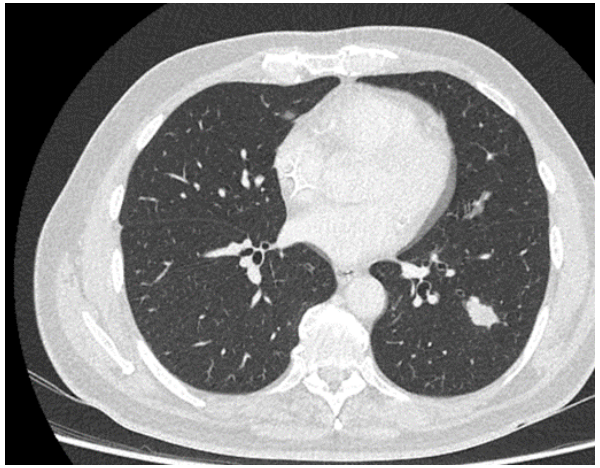
Leitlinie
Plattenepithelkarzinome

Konrad Klinghammer

ONKOPEDIA – Online-Seminar

11.7.2025



Offenlegung Interessenskonflikte

1. Anstellungsverhältnis oder Führungsposition
Arbeitsgruppensprecher der AIO Kopf Hals Gruppe

2. Beratungs- bzw. Gutachtertätigkeit
GBA, MSD, Merck Serono, BMS, Roche, Novartis; astellas, gsk, Biontech, BeiGene, Pfizer, LeoPharma

3. Besitz von Geschäftsanteilen, Aktien oder Fonds
keine

4. Patent, Urheberrecht, Verkaufslizenz
keine

5. Honorare
MSD, Merck Serono, BMS, gsk, Biontech,

6. Finanzierung wissenschaftlicher Untersuchungen
Merck Serono

7. Andere finanzielle Beziehungen
keine

8. Immaterielle Interessenkonflikte
Leitlinienautor AWMF Speicheldrüsen, Mundhöhle, onkopedia Speicheldrüse und Plattenepithelkarzinome

Agenda

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Aufbau

- Fallbeispiel 1
- Epidemiologie
- Biologie
- Klinisches Bild
- Diagnostik
- Therapie
  - im kurativen Setting
  - im palliativen Setting

Fallbeispiel

Leitlinie

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männlich, Alter 65 Jahre

Hypopharynxkarzinom

Tumorformel: cT3, cN2b, cM0.

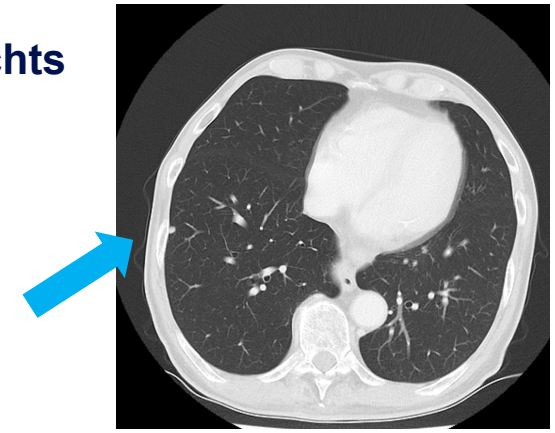
Histologie: Nicht verhornendes invasives Plattenepithelkarzinom, Ki-67: 40 %, p16 negativ, PD-L1 CPS 6

ND: Leberzirrhose mit Zn TIPPS Anlage

08.-10.2021 Definitive Radiochemotherapie nach HART kumulativen Gesamtdosis von 72 Gy im Bereich des Primärtumors und der Lymphknotenmetastase sowie der elektiven Lymphabflusswege zervikal beidseits.

Simultane Chemotherapie Cisplatin 180 mg/m² KOF kumulativ.

17.01.2022 Staging-CT - neue metastasensuspekte Raumforderungen pulmonal rechts



Einstiegsfrage

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Was würden Sie jetzt machen?

Fragen an die Teilnehmer

Frage1: stereotaktische RT

Frage 2: VATS

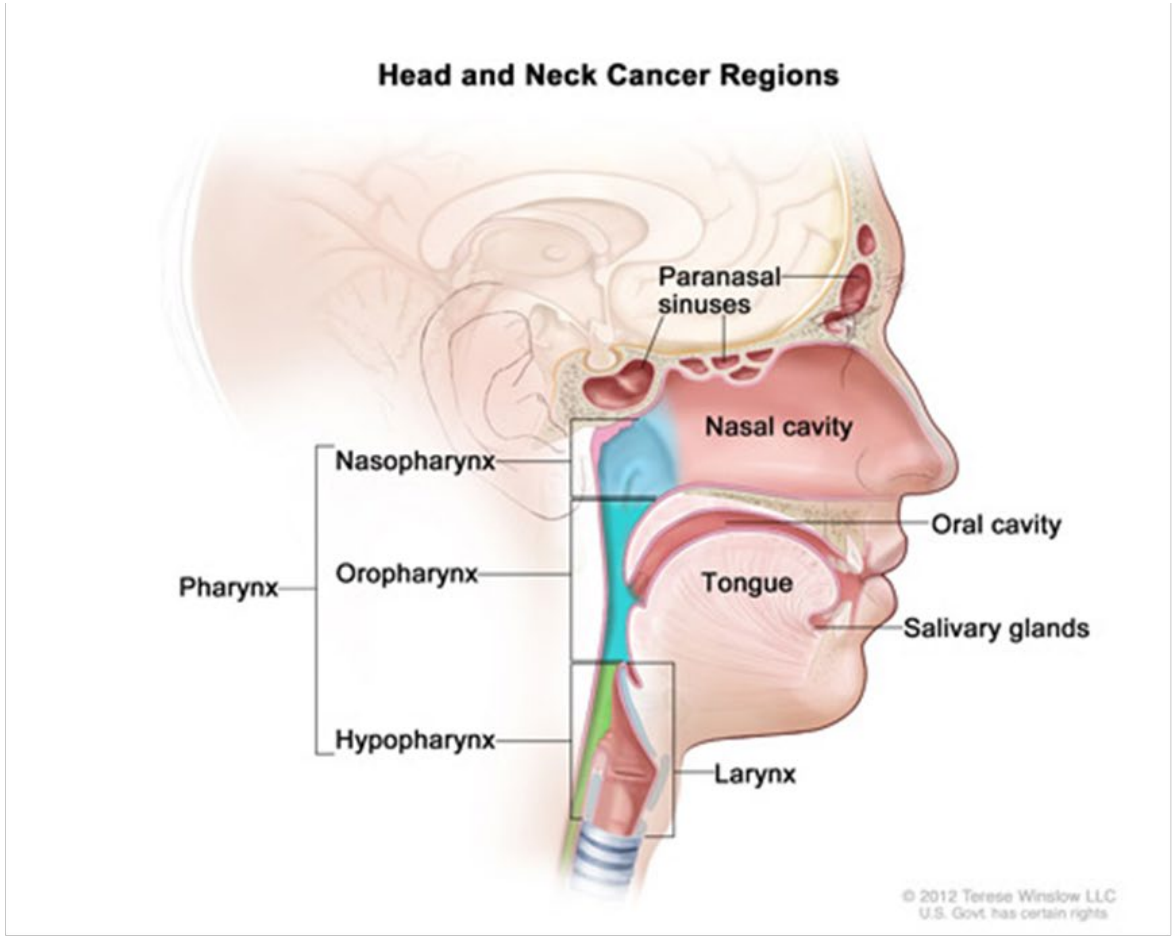
Frage 3: watch and wait

Frage 4: Immuntherapie

Frage 5: Chemo – Cetuximab Kombination

Frage 6: Chemo Pembrolizumab Kombination

Kopf-Hals Karzinome – heterogene Tumore!



