Head and neck oncology in maxillofacial surgery

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Antwerpen

29/11/2025

Nobel Biocare™

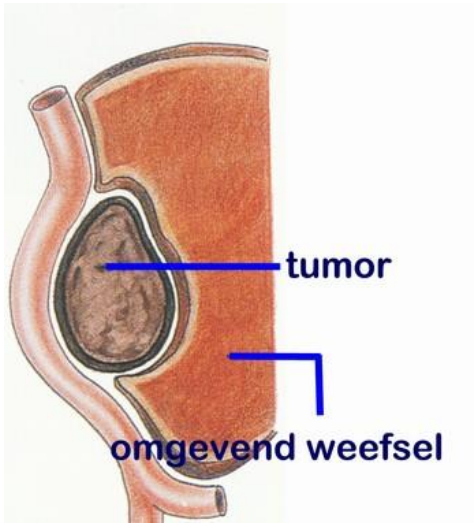
Experience the future of dental care

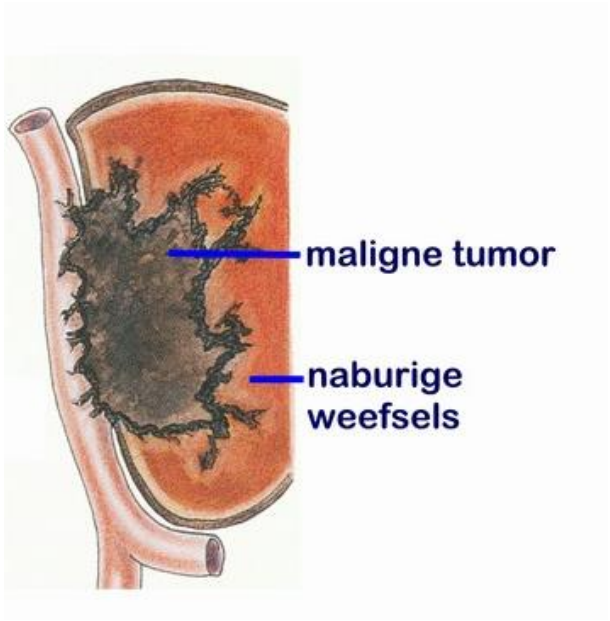
What is head and neck oncology?

