



Head and neck virus-induced cancers: current management and perspectives

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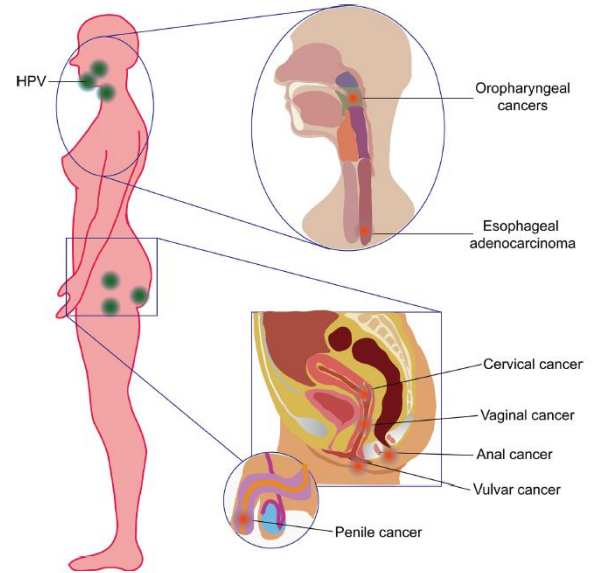
Disclosures

- **Participated in Advisory Boards sponsored by:**

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Background

- **Virus-induced head and neck cancers:**
 - **UCNT:**
 - * **EBV**
 - * Most of NPC
 - * Some **lymphomas**
 - **Oropharyngeal squamous cell carcinoma:**
 - * **HPV16** mainly
 - * Younger patients
 - * Other **GI** and **GU** cancers



Prognosis of stage III-IV disease

@5 years	NPC	HPV+ OPC	HNSCC
OS	80%	85%	60%
RFS/PFS	70%	80%	50%
Locoregional recurrence	10%	10%	30%
Distant metastases	20%	10%	20%

AJCC classification

Stage	NPC	HPV+ OPC	HPV- OPC
I	T: oropharynx, nasal cavity N0	T<4cm N<6cm ipsilateral	T<2cm N0
II	T: parapharynx, muscles N<6cm bilateral	T<4cm, epiglottis N<6cm bilateral	T<4cm N0
III	T: skull base N<6cm bilateral	T: larynx, mouth N>6cm	T>4cm, epiglottis 1N+ ipsilateral <3cm
IV	T: brain, cranial nerves N>6cm	T: anywhere N: any	T: anywhere Multiple N, >3cm

AJCC classification

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Treatment

Stage	NPC	HPV+ OPC	HPV- OPC
I	T: oropharynx, nasal cavity N0	T: ... N: ... ipsilateral	T<2cm N0
II	T: parapharynx, muscles N<6cm bilateral	T<4cm ... N<6cm ...	T<4cm N0
III	T: skull base N<6cm bilateral	T: larynx ... N>6cm ...	T>4cm, epiglottis 1N+ ipsilateral <3cm
IV	T: brain, cranial nerves N>6cm	T: ... N: ...	T: anywhere Multiple N, >3cm

Treatment

Stage	NPC	OPC (both HPV+ & HPV-)
I	T: oropharynx, nasal cavity N0	T<2cm N0
II	T: parapharynx, muscles N<6cm bilateral	T<4cm N0
III	T: skull base N<6cm bilateral	T>4cm, epiglottis 1N+ ipsilateral <3cm
IV	T: brain, cranial nerves N>6cm	T: anywhere Multiple N, >3cm

Unimodal

Multimodal

Treatment strategies – stage III/IV

@5 years	NPC	HPV+ OPC
OS	80%	85%
RFS/PFS	70%	80%
Locoregional recurrence	10%	10%
Distant metastases	20%	10%