Plattenepithelkarzinome
90%

Speicheldrüsenkarzinome
8%

Epidemiologie

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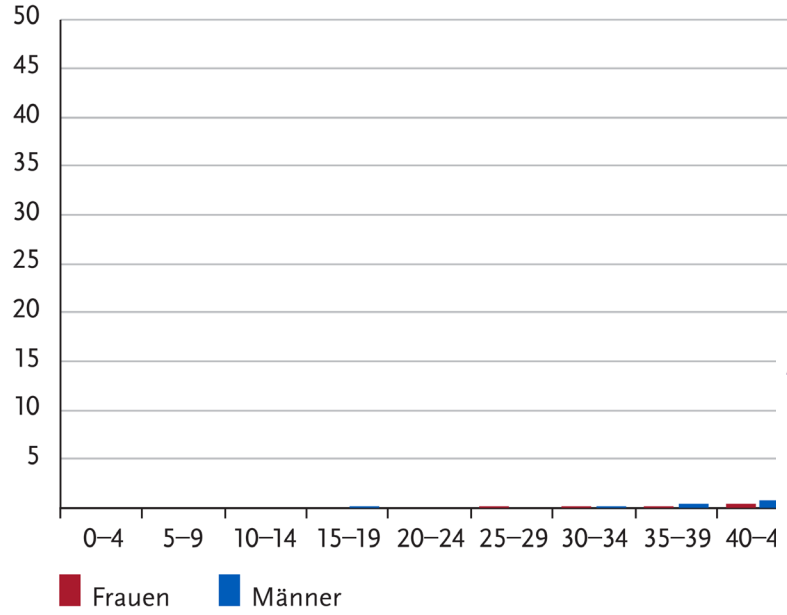
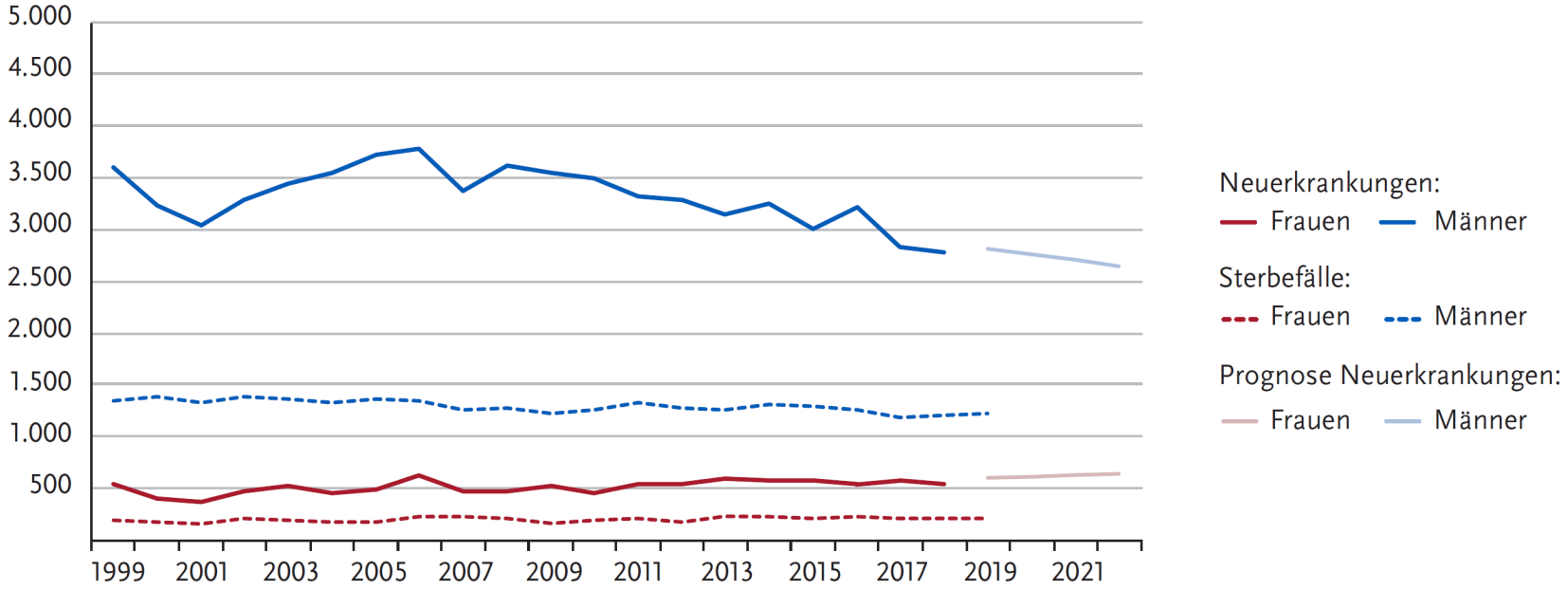
6. häufigste Tumorerkrankung

Altersspezifische Neuerkrankungsraten nach Geschlecht, ICD-10 C32, Deutschland 2017–2018
je 100.000



Absolute Zahl der Neuerkrankungs- und Sterbefälle nach Geschlecht, ICD-10 C32, Deutschland 1999–2018/2019, Prognose (Inzidenz) bis 2022