Epidemiology

Head and neck cancer

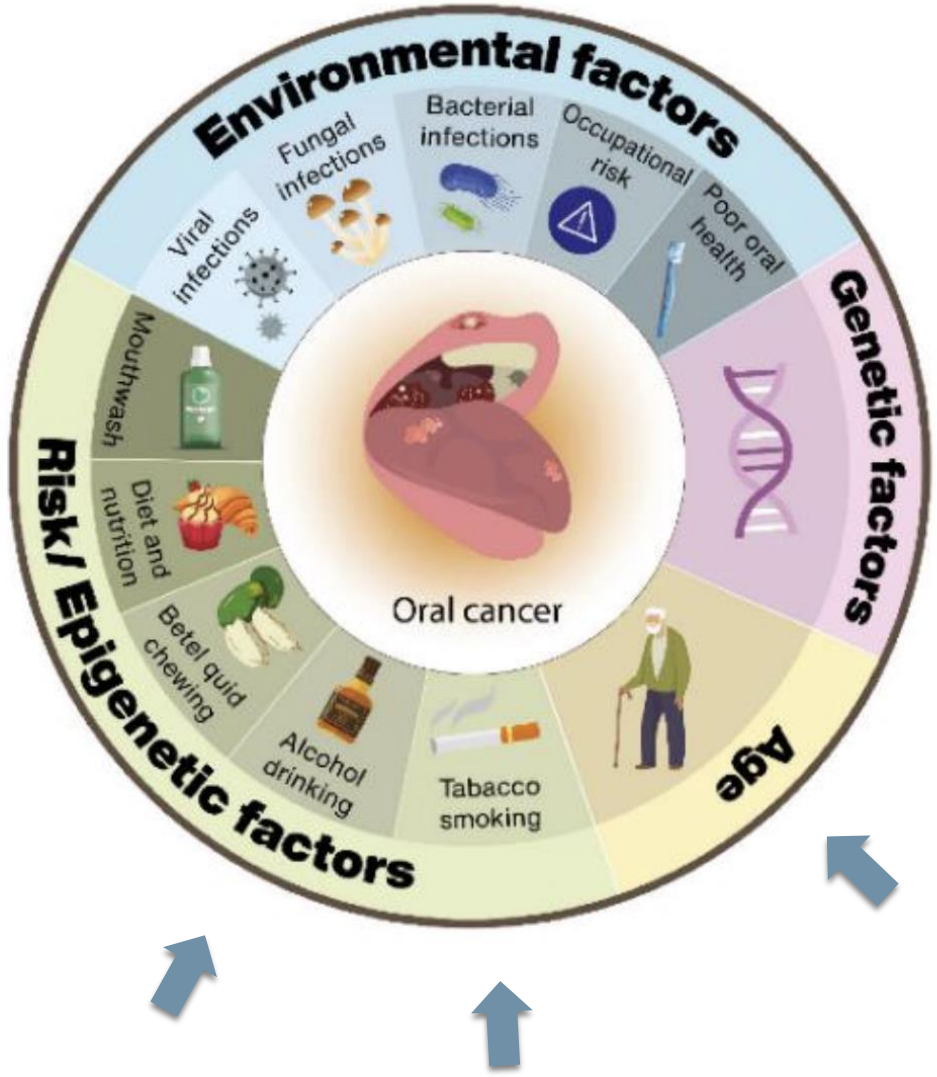
Epidemiology





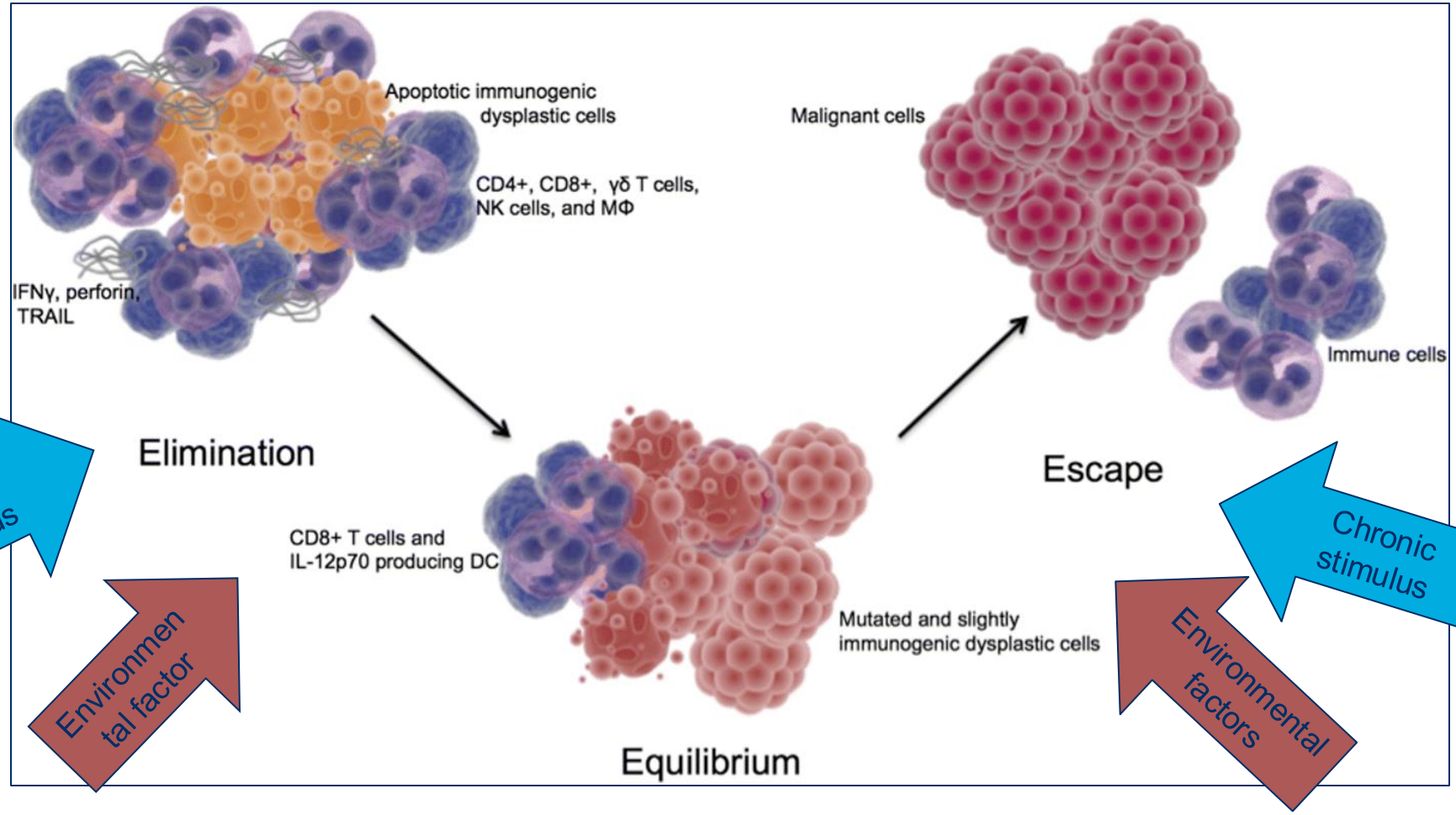
Head and neck cancer

Epidemiology



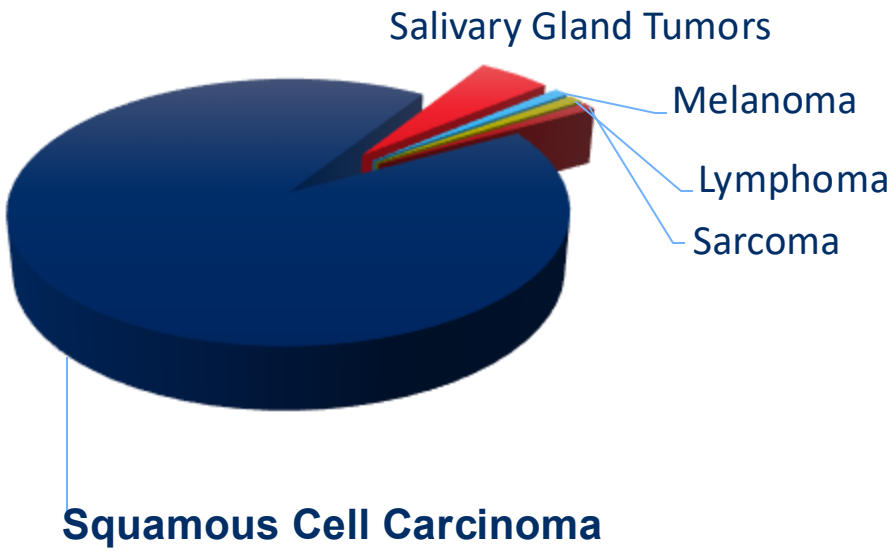
Head and neck cancer

Epidemiology



Head and neck cancer

Pathology

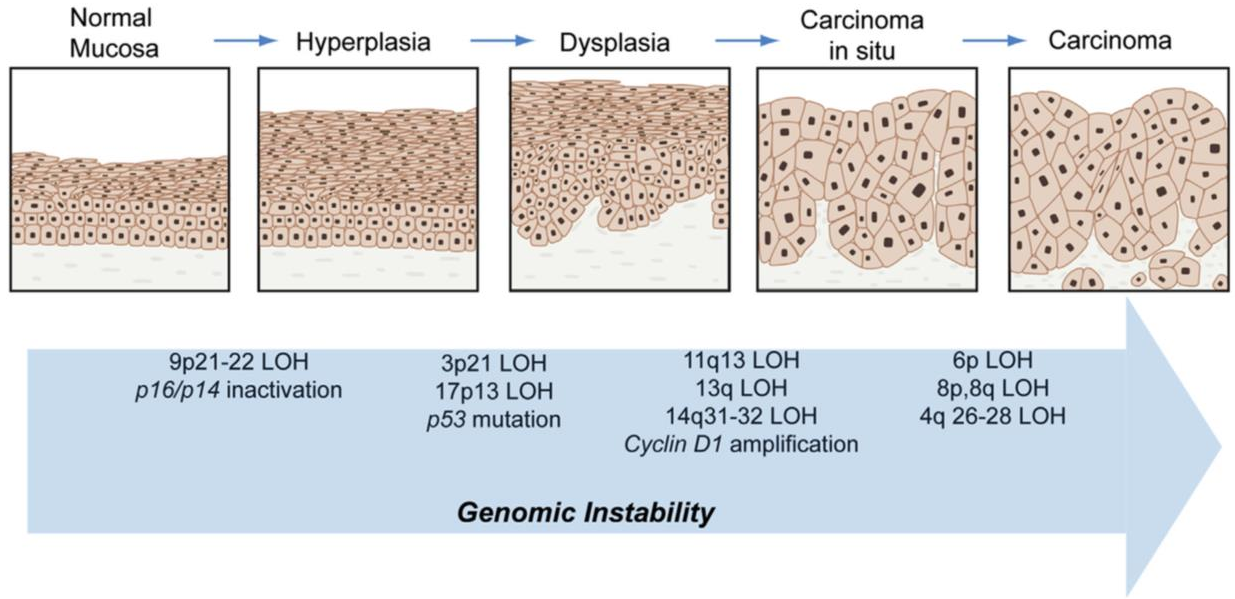


Head and neck cancer

Pathology

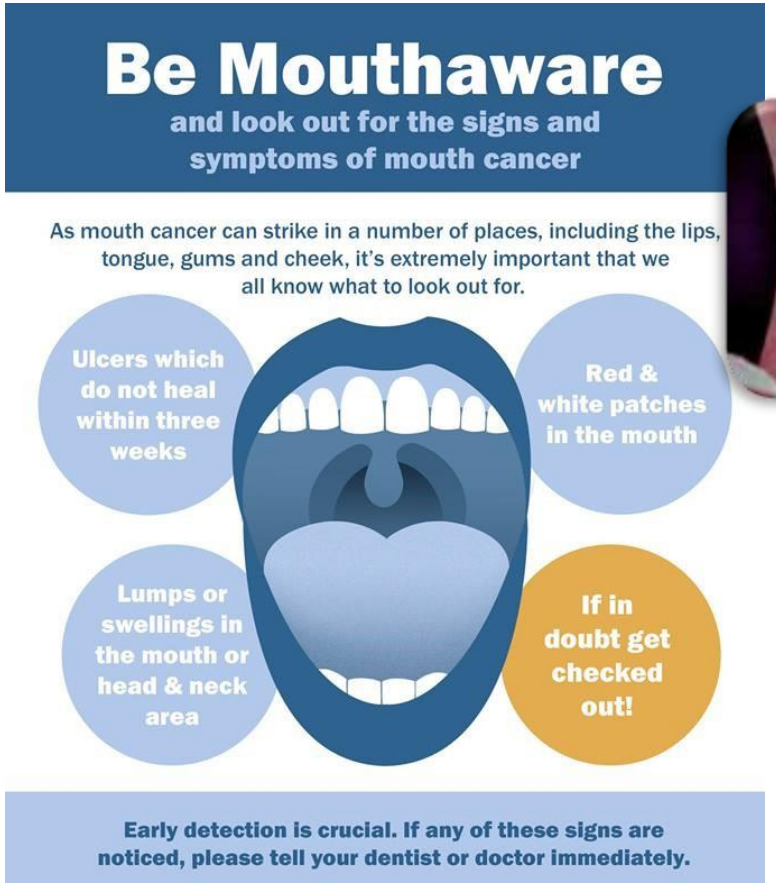
SQUAMOUS CELL CARCINOMA PRECURSORS

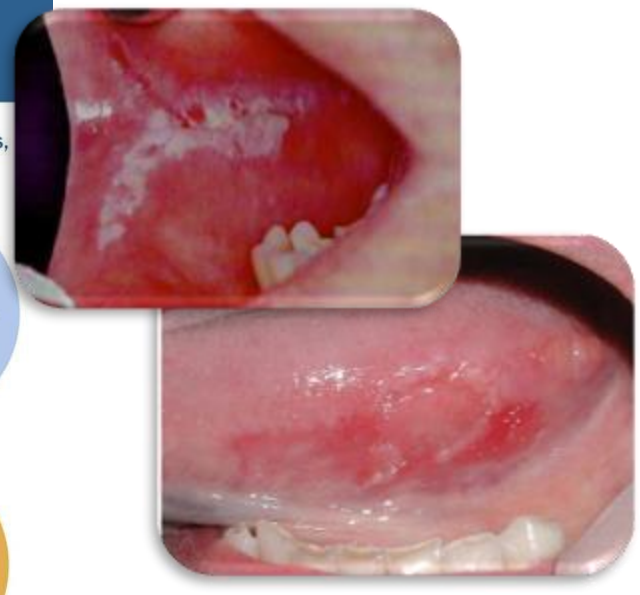
- **Leukoplakia and erythroplakia**
  - **= White and red patches**
- **Squamous hyperplasia**
  - **= Reactive thickened squamous epithelium**
- **Squamous dysplasia**
  - **WHO: Mild, (Moderate), Severe**



Head and neck cancer

Pathology





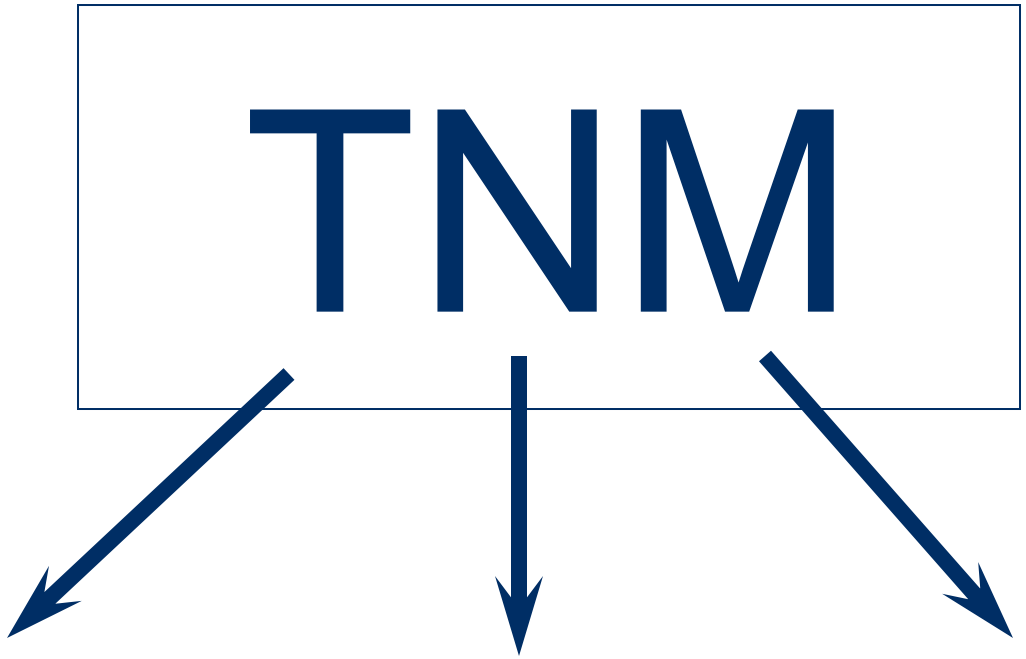
Mostly ASYMPTOMATIC

Head and neck cancer

staging

(UICC & AJCC)

UICC: **Union International Contre le Cancer**
AJCC: **American Joint Committee for Cancer**



Tumor

Neck Node

Metastasis

Head and neck cancer

staging

Cancer of the mucosal lip and oral cavity TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor ≤2 cm with depth of invasion (DOI)* ≤5 mm
T2	Tumor ≤2 cm, with DOI* >5 mm and ≤10 mm; **or** Tumor >2 cm and ≤4 cm, with DOI* ≤10 mm
T3	Tumor >2 cm and ≤4 cm with DOI* >10 mm; **or** Tumor >4 cm with DOI* ≤10 mm
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease. Tumor >4 cm with DOI* >10 mm; **or** Tumor invades adjacent structures only (eg, through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face). *NOTE:* Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4.
T4b	Very advanced local disease. Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery.
* DOI is depth of invasion and **not** tumor thickness.	

Size + Depth

Head and neck cancer

staging

Regional lymph nodes (N)	
Clinical N (cN)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension ENE(–)
N2	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–); **or** Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–); **or** In bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
N2a	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension, and ENE(–)
N2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension, and ENE(–)
N2c	Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, and ENE(–)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(–); **or** Metastasis in any node(s) and clinically overt ENE(+)
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(–)
N3b	Metastasis in any node(s) and clinically overt ENE(+)
NOTE: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(–) or ENE(+).	

Size + Number

Treatment of head and neck oncology

Head and neck cancer

Treatment

Surgery is generally preferred

- easily accessible
- Increased reconstructive options with acceptable functional outcomes
- pathology available for adjuvant treatment selection

Head and neck cancer

Treatment

Reprint of "Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up"☆

J.-P. Machiels[a,b,1], C. René Leemans[c,1], W. Golusinski[d], C. Grau[e], L. Licitra[f], V. Gregoire[g], on behalf of the EHNS Executive Board, ESMO Guidelines Committee, ESTRO Executive Board*

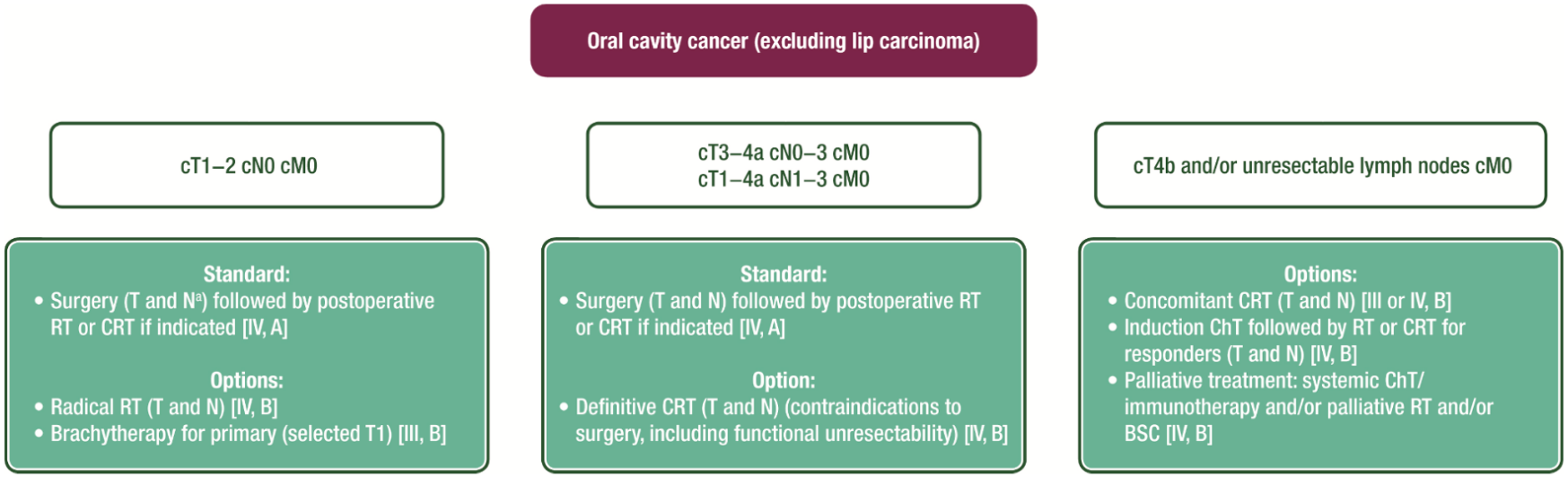


Figure 1. Management of oral cavity cancer (stage I–IVB) excluding lip carcinoma. BSC, best supportive care; ChT, chemotherapy; CRT, chemoradiotherapy; DOI, depth of invasion; M, metastasis; N, node; RT, radiotherapy; T, tumour. [a] If DOI < 10 mm: sentinel lymph node biopsy is a valid option; if DOI < 5 mm and cT1N0, active surveillance of the neck is a valid option.