De-escalation

Intensification

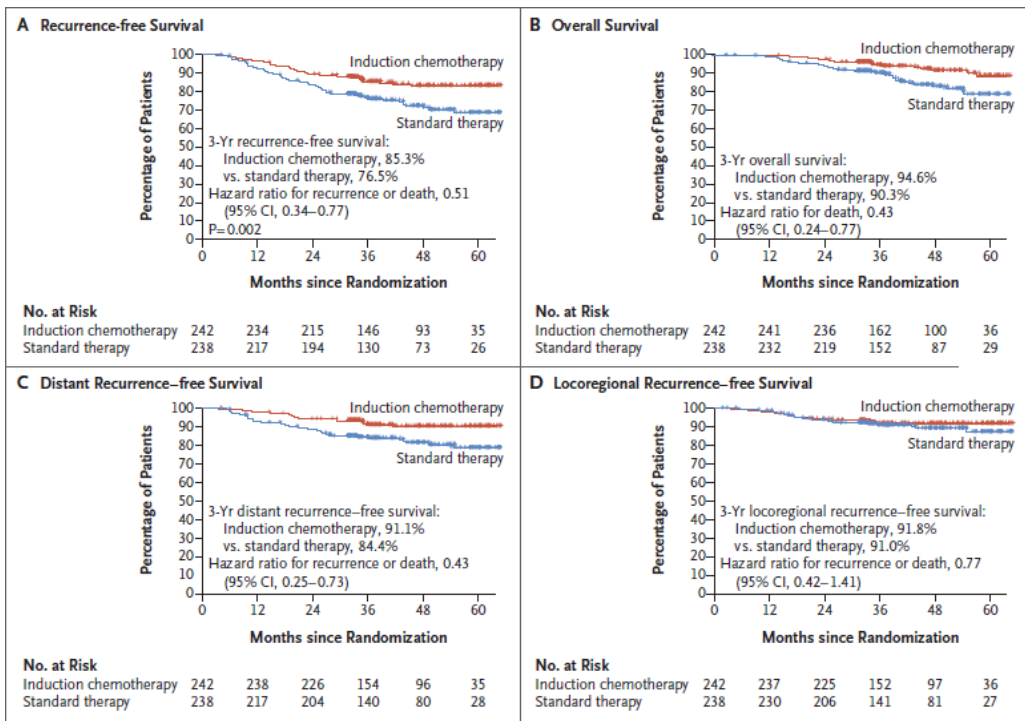


NPC – stage III/IV

Gem + Cis x3 → RCT



RCT



Treatment strategies – stage III/IV

@5 years	NPC	HPV+ OPC
OS	80% 90%	85%
RFS/PFS	70% 85%	80%
Locoregional recurrence	42% 8%	10%
Distant metastases	20% 10%	10%

De-escalation

Intensification



HPV+ OPC – stage III/IV

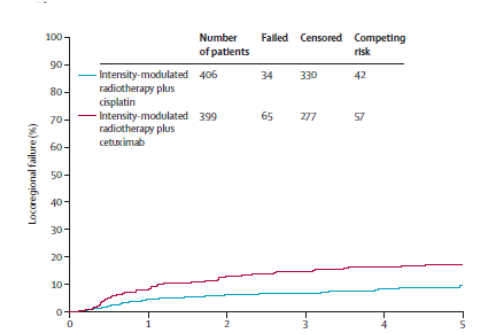
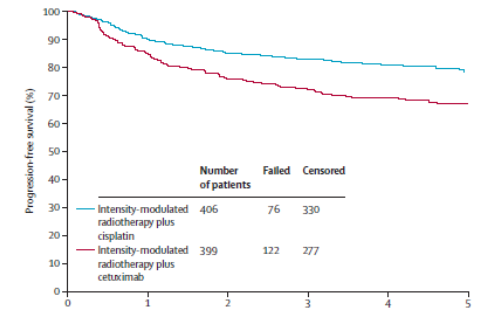
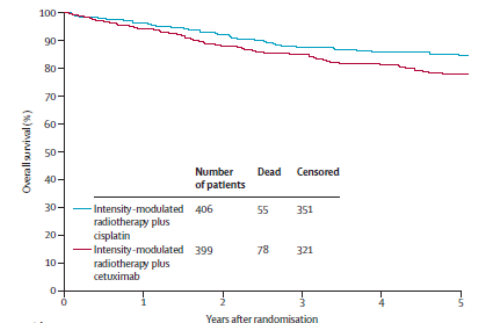
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**RT +
Cetuximab**