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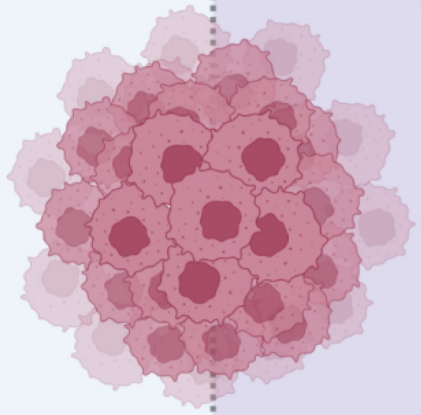
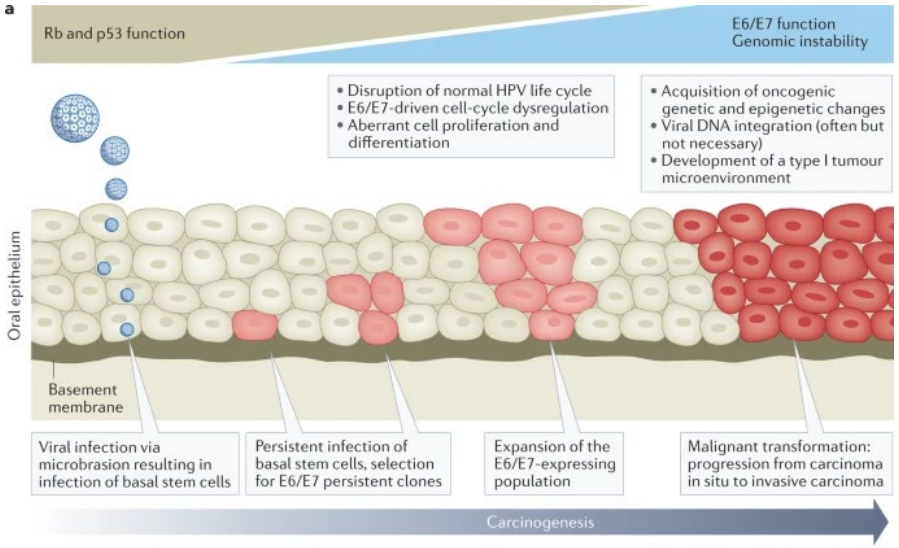
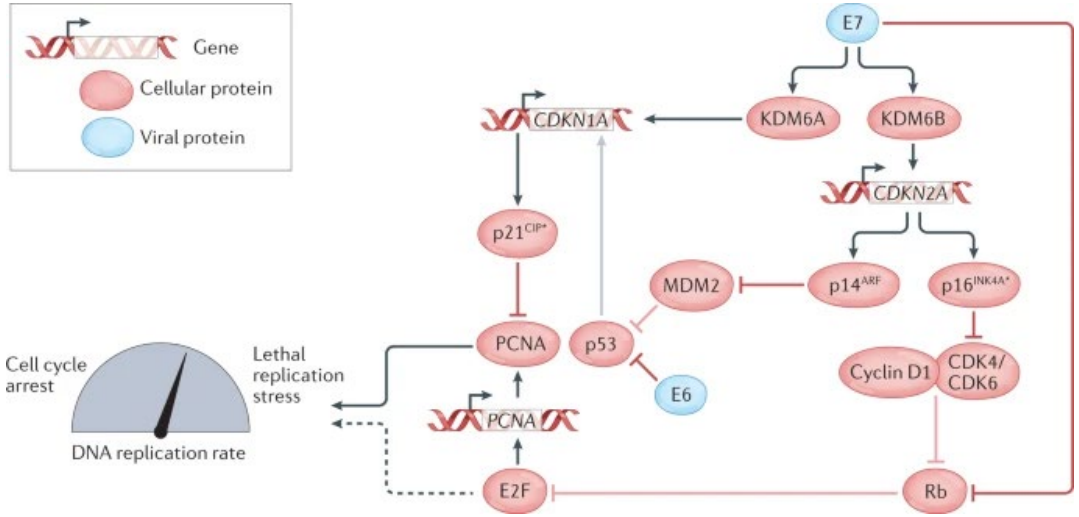
HPV negativ vs. HPV positiv

HPV+	HPV-
Amplification	**Amplification**
E2F1	*EGFR*
TNFRSF1	*HER2/ ERBB2*
ALG3	*FGFR1*
IGF2BP2	*TERT*
	JAK2
Loss	**Loss**
TRAF3	*CDKN2A*
BIRC3	*LRP1B*
ATM	*PTEN*
SMAD9	*NOTCH1*
EZH2	*SMAD4*
Mutation	**Mutation**
PIK3CA	*TP53*
FGFR3	*CDKN2A*
MLL2/3	*NRF2*
NOTCH1	*KEAP1*







Therapie im kurativen Setting

- Mundhöhlenkarzinome primär operativ
- Pharynxkarzinome chirurgische Therapie gegenüber der definitiven Bestrahlung hinsichtlich des onkologischen Ergebnisses gleichwertig

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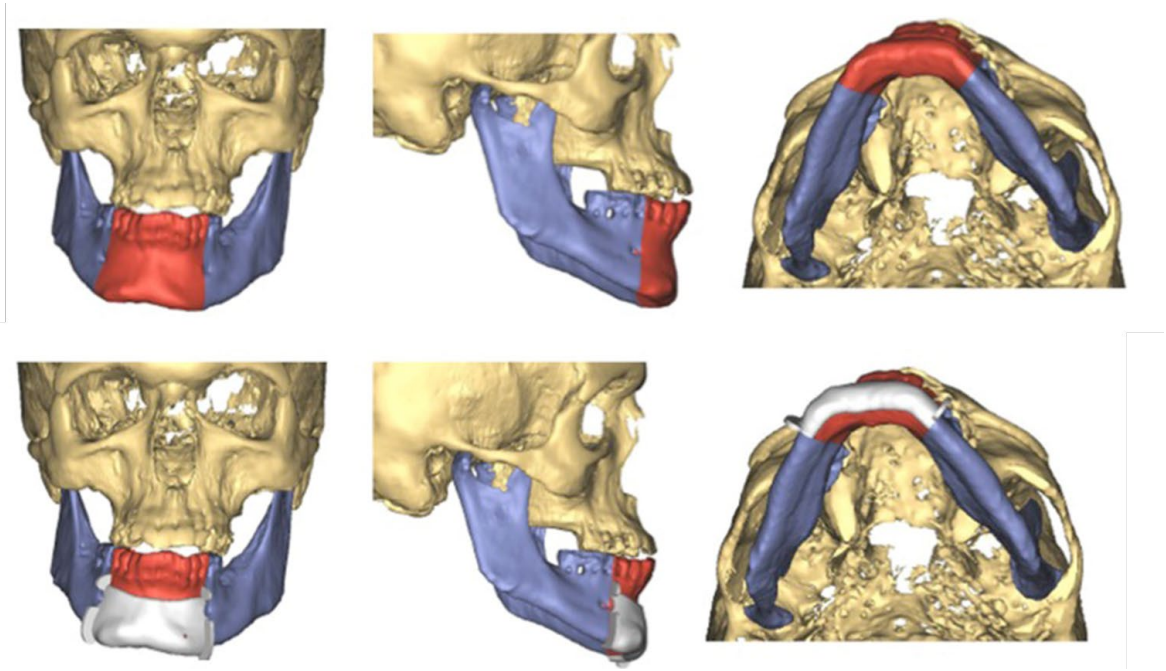
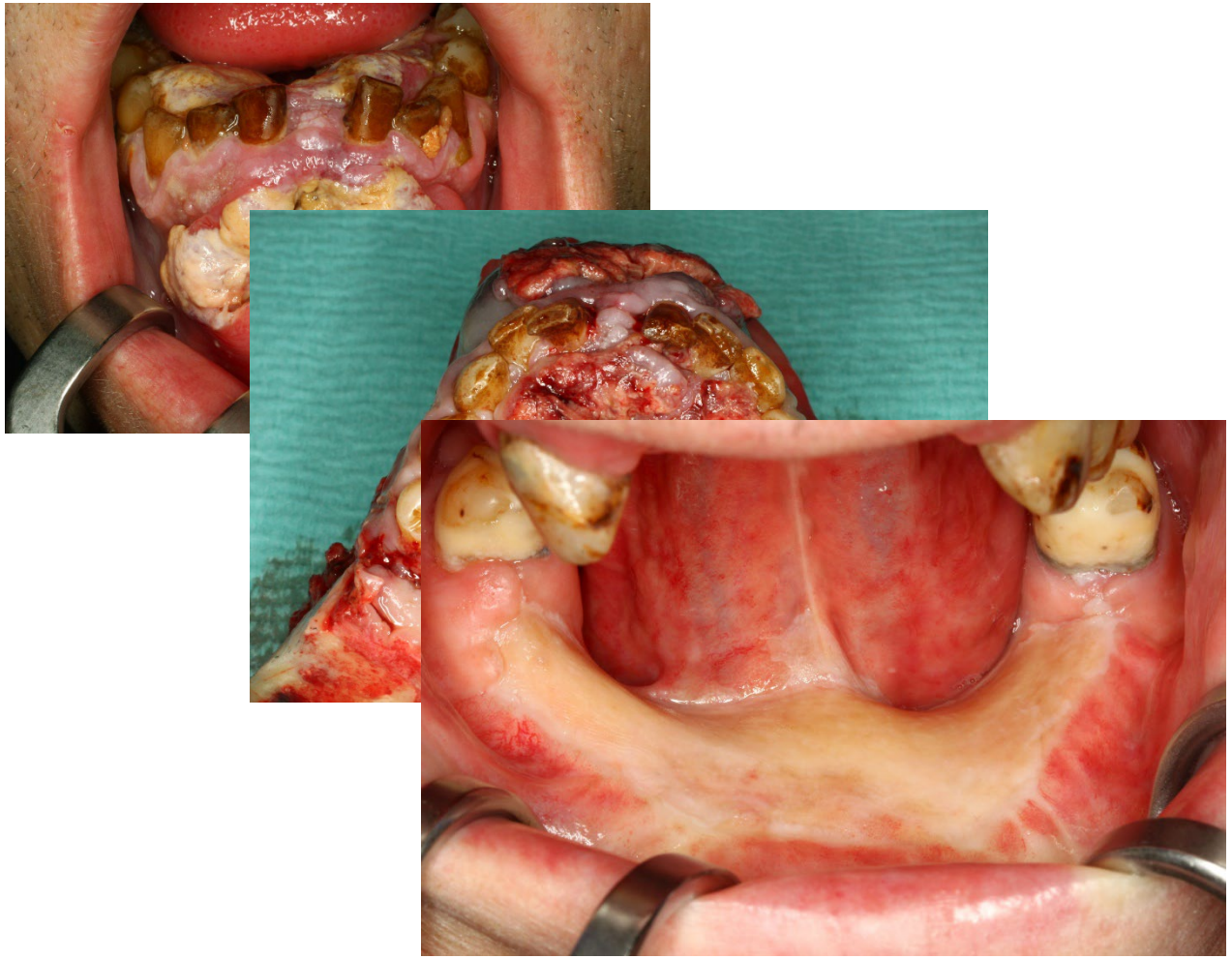
Operative Therapie