Surgical treatment of head and neck oncology

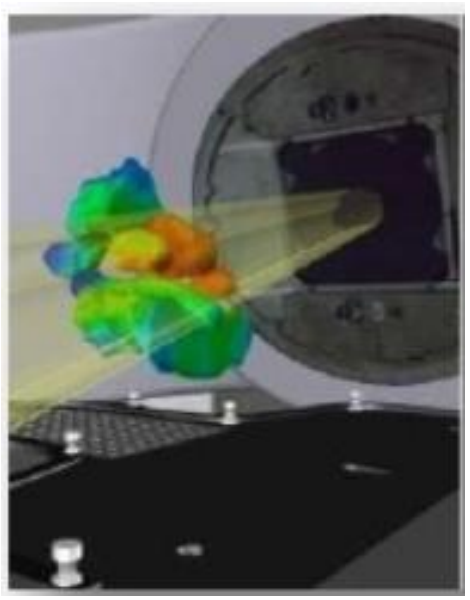

Resection
Neck dissection
Reconstruction

Radiotherapy in head and neck oncology

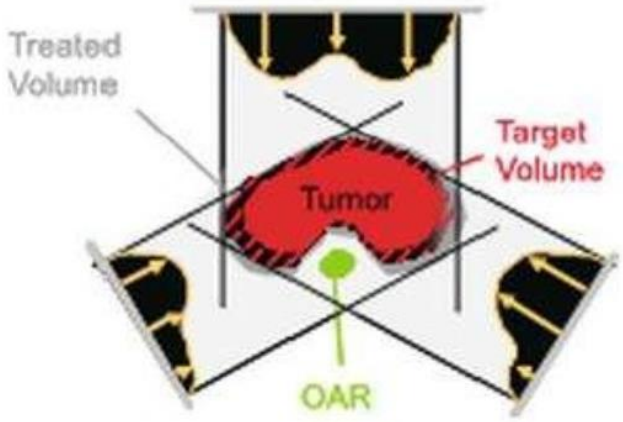
Head and neck cancer

Radiotherapy

External beam radiotherapy



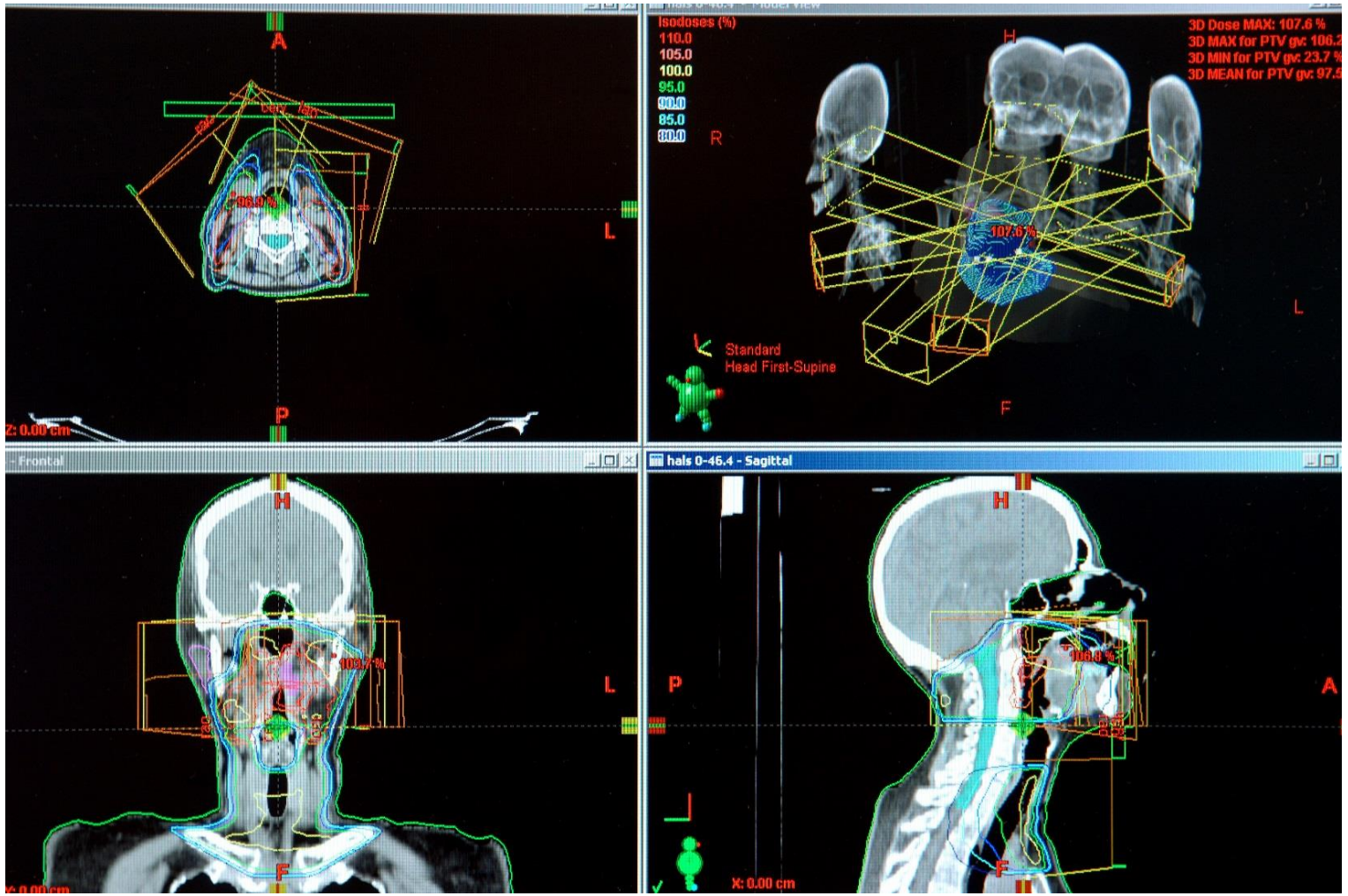
IMRT



Head and neck cancer

Radiotherapy

External beam radiotherapy



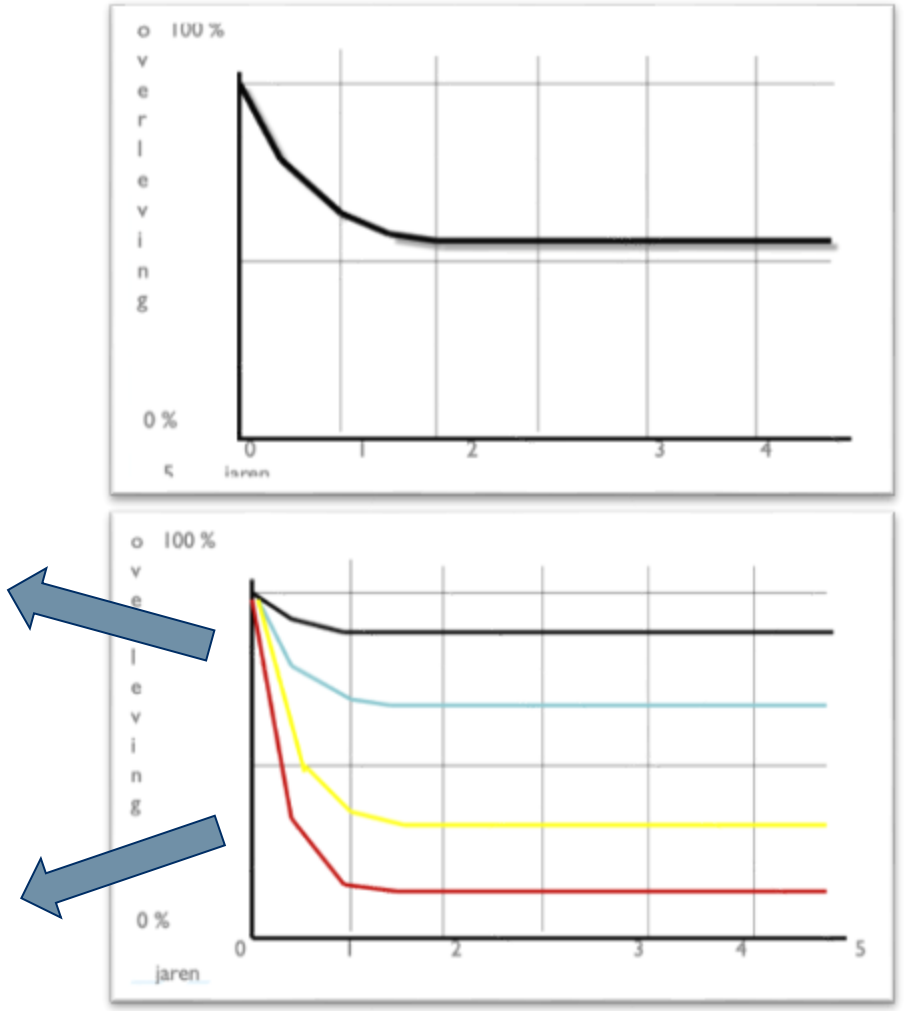
The role of medical oncology in HNSCC to date

Hitherto role for medical oncology in HNSCC

58% survival in
5 years

40% stage I en II
- High cure rate 80 - 90%
- Monomodal therapy

60% stage III en IV
- Lower cure rate 40 - 50%
- Multimodal therapy



Güneri P, Epstein JB. Late stage diagnosis of oral cancer: Components and possible solutions. Oral Oncol (2014), http://dx.doi.org/10.1016/j.oraloncology.2014.09.005

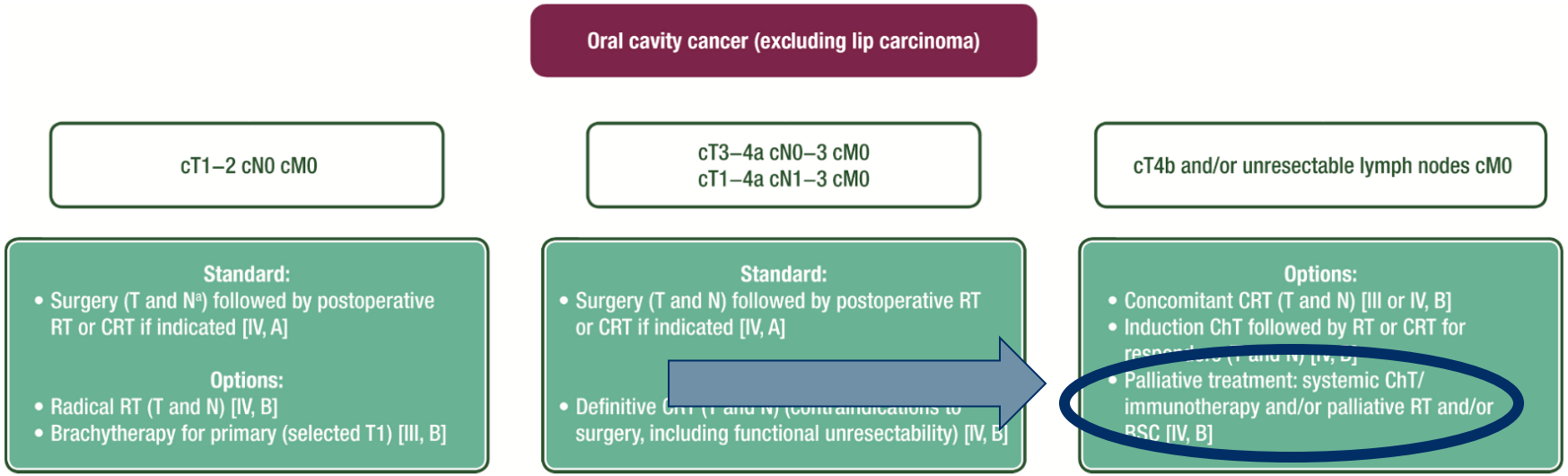
Hitherto role for medical oncology in HNSCC