**RT +
Cisplatin**



Treatment strategies – stage III/IV

@5 years	NPC	HPV+ OPC
OS	80% 90%	85% 80%
RFS/PFS	70% 85%	80% 70%
Locoregional recurrence	12% 8%	10% 20%
Distant metastases	20% 10%	8% 12%

De-escalation

Intensification

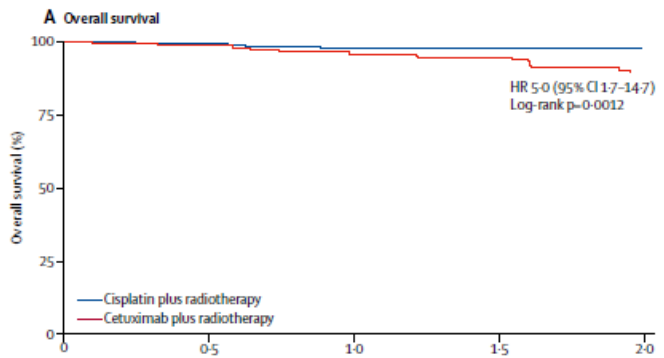
HPV+ OPC – stage III/IV

De-ESCALaTE

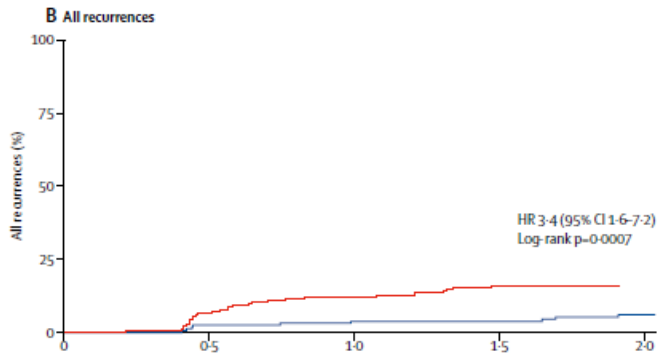


RT +
Cetuximab

RT +
Cisplatin



	Time since randomisation (years)				
Number at risk	0	0.5	1.0	1.5	2.0
Cisplatin plus radiotherapy	166	160	154	147	118
Cetuximab plus radiotherapy	168	163	156	144	109



	Time since randomisation (years)				
Number at risk	0	0.5	1.0	1.5	2.0
Cisplatin plus radiotherapy	166	156	148	141	109
Cetuximab plus radiotherapy	168	152	41	128	101

Recurrent and/or metastatic setting

	NPC	HPV+ OPC	HNSCC
Median OS	24 mo	16 mo	12 mo
Locoregional recurrence	30%	30%	70%
Distant metastases	70%	70%	30%



Anti-PD1/PD-L1 therapy

Study	ORR	DoR	Median PFS	Median OS
NPC				
KN-028	26%	17 mo	3.7 mo	17 mo
POLARIS-02	21%	13 mo	1.9 mo	17 mo
HPV+ HNSCC				
KN-012	32%	-	4.0 mo	-
KN-055	16%	NR	2.1 mo	8.0 mo
CM-141	16%	-	-	9.1 mo
HPV- HNSCC				
KN-012	14%	-	2.0 mo	-
KN-055	15%	7 mo	2.1 mo	8.0 mo
CM-141	8%	-	-	7.5 mo