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Definitive Strahlentherapie

- Einzeldosen 2 Gy kumulativ im fortgeschritten Stadium bis 72 Gy
- Cisplatin 40 mg/m² wöchentlich genauso effektiv wie 100 mg/m² q3w – kumulativ sollten min. 200 mg/m² erreicht werden

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Therapie im adjuvanten Setting

Indikation für adjuvante Radiotherapie orientiert sich an dem Vorliegen von Risikofaktoren:

- pT≥3
- pN2 oder pN3 oder >1 LK (pN1) bei HPV pos
- Perineurale Invasion (Pn1)
- Lymphovaskuläre Invasion (V1)

Indikation zur Radiochemotherapie:

- Extrakapsuläres Wachstum (ECE+)
- Tumorfreier Resektionsrand < 5 mm oder R1

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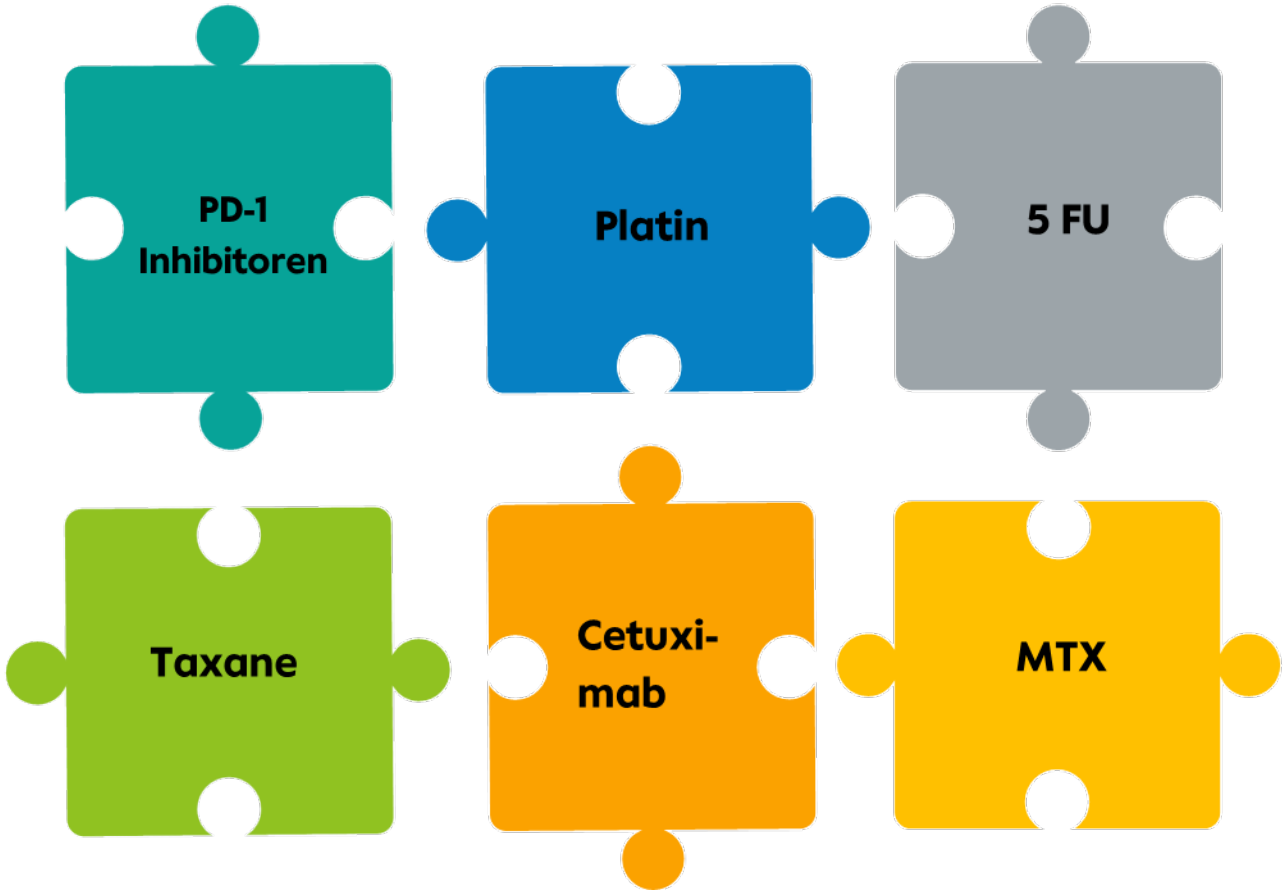
Therapie im palliativen Setting