Chemotherapy for HNSCC

- Remission in +/- 70 % of patients
- But not curative

Hitherto role for medical oncology in HNSCC

Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma



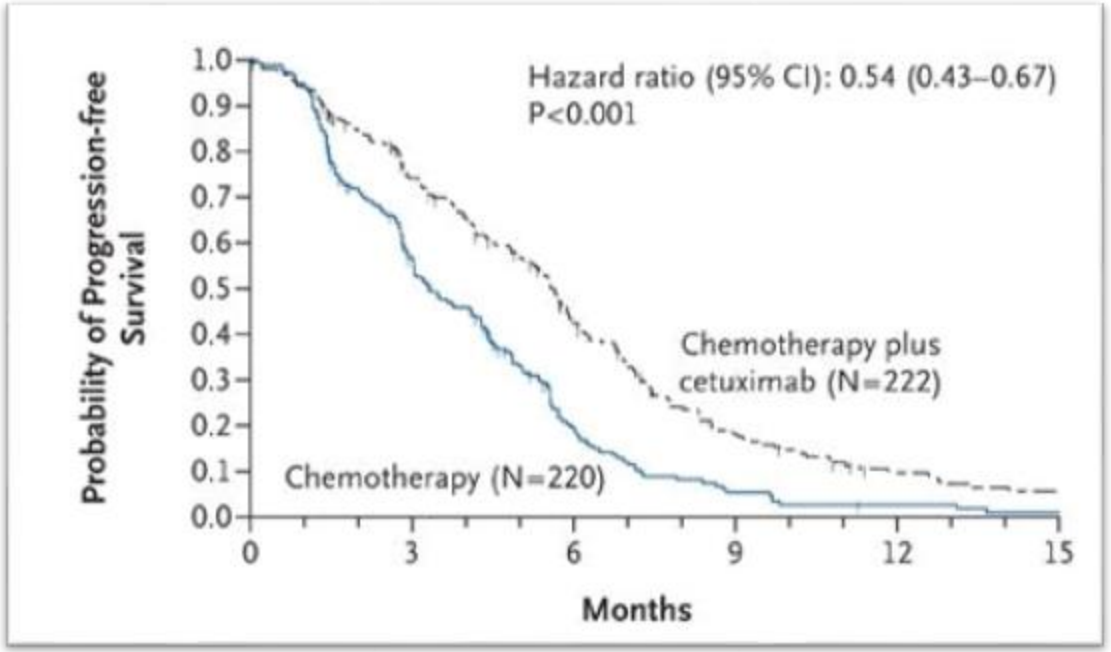
Hitherto role for medical oncology in HNSCC

Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

First line treatment

- **Historically = platinum-based combinations**
- **Cetuximab**

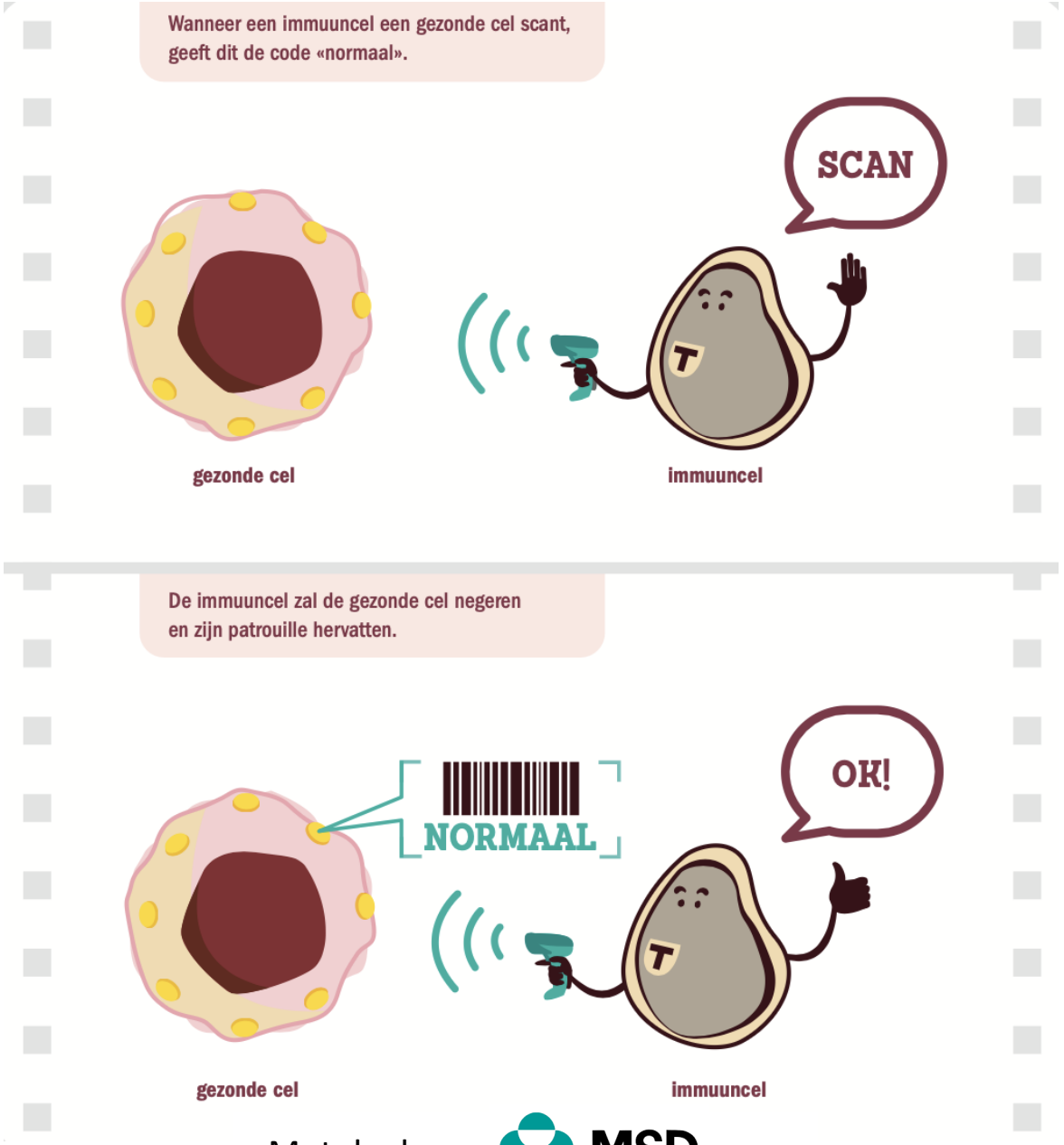
EXTREME



Hitherto role for medical oncology in HNSCC

Met dank aan MSD

Hitherto role for medical oncology in HNSCC



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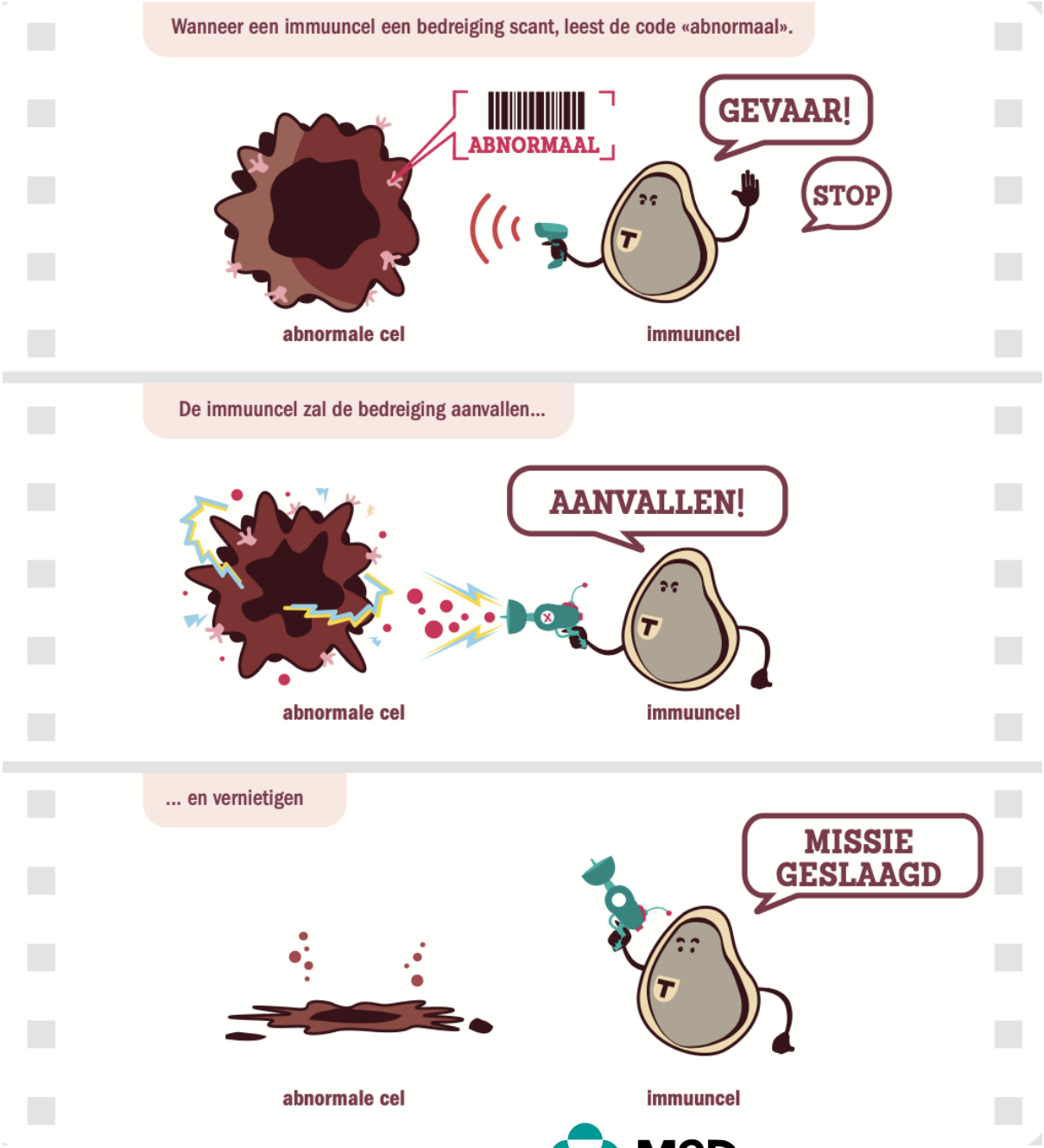


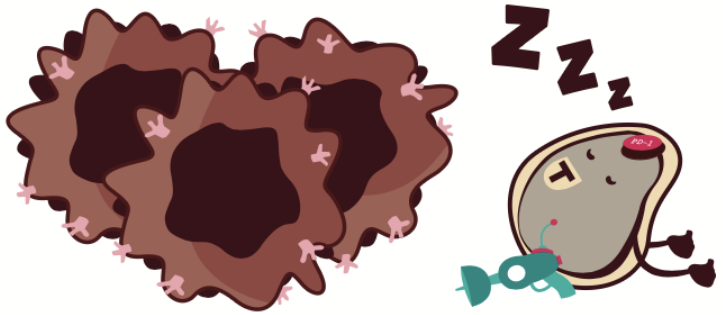
Met dank aan MSD

Hitherto role for medical oncology in HNSCC

Tijdens de ontwikkeling van een kanker, leren de kankercellen om aan het immuunsysteem te ontsnappen. Een mechanisme dat vaak gebruikt wordt door kankercellen is een "**STOP signaal**" waarmee ze op de "**UIT-knop**" van de immuuncellen kunnen duwen.

