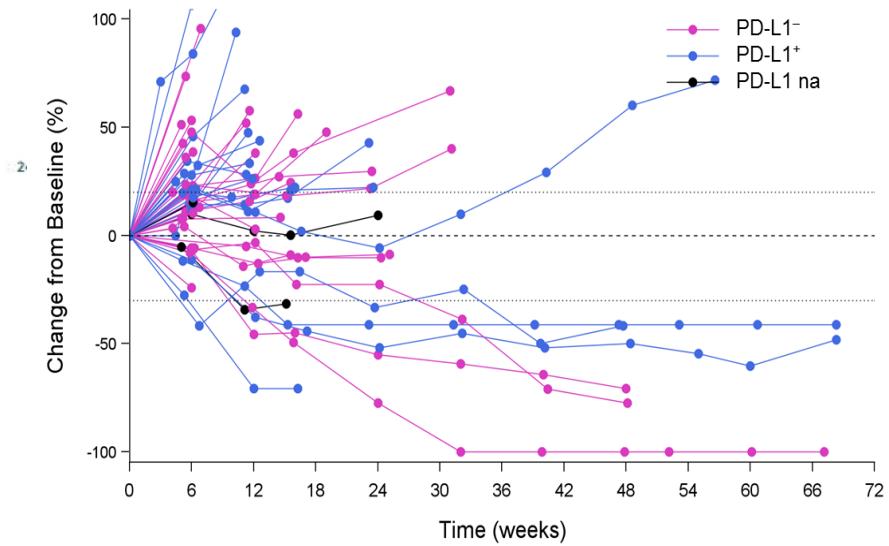
# anti-PD1 and anti-PD-L1 in recurrent head and neck cancer

Pembrolizumab Anti-PD-1	Total N=117	HPV+ N=34	HPV- N=81
ORR	24.8%	20.6%	27.2%

MEDI4736 Anti-PD-L1	Total N=62	PD-L1+ N=22	PD-L1- N=37
ORR	11%	18%	8%



Pembrolizumab



MEDI4736

# PD-L1 positive recurrent nasopharyngeal cancer

Pembrolizumab	N=27
ORR	22%

# Conclusions

- The Cancer Genome Atlas project
- Anti-EGFR mAb with radiotherapy and HPV
- Nasopharyngeal cancer: plasma EBV
- Oral cavity : elective neck dissection
- Recurrent/metastatic disease: immunotherapy