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Kriterien zur Therapieselektion

Patientenfaktoren

- Alter
- Patientenwunsch
- ECOG/Performance
- Behandlungsplan
- soziales Umfeld

Tumorfaktoren

- Schmerz
- Zeit seit der letzten Therapie
- Blutungsrisiko
- Tumorgröße
- PD-L1 Expression

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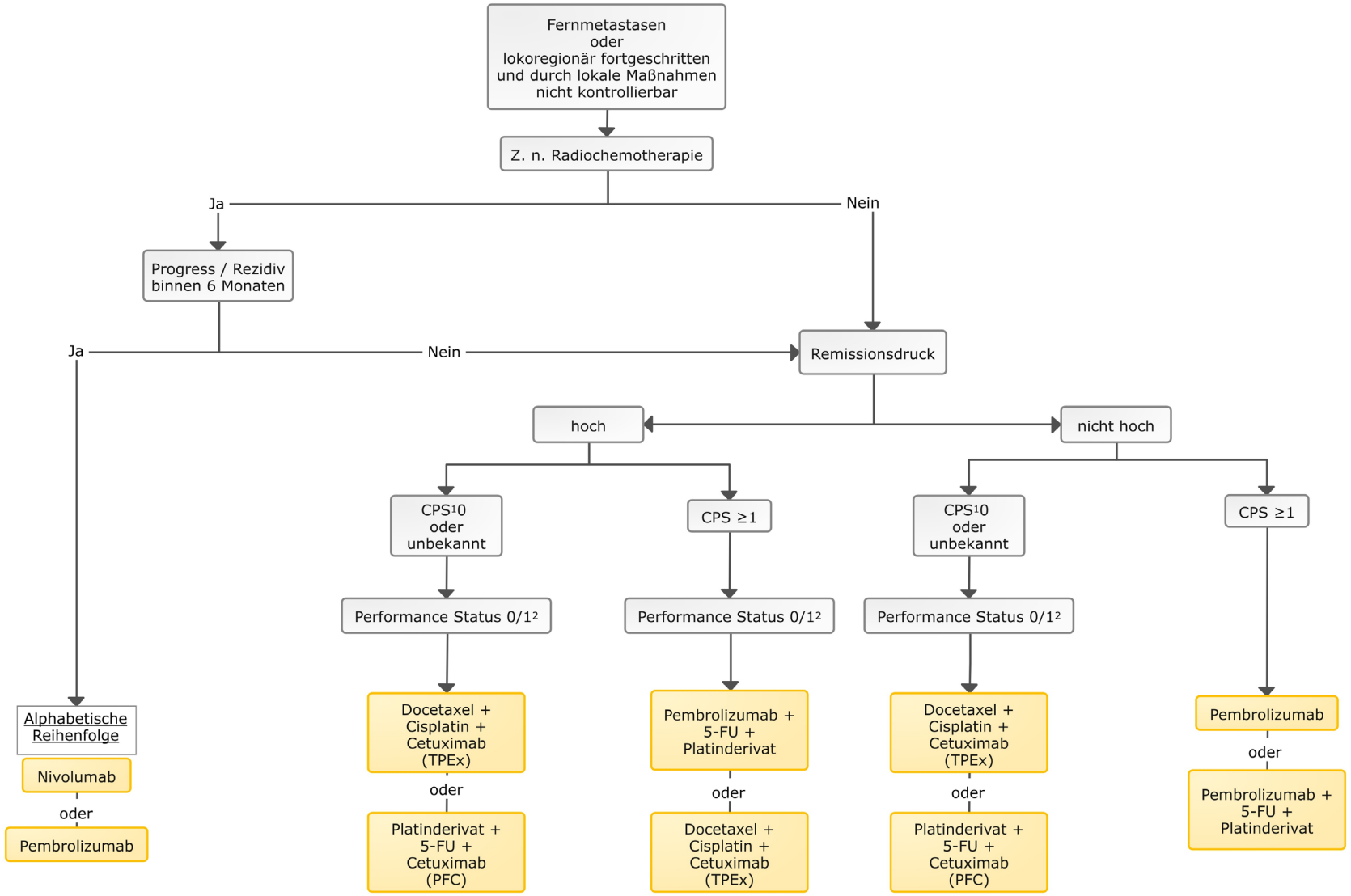
Kriterien zur Therapieselektion



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Study Design of KEYNOTE-048 (NCT02358031)

Key Eligibility Criteria

- SCC of the oropharynx, oral cavity, hypopharynx, or larynx
- R/M disease incurable by local therapies
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment[a]
- Known p16 status in the oropharynx[b]

R (1:1:1)

Pembrolizumab monotherapy → Pembrolizumab 200 mg Q3W for up to 35 cycles

Pembrolizumab + chemotherapy → Pembrolizumab 200 mg + Carboplatin AUC 5 or Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days for 6 cycles (Q3W) → Pembrolizumab 200 mg Q3W for ≤35 cycles total

EXTREME → Cetuximab 250 mg/m² QW[d] + Carboplatin AUC 5 or Cisplatin 100 mg/m² + 5-FU 1000 mg/m²/d for 4 days for 6 cycles (Q3W) → Cetuximab 250 mg/m² QW

Stratification Factors

- ECOG PS (0 vs 1)
- p16 status in oropharynx (positive vs negative)
- PD-L1 expression[a] TPS (≥50% vs <50%)

Primary end points: OS[c], PFS[c]
Secondary end points: ORR[c], safety
Exploratory end point: DOR