kankercel immuuncel

Hierdoor vallen de **immuuncellen in slaap** en kunnen de kankercellen ongestoord verder delen en zich verspreiden in het lichaam.



kankercellen immuuncel

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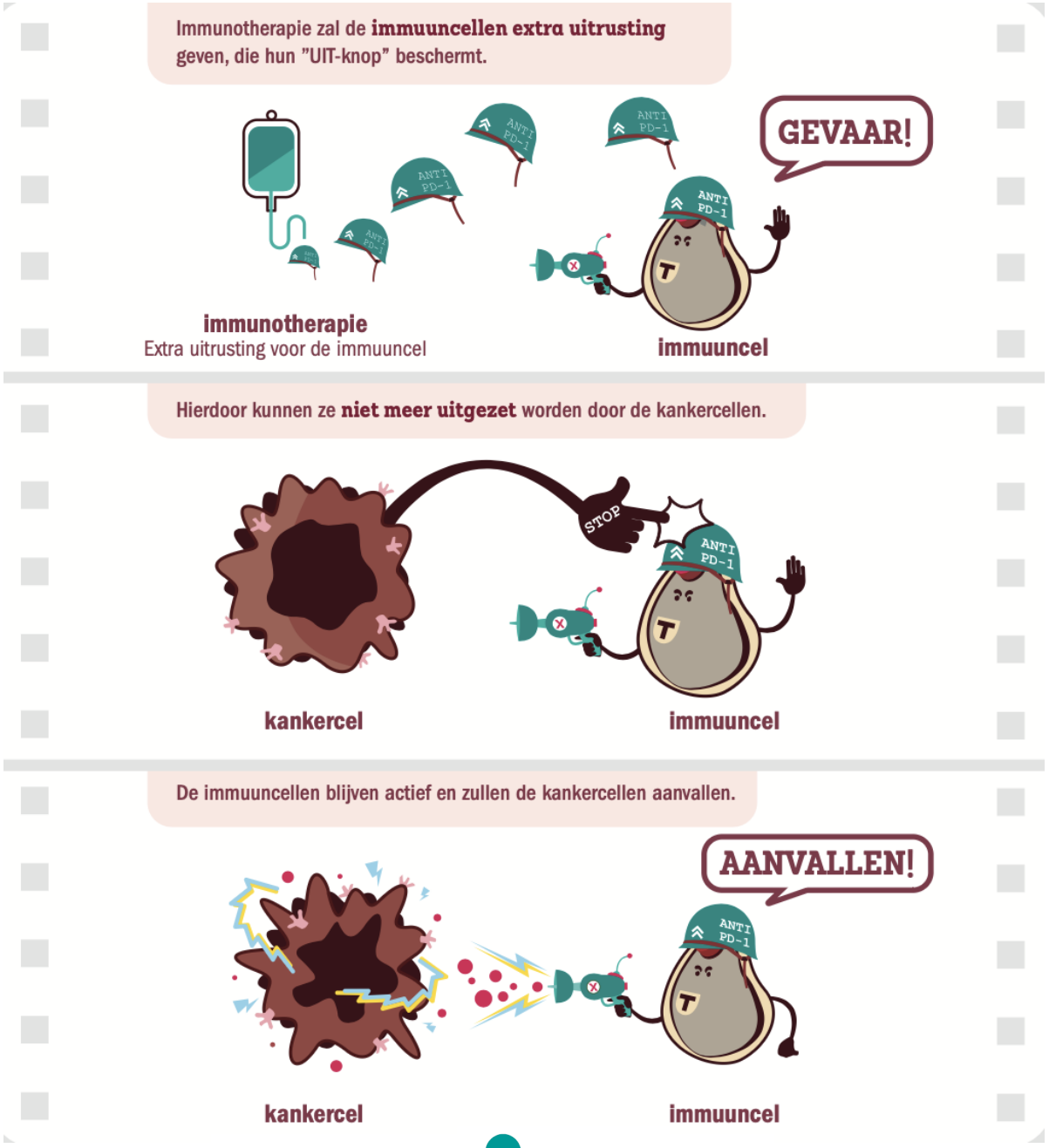
Hitherto role for medical oncology in HNSCC



Met dank aan MSD

Immune system

Hitherto role for medical oncology in HNSCC

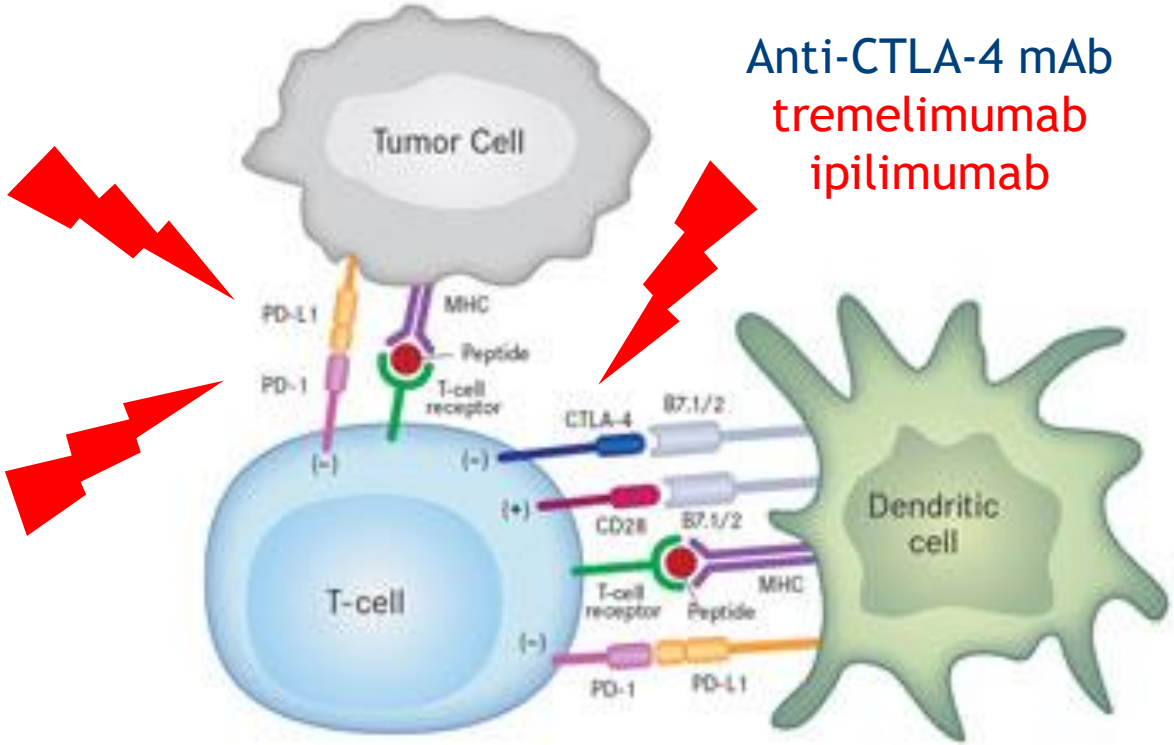
CTLA-4 (cytotoxic T lymphocyte-associated protein 4 = CD152)**/B7** (=CD80/86)

PD-1 (programmed cell death protein 1)**/PD-L1**(programmed cell death ligand 1)

Anti-PD-L1 mAb
durvalumab
atezolizumab
avelumab

Anti-PD-1 mAb
nivolumab
pembrolizumab

Anti-CTLA-4 mAb
tremelimumab
ipilimumab



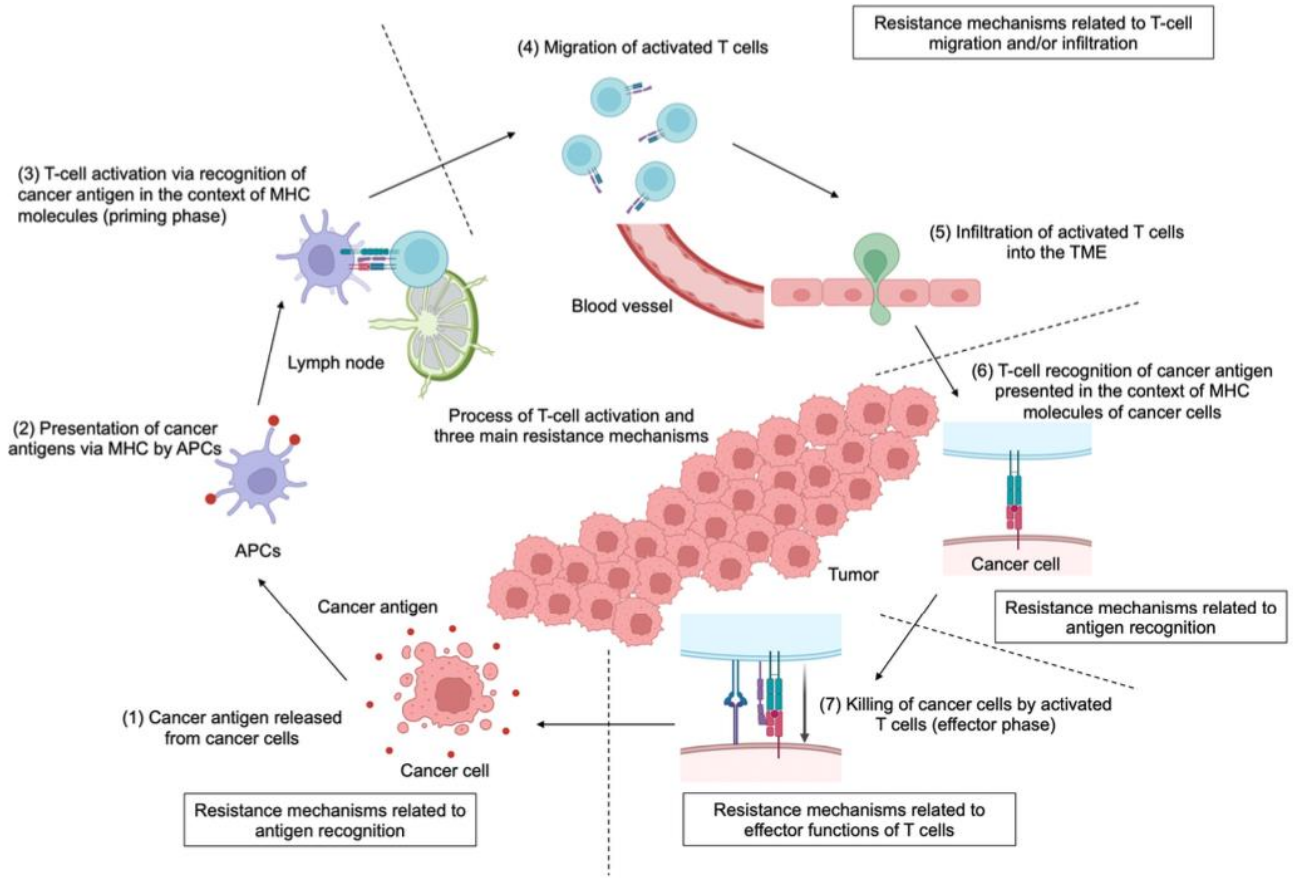
http://www.nature.com/nature/journal/v515/n7528/full/515496a.html
http://www.nature.com/nrc/journal/v12/n4/fig_tab/nrc3239_F1.html