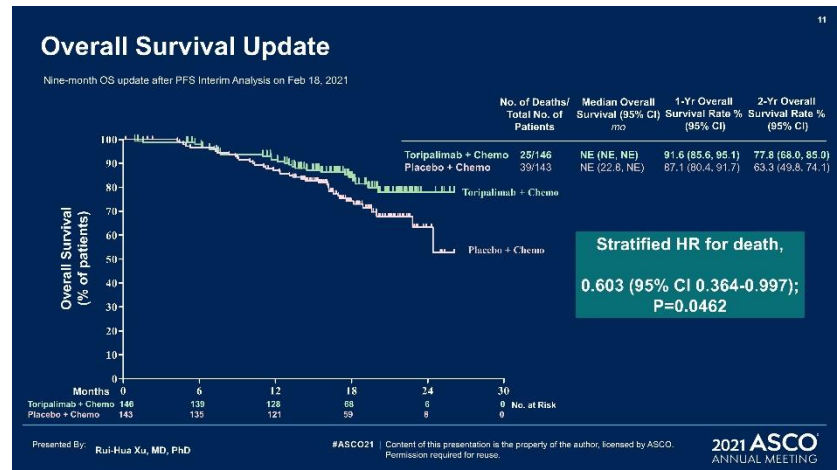
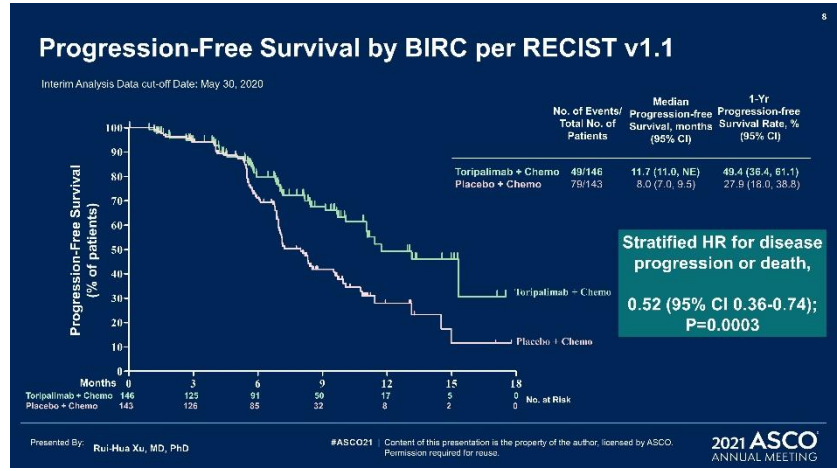
NPC – SOC 1st line