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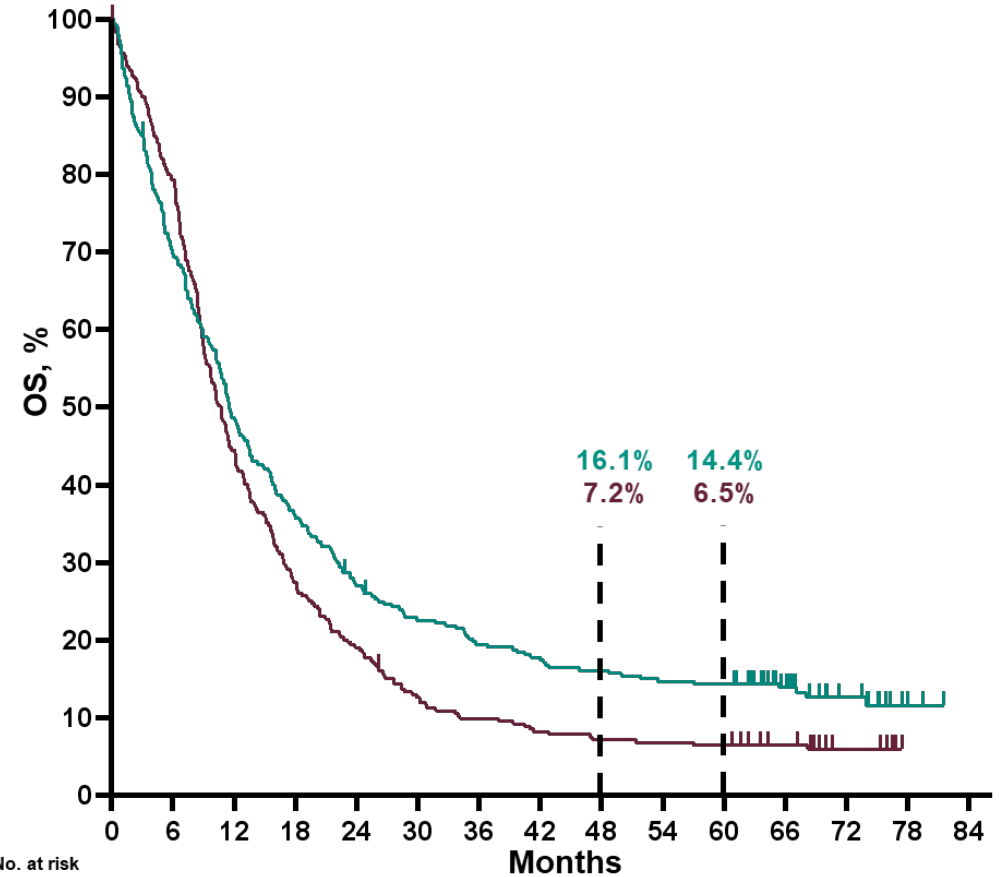
Overall Survival in the ITT Population

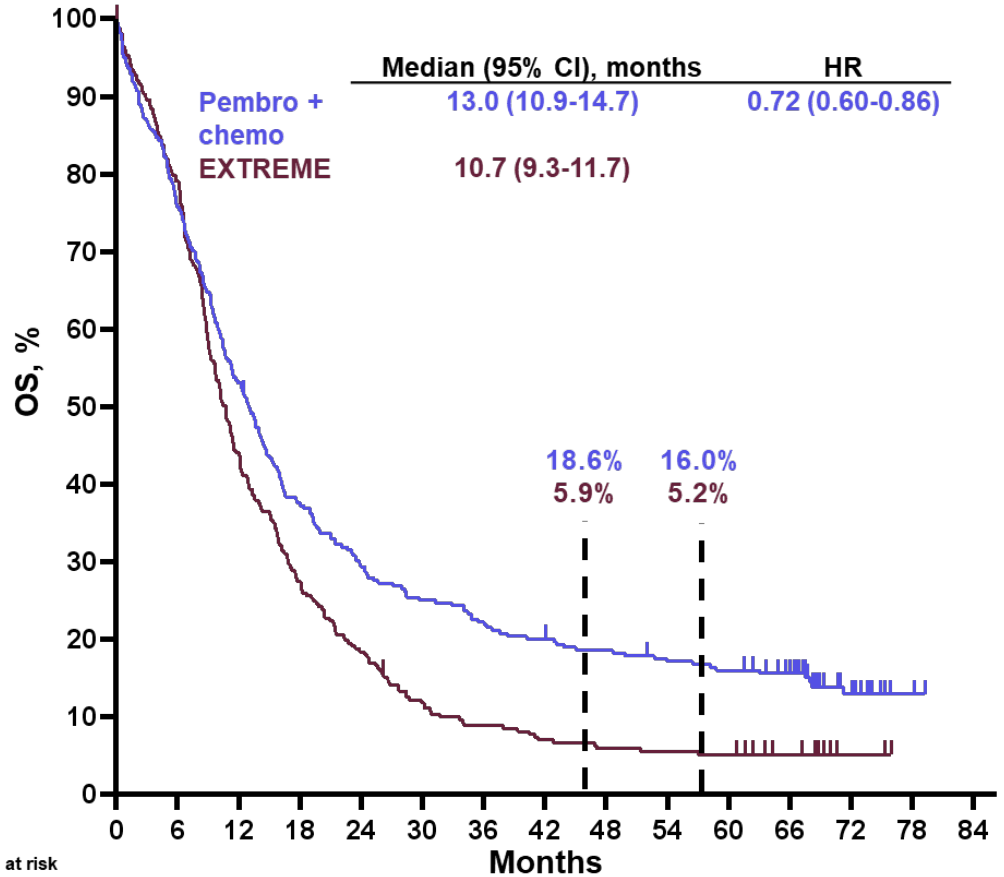
Pembrolizumab mono



No. at risk															
Pembro	301	209	146	108	80	66	57	51	47	43	42	28	13	3	0
EXTREME	300	237	133	82	57	37	29	24	21	20	19	14	6	0	0

Data cutoff date February 21, 2022.

Pembrolizumab + Chemotherapie



No. at risk															
Pembro + chemo	281	213	149	105	82	70	62	56	51	46	43	36	15	2	0
EXTREME	278	219	122	76	51	32	24	19	16	15	14	9	2	0	0

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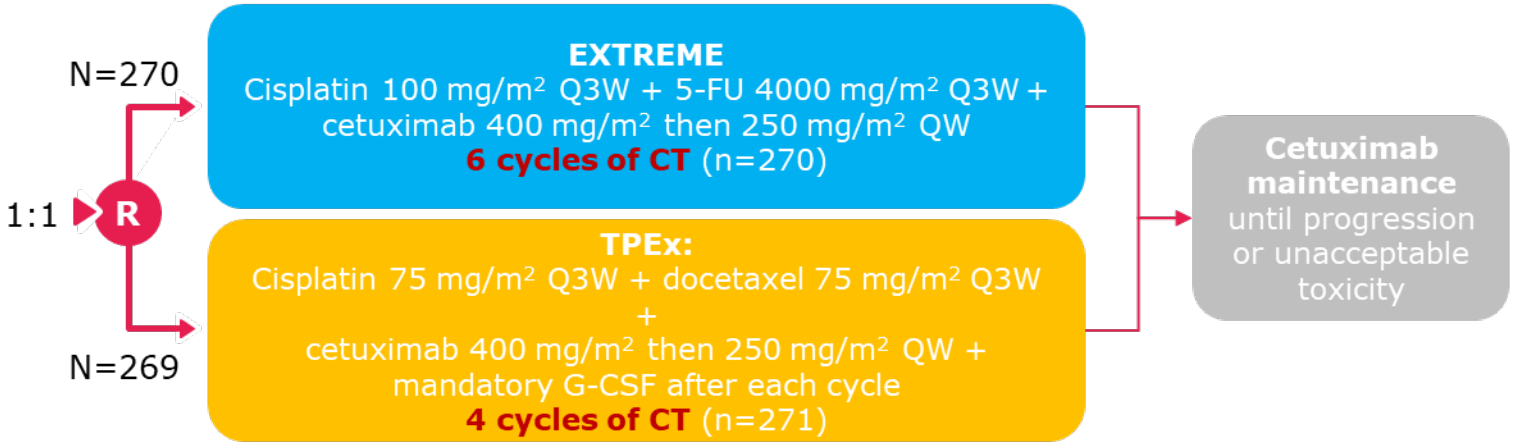
TPExtreme study design (NCT 02268695)