Hitherto role for medical oncology in HNSCC

Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

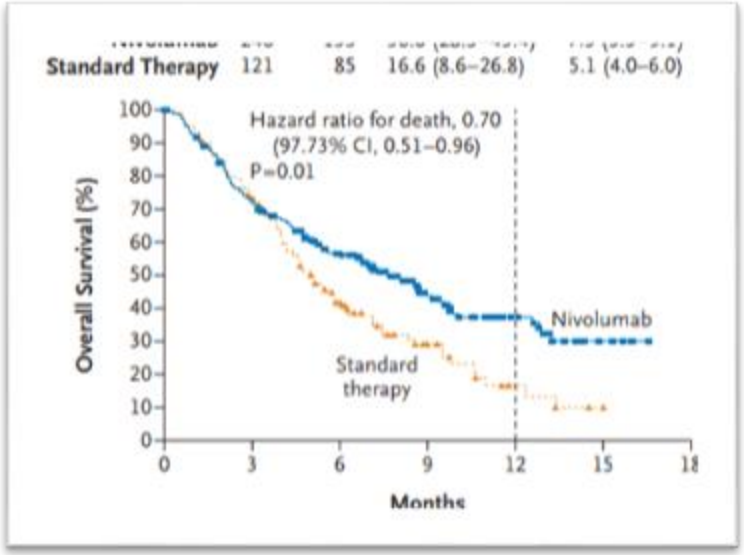
First line treatment

- **Backbone = pembrolizumab**



Hitherto role for medical oncology in HNSCC

CheckMate 141



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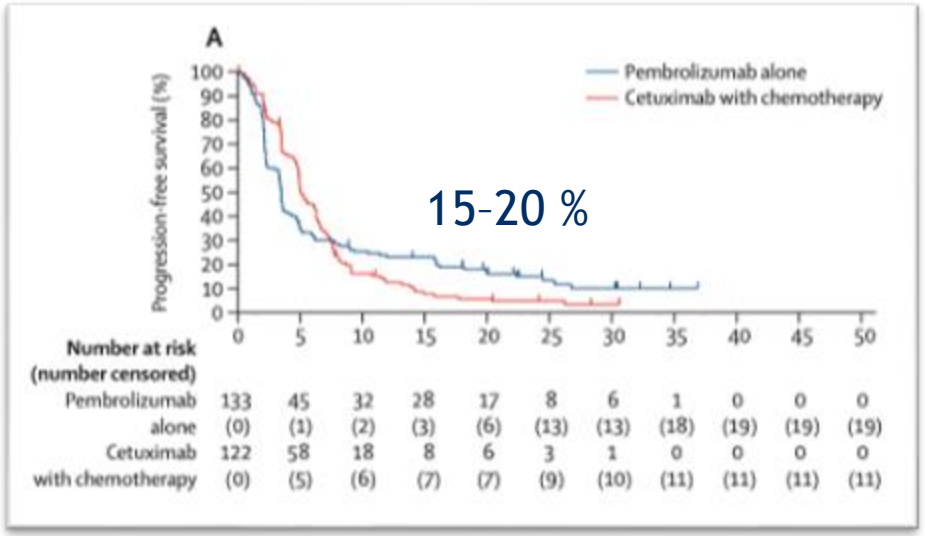

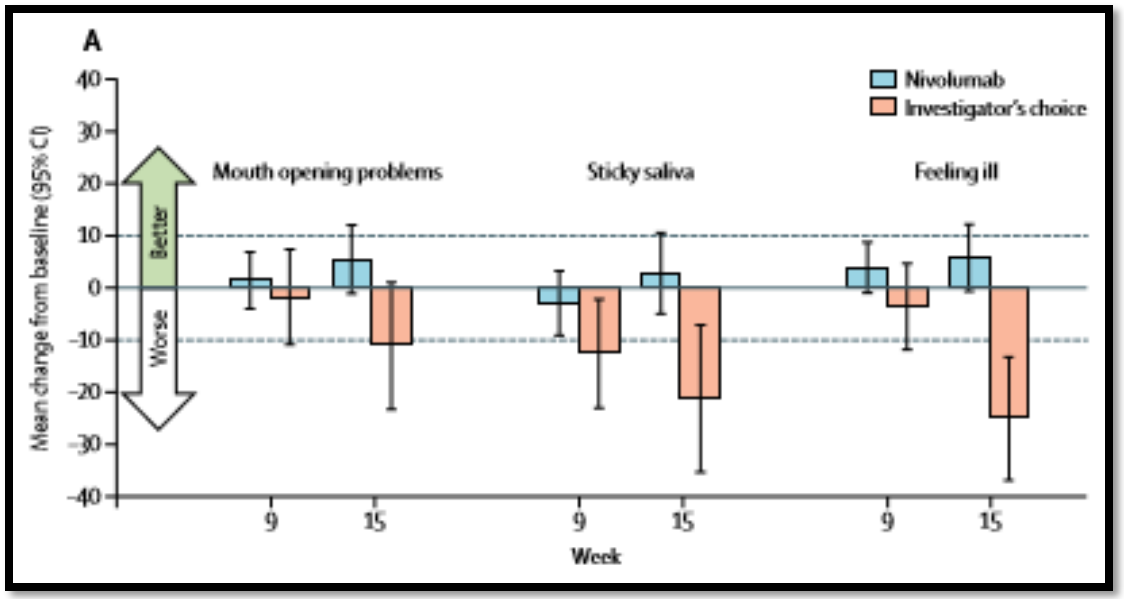

Rationale for change

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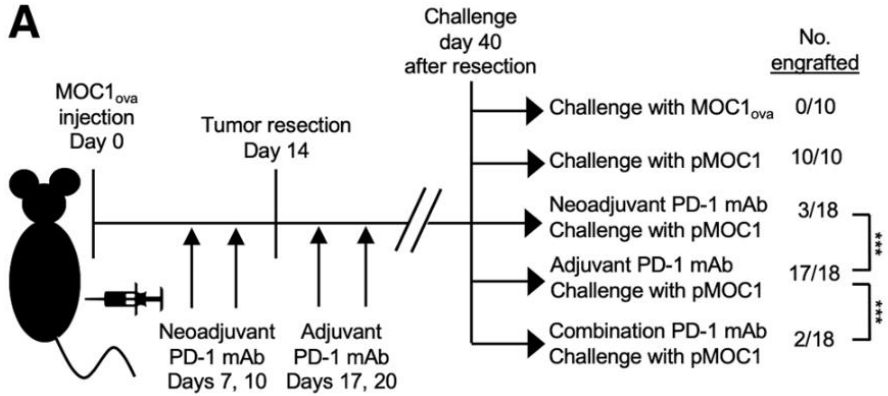
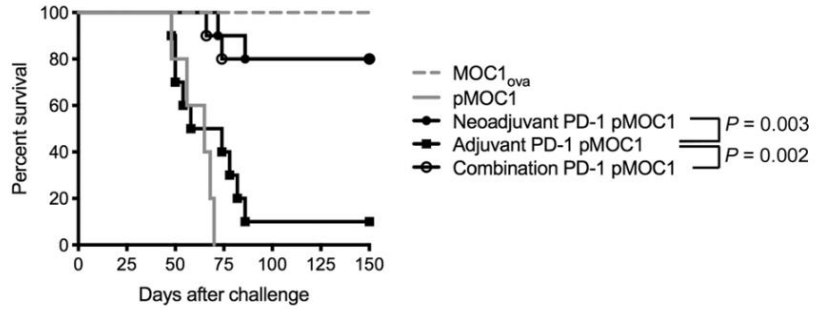
Rationale for change

- Need to improve OS from current SoC
- Clear activity from ICI's in R/M HNSCC but costly and limited proportion of patients are actually responding
- Preclinical date supports that neoadjuvant use of ICI's **may be more effective:**
    - **Amount of responders** may increase since response can be mounted in a treatment naïve patients
    - **Radiological response** may alter sugery
    - **Pathological response** may reduce the need for adjuvant approaches

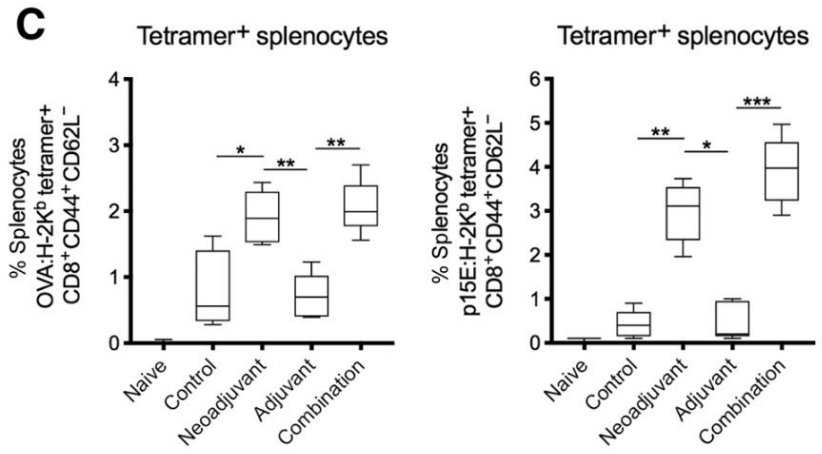
Rationale for change

Friedman 2020





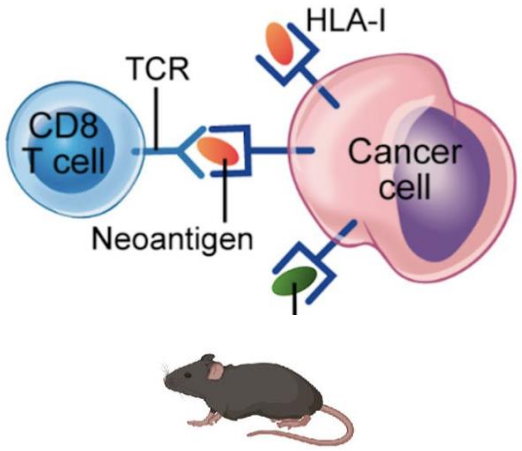
CD 8+ T cells

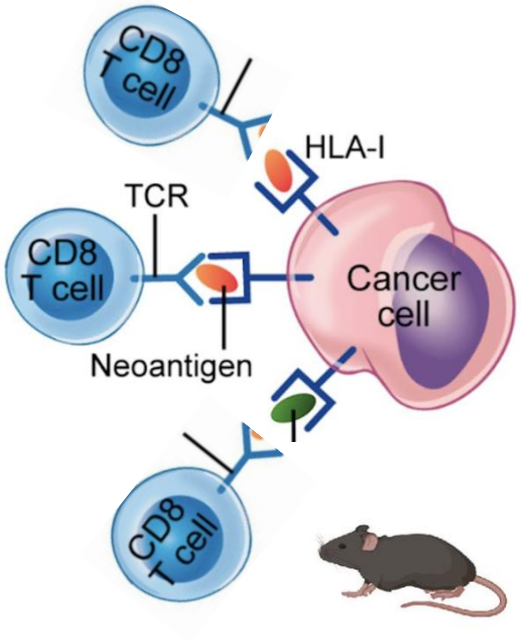


Rationale for change

Friedman 2020

- **Breaks T-cell immunodominance** → broadens clone repertoire
- Durable memory on rechallenge