JUPITER-02

R

Gem + Cis + Toripalimab

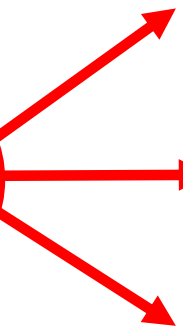
Gem + Cis





HNSCC – SOC 1st line

KN-048



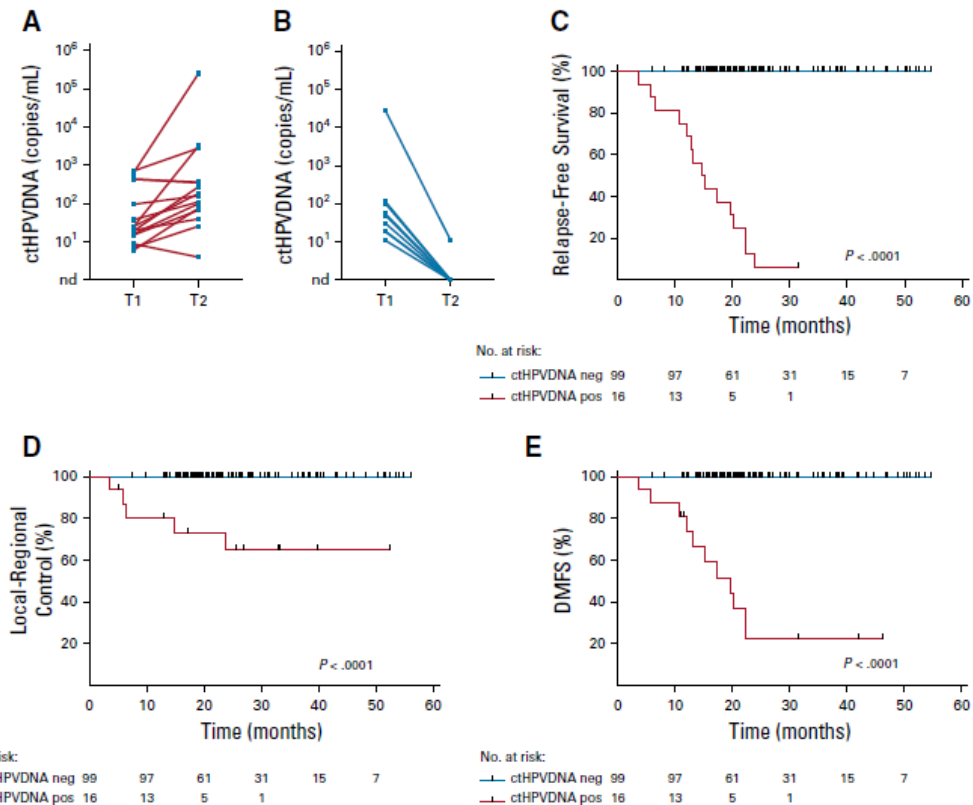
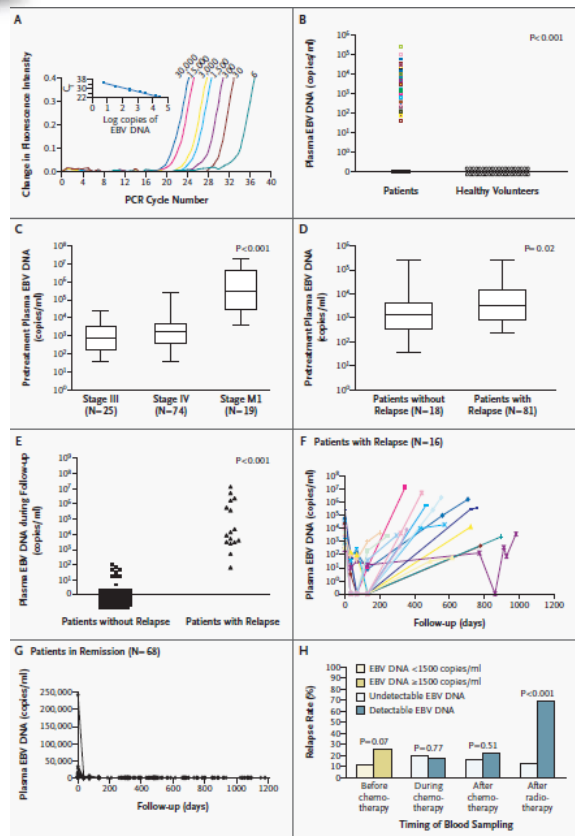
**Cis + 5-FU
+ Pembro**

Pembro

**Cis + 5-FU +
Cetuximab**

	OS HR (95%CI)	PFS HR (95%CI)	ORR Experimental	ORR Standard
P versus EXTREME				
CPS ≥20 (40%)	0.58 (0.44-0.78)	0.99 (0.75-1.29)	23%	36%
CPS 1-19 (45%)	0.86 (0.66-1.12)	1.25 (0.96-1.61)	15%	34%
CPS 0 (15%)	1.51 (0.96-2.37)	4.31 (2.63-7.08)	5%	42%
CPS ≥1 (85%)	0.74 (0.61-0.90)	-	19%	35%
Total	0.83 (0.70-0.99)	1.34 (1.13-1.59)	17%	36%
P+C versus EXTREME				
CPS ≥20 (40%)	0.60 (0.45-0.82)	0.73 (0.55-0.97)	43%	38%
CPS 1-19 (45%)	0.71 (0.54-0.94)	0.93 (0.71-1.21)	29%	34%
CPS 0 (15%)	1.21 (0.76-1.94)	1.46 (0.93-2.30)	31%	40%
CPS ≥1 (85%)	0.65 (0.53-0.80)	0.82 (0.67-1.00)	36%	36%
Total	0.72 (0.60-0.87)	-	36%	36%

EBV & HPV ctDNA





Conclusions

- **Virus-induced head and neck cancers** have a better **prognosis**
- In the **locally advanced** setting, **de-escalation** in **HPV+ OPC** has failed, whereas **intensification** has improved **NPC** patients outcome
- **Immunotherapy** has become standard of care in these cancers in the **recurrent and/or metastatic** setting
- It is not clear whether **immunotherapy** has more efficacy in **virus-induced head and neck cancers** as compared to HPV- HNSCC