Key eligibility criteria

- R/M HNSCC not suitable for locoregional treatment
- Age 18-70 years
- PS 0-1
- Creatinine clearance >60 ml/min
- Prior cisplatin ≤300mg/m2
- No Anti-EGFR for 1 year

Minimization factors

- PS
- Metastatic status
- Previous cetuximab
- Country



Primary endpoint:
OS

Secondary endpoints:
PFS, ORR at 12 weeks, QoL, safety, compliance

Exploratory endpoints:
2L treatment, prognostic factors for OS, medico-economic factors

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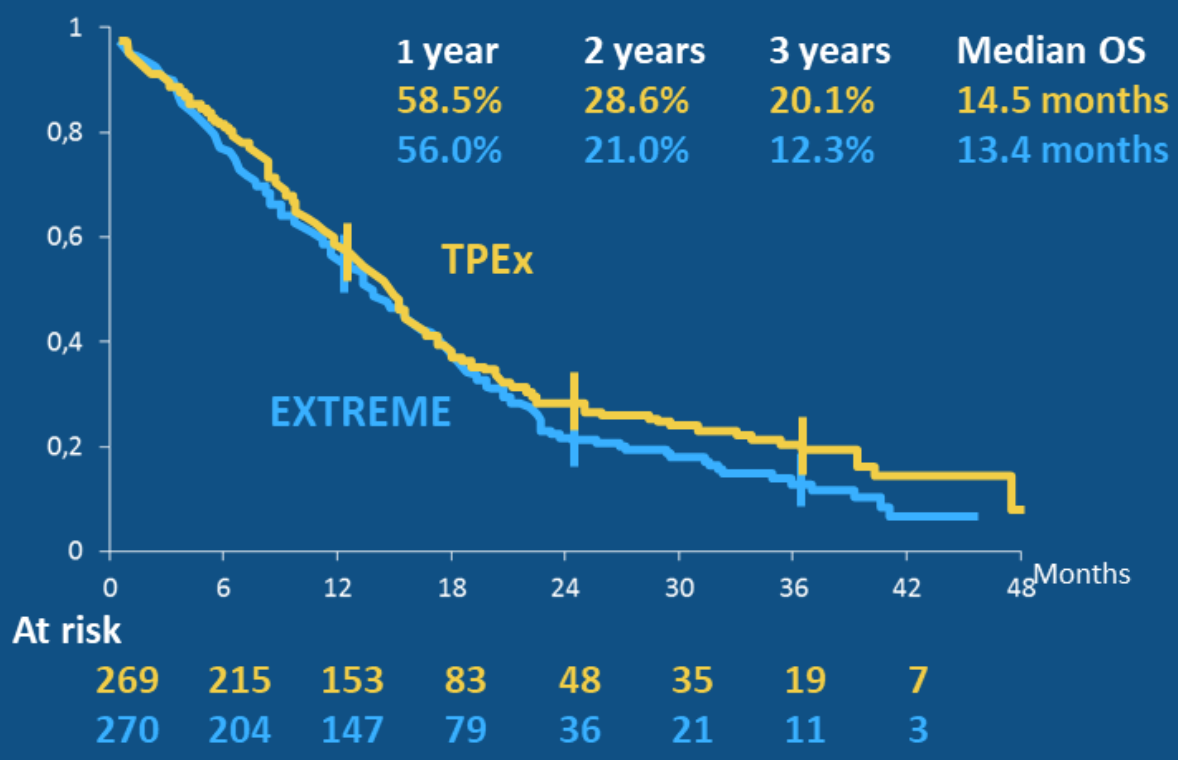

Median OS higher than expected:
14.5 months in TPEx arm and
13.4 months in EXTREME arm

Hazard ratio TPEx vs EXTREME:
HR=0.87 (95% CI: 0.71-1.05)
p-value=0.15

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Systemtherapie nach Immuntherapie

Patients with R/M SCCHN after 1L pembrolizumab failure

- ≥18 years old
- ECOG PS 0–2
- Measurable disease per RECIST v1.1
- Adequate organ function

N=57 →

Until PD or unacceptable toxicity:

Paclitaxel 175 mg/m^2 q21 days
+ cetuximab 400 mg/m^2 (loading dose) followed by 250 mg/m^2 weekly*

Key exclusion criteria:

- Prior taxane or cetuximab therapy, except for induction therapy for locally advanced disease ≥6 months prior

Endpoints

- **Primary:** ORR
- **Secondary:** DOR, DCR, BOR, PFS, OS, AEs

Characteristics	Number of Patients (%)
Sex	
Male	48 (84.2%)
Female	9 (15.8%)
Median age (range) years	64 (28-81)
Primary tumor site	
Oral cavity	17 (29.8%)
Laryngeal carcinoma	6 (10.5%)
Hypopharyngeal carcinoma	9 (15.8%)
Oropharyngeal carcinoma	25 (43.9%)
P16 status (oropharyngeal carcinoma)	
positive	11 (44.0%)
negative	14 (56.0%)
Disease Status	
Recurrent	23 (40.4%)
Metastatic	17 (29.8%)
Recurrent and Metastatic	17 (29.8%)
ECOG Status	
0	28 (49.1%)
1	25 (43.9%)
2	4 (7.0%)
Previous first line therapy	
Pembrolizumab Monotherapy (P)	29 (50.9%)
Pembrolizumab plus Chemotherapy (P+C)	28 (49.1%)
PD-L1 Status	
CPS ≥1	55 (100%)
CPS 1-19	24 (43.6%)
CPS ≥ 20	31 (56.4%)
CPS unknown	2

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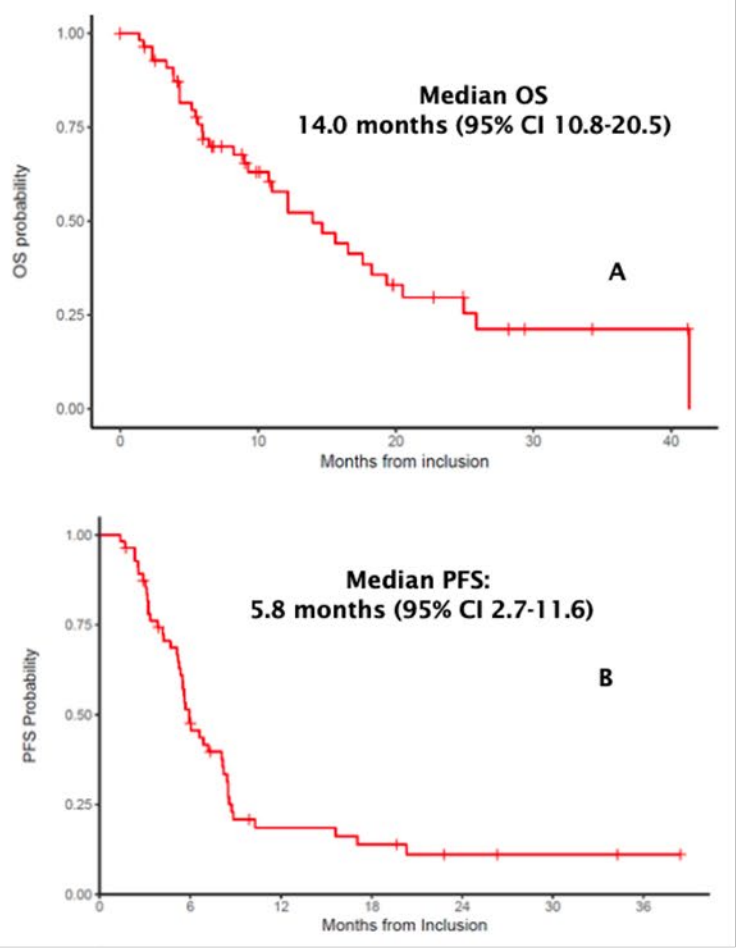
Therapie