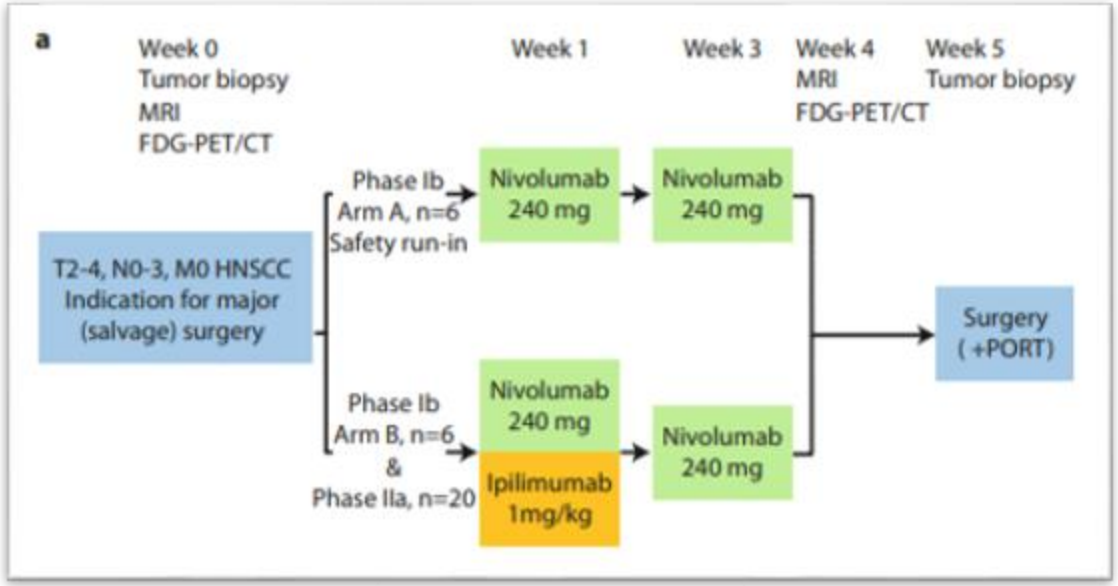




Rationale for change

IMCISION

- **Randomized study with 32 patients**
  - nivolumab (N)
  - combination with ipilimumab (N+I)
- **2 cycles**
  - Week 1
  - Week 3
- **Surgery**
  - 27 days
- **APO**
  - Resection up to the initial tumor margins
  - PORT as SOC based on initial cTNM and not pTNM



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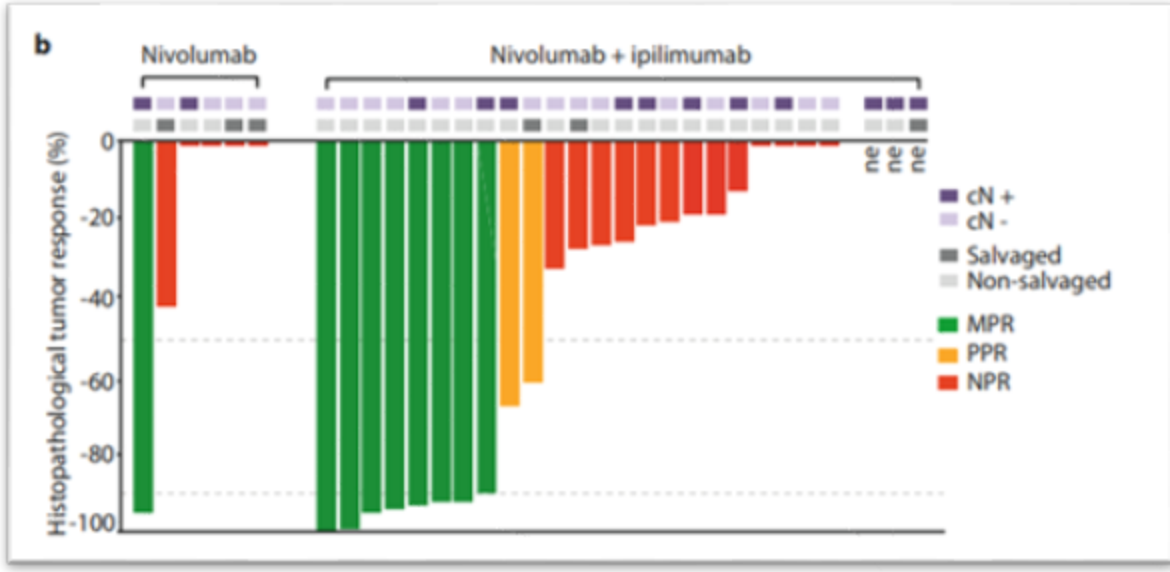
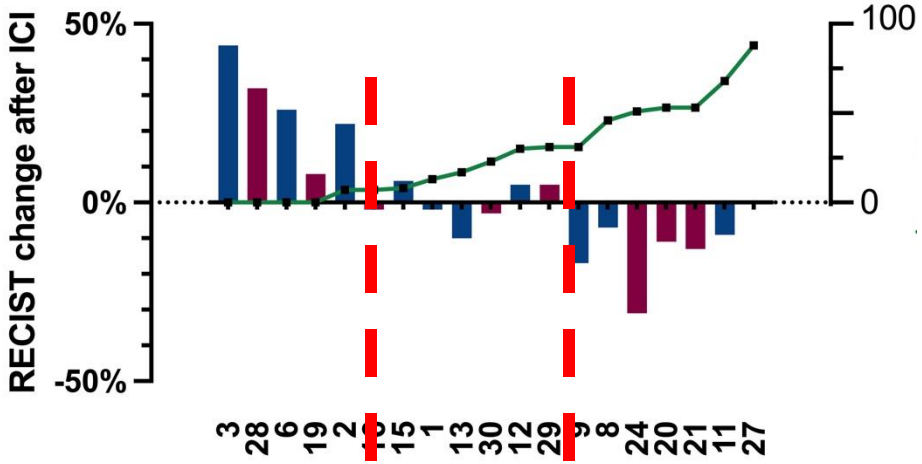


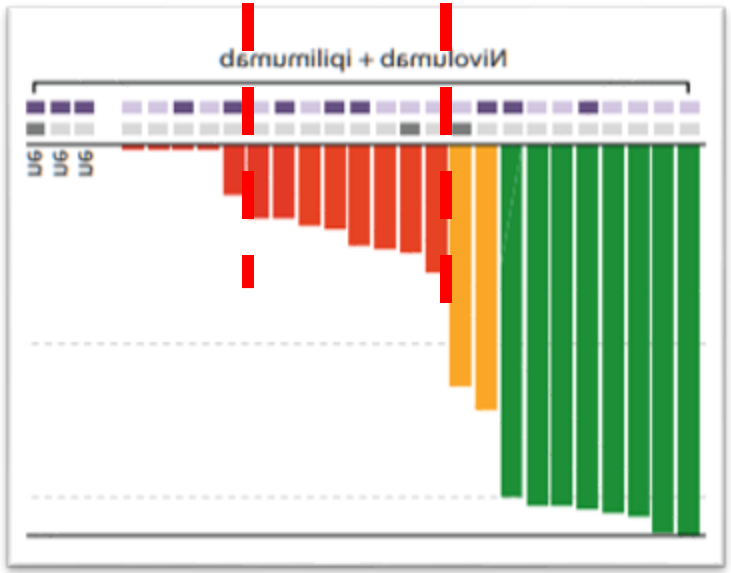
Major pathological response
17% mono
35% combo

Rationale for change

DUTRELASCO

- **20 patients**
  - durvalumab (D) (n=10)
  - combination with tremelimumab (DT (n=10)
- **7 cycles**
  - 14 days prior to surgery
  - 6 adjuvant cycles
- **Surgery**
  - 14 days
- **APO**
  - Resection up to the initial tumor margins
  - PORT as SOC based on initial cTNM and not pTNM





Recent Breakthroughs in HNSCC

Key Advances from Recent Trials

Uppaluri KN689 AACR 2025

KEYNOTE-689 Study

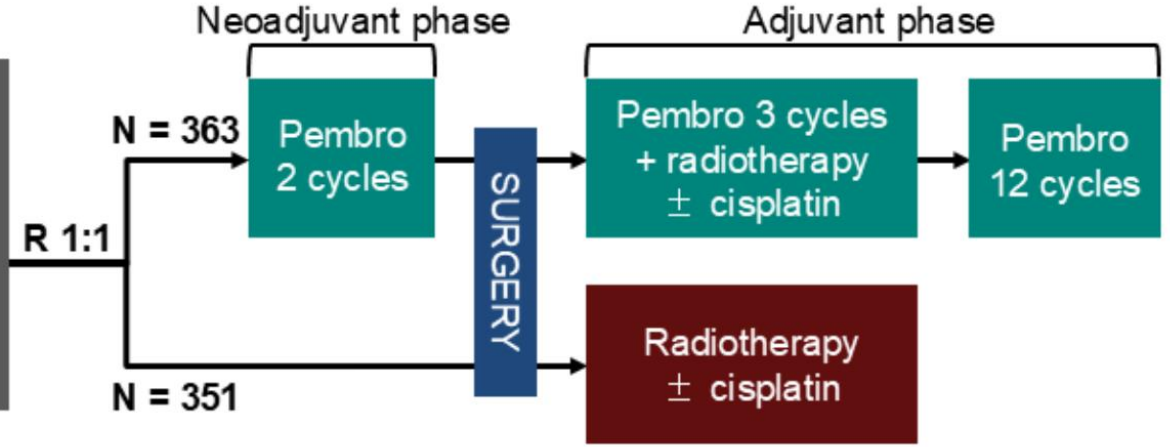
NCT03765918

AACR American Association for Cancer Research ANNUAL MEETING 2025 CHICAGO

APRIL 25–30 | AACR.ORG/AACR2025 | #AACR25

Key Eligibility Criteria

- Adults with resectable LA HNSCC
  - Larynx/hypopharynx/oral cavity stage III/IVA
  - Oropharyngeal stage III/IVA p16−
  - Oropharyngeal stage III T4 N0-2 p16+
- ECOG PS 0 or 1
- Tumor tissue for PD-L1 testing[a]



Stratification factors

- Primary tumor site (oropharynx/oral cavity vs larynx vs hypopharynx)
- Tumor stage (III vs IVA)
- PD-L1 TPS[a] (≥50% vs <50%)

Primary endpoint: EFS per RECIST 1.1 by BICR

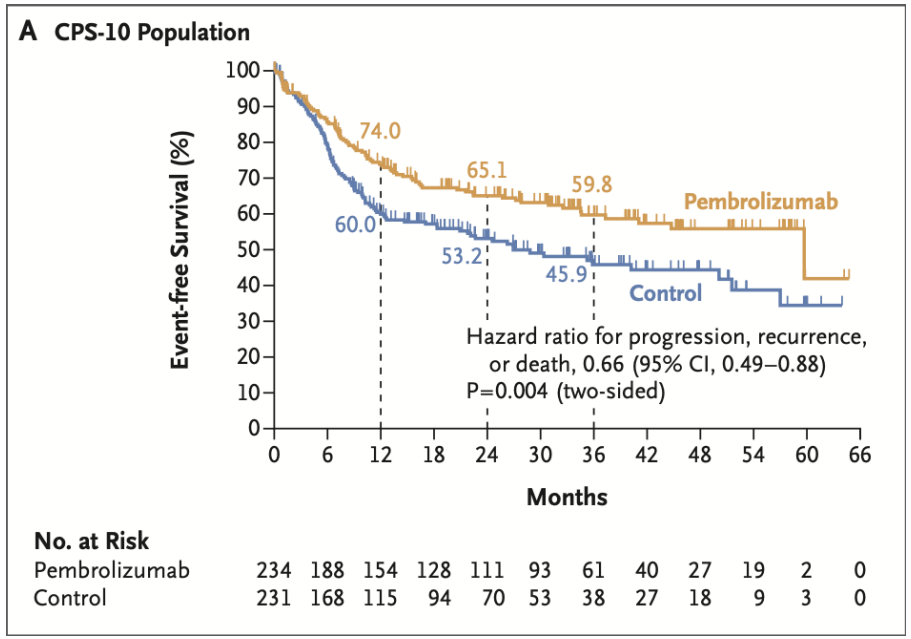
Key secondary endpoints: Major pathological response (mPR; ≤10% residual invasive SCC in resected primary tumor and all sampled regional lymph nodes) by BIPR and OS