neuer Standard nach Immuntherapie



Best Response	Number of Patients (n=57)	Percentage
CR 95% CI	8	14.0% 1.75% to 27.98%
PR 95% CI	19	33.33% 21.05% to 47.28%
Stable Disease 95% CI	14	24.6% 12.28% to 38.51%
Progressive Disease 95% CI	13	22.8% 10.53% to 36.75%
Not evaluable	3	5.26%
Overall Response Rate 95% CI		47.4% 34.0% to 61.0%
Disease Control Rate (CR+PR+SD) 95% CI		71.9% 58.5% to 83.0%

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Was ändert sich 2025?

Multi-center, randomized, open-label study of pembrolizumab as neoadjuvant therapy and as adjuvant therapy in combination with standard RT (± cisplatin) in newly diagnosed resectable stage III or IVA (locally advanced) HNSCC[1,2]

Eligibility Criteria

- Age ≥18 years
- Newly diagnosed resectable stage III or IVA HNSCC
- ECOG PS 0–1
- Available tumor tissue sample
- No prior anti–PD-1, PD-L1, or PD-L2 therapy or RT

Stratification Factors

- Primary tumor site (oropharynx/oral cavity vs larynx vs hypopharynx)
- Tumor stage (III vs IVA)
- HPV p16 status (oropharynx p16–positive vs oropharynx p16–negative or larynx/hypopharynx/oral cavity HNSCC)
- PD-L1 TPS (≥50% vs <50%)

Randomization 1:1 N=704

Neoadjuvant Phase → **Adjuvant Phase**

Pembrolizumab 200 mg IV Q3W (2 cycles) → Surgery → High risk: Pembrolizumab 200 mg IV Q3W (15 cycles) + RT + cisplatin[a]; Low risk: Pembrolizumab 200 mg IV Q3W (15 cycles) + RT

No neoadjuvant therapy → Surgery → High risk: RT + cisplatin[a]; Low risk: RT

End Points

Primary
- mPR rate
- EFS

Secondary
- OS
- Pathological CR rate
- Safety
- QoL

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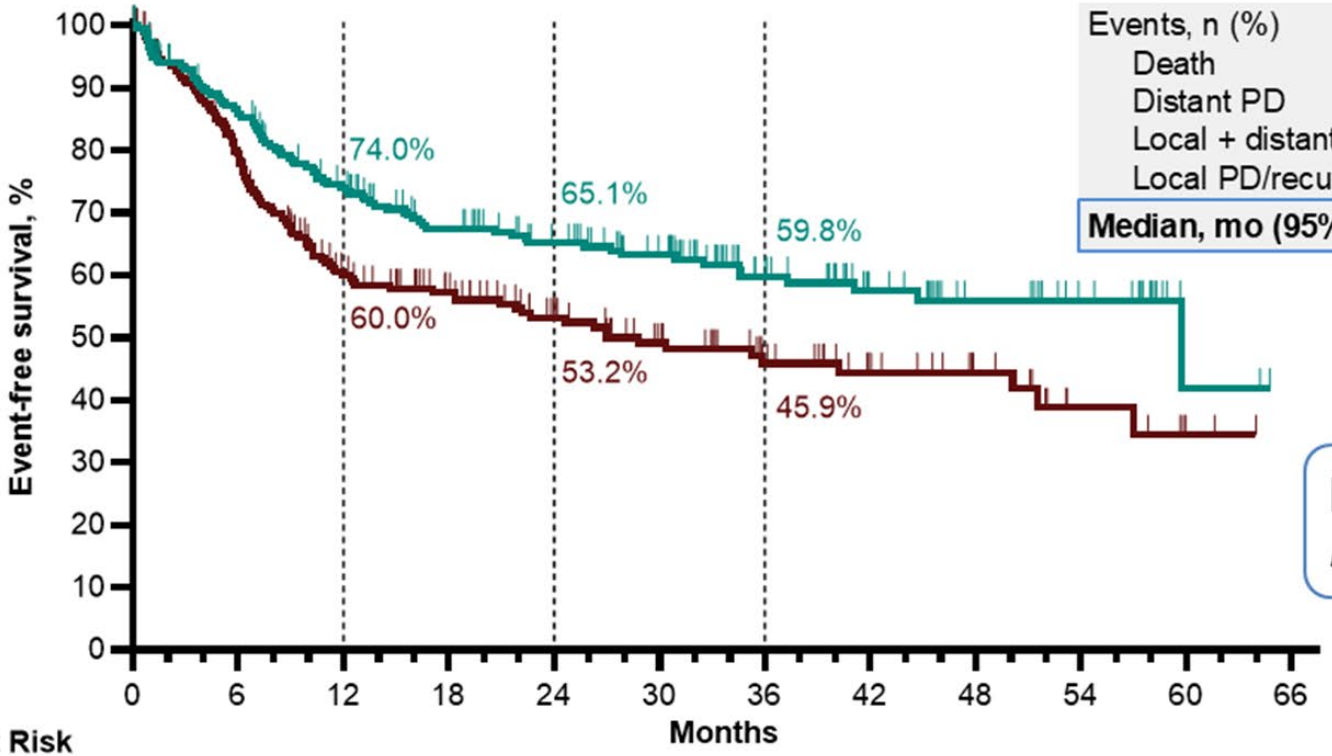
Uppaluri KN689 AACR 2025

Primary Endpoint: EFS

CPS ≥10 Population



	Pembro + SOC (N = 234)	SOC (N = 231)
Events, n (%)	85 (36.3)	107 (46.3)
Death	43 (18.4)	37 (16.0)
Distant PD	15 (6.4)	39 (16.9)
Local + distant PD	2 (0.9)	2 (0.9)
Local PD/recurrence	25 (10.7)	29 (12.6)
Median, mo (95% CI)	**59.7 (41.1–NR)**	**26.9 (18.3–51.5)**

HR 0.66, 95% CI 0.49–0.88, *P*=.0022*

No. at Risk												
Pembro + SOC	234	188	154	128	111	93	61	40	27	19	2	0
SOC	231	168	115	94	70	53	38	27	18	9	3	0

Data cutoff date: 25 July 2024

NR, not reached.
*Significance boundary was met at IA1.

Fallbeispiel

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