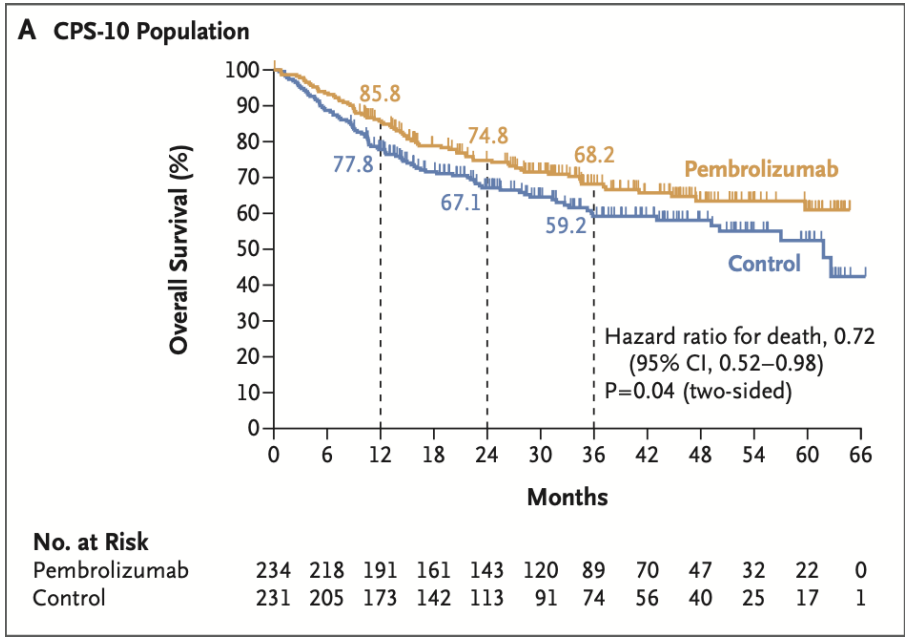
Other secondary endpoints include: Safety

Universiteit Antwerpen UZA ZMACK

Key Advances from Recent Trials

KEYNOTE-689 Study





Key Advances from Recent Trials

KEYNOTE-689 Study

		Pembro + SOC	SOC
Study start	Participants randomized (Dec 2018-Oct 2023), N	363	351
Neoadjuvant therapy	Received ≥1 dose of neoadjuvant pembrolizumab, n (%)	360 (99.2)	2[a] (0.6)
	Completed 2 cycles of pembrolizumab, n (%)	341 (93.9)	1 (0.3)
	Permanently discontinued all study therapy at this phase, n (%)	30 (8.3)	0
In-study therapy	Underwent surgery, n (%)	322 (88.7)	308 (87.7)
	Completed surgery	321 (88.4)	308 (87.7)
	Tumor found to be surgically unresectable	1 (0.3)	0
	Permanently discontinued all study therapy at this phase, n (%)	55 (15.2)	41 (11.7)
	Postoperative risk assessment by BIPR, n (%)		
	High-risk features present	118 (32.5)	156 (44.4)
	Low risk (no high-risk features present)	196 (54.0)	148 (42.2)
	Missing	49 (13.5)	47 (13.4)
Adjuvant therapy	Received ≥1 dose of adjuvant therapy after surgery, n (%)	267 (73.6)[b]	267 (76.1)[b]
	Started radiotherapy	266 (73.3)	267 (76.1)
	Started pembrolizumab	248 (68.3)	0
	Started cisplatin	100 (27.5)	132 (37.6)
	Permanently discontinued all study therapy at this phase, n (%)	109 (30.0)	14 (4.0)
All study treatment	Completed all study treatment, n (%)	155 (42.7)	261 (74.4)
	Treatment ongoing, n (%)	11 (3.0)	0

Key Advances from Recent Trials

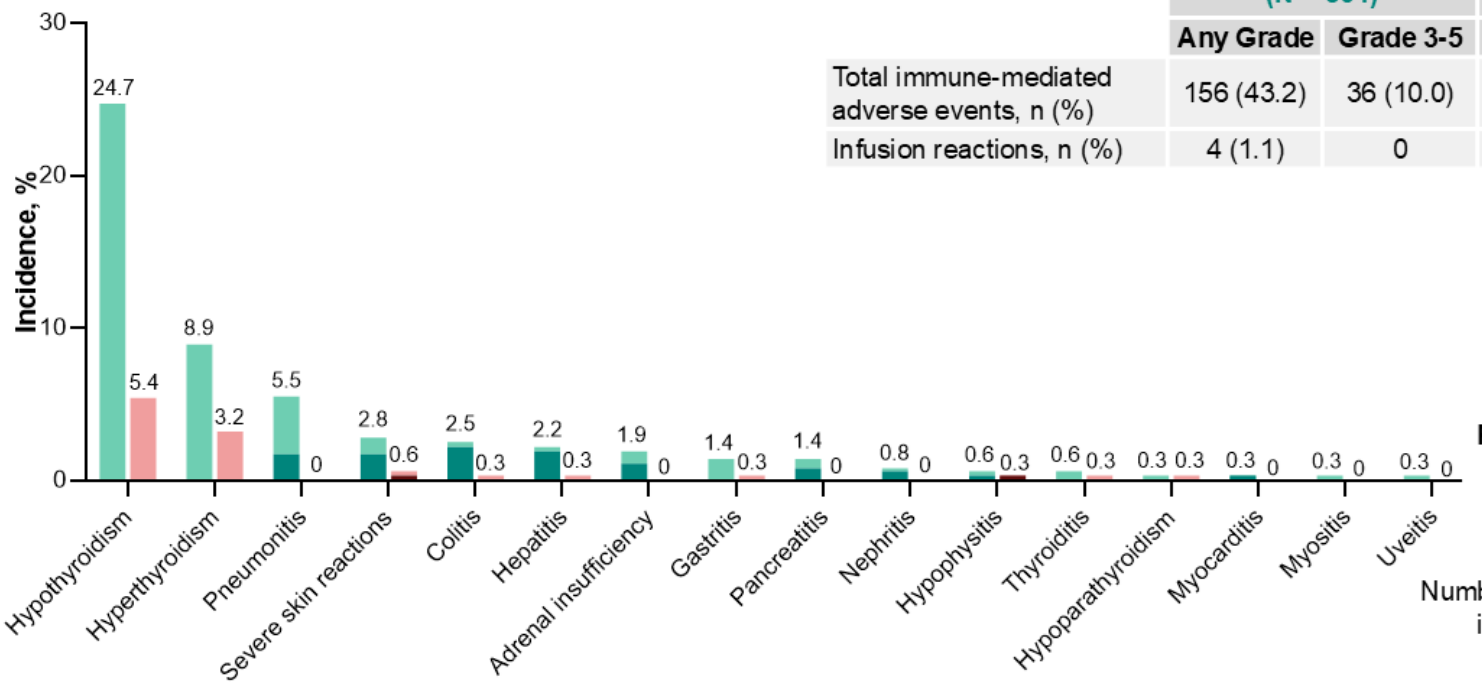
KEYNOTE-689 Study

Uppaluri KN689 AACR 2025

Immune-Mediated AEs

As-Treated Population

	Pembro + SOC (N = 361)		SOC (N = 315)	
	Any Grade	Grade 3-5	Any Grade	Grade 3-5
Total immune-mediated adverse events, n (%)	156 (43.2)	36 (10.0)	32 (10.2)	2 (0.6)
Infusion reactions, n (%)	4 (1.1)	0	2 (0.6)	0



Numbers above bars show total incidence of any-grade AE.

One grade 5 event of pneumonitis occurred.

Data cutoff date: 25 July 2024

Immune-mediated AEs are based on a list of preferred terms intended to capture known risks of pembro considered regardless of attribution to study treatment by investigator.

Key Advances from Recent Trials

IMPACT OF TIME OF DAY

Paul Clement

	Total	Early in the day (≤13h)	Late in the day (>13h)
Cycles			
C1	255	126 (49%)	129 (51%)
C2	242	109 (45%)	133 (55%)
C3	224	73 (33%)	151 (67%)
C1C2	242	62 (26%)	180 (74%)

Table 1: Distribution of Infusion Administration Across Treatment Cycles C1, C2, and C3.

Key Advances from Recent Trials

IMPACT OF TIME OF DAY

Paul Clement

- **Circadian gating of antitumour immunity.**
  - Aligning PD-1 blockade with the “active” immune phase enhances effector function.
  - Circulating $CD8^+$, $CD4^+$, NK and dendritic cells show day–night variation with higher morning trafficking
  - PD-1/PD-L1 axis is time-dependent (changes in PD-1 expression and TCR signalling thresholds)
- **Morning timing, especially during the first 2 cycles**
- **Pharmacokinetics are not the driver.**
  - nivolumab/pembrolizumab have a long half-live

Future practices

Future

FAGG approval

Available under MNP since 28/08/2025

Keytruda - pembrolizumab

Voor behandeling van resecteerbaar stadium III-IVA lokaal gevorderd plaveiselcelcarcinoom van het hoofd en hals gebied als neoadjuvante behandeling, voortgezet als adjuvante behandeling in combinatie met radiotherapie met of zonder cisplatine, en vervolgens als monotherapie bij volwassenen waarvan de tumoren PD-L1 tot expressie brengen met een CPS ≥ 1.

Reïmbursement pending…

Future

Practicalities

- **Include patients from the first presentation**
  - Stage III-IV HNSCC
  - THAT CAN WAIT
- **Sequential Imaging**
  - DWI + perfusion MRI imaging
  - 18-FDG-PET
- **Morning dosing of ICI**
- **Surgery week 5-6**
  - Early surgery only if progression after 1 dose:
- **Keep data centralized**
  - VWHHT?

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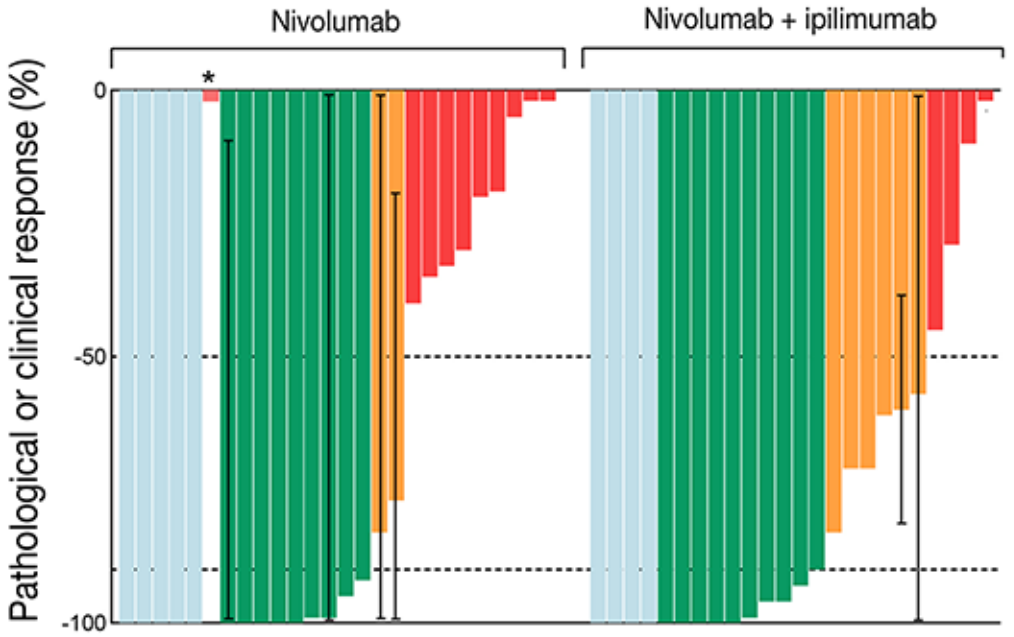
Future

Open questions

- What about the complete responders?

IMCISION

MATISSE



9 of the 50 patients withdrew consent to surgery and RT
all 9 remained cancer-free after 18 months,

Questions?

Feel free to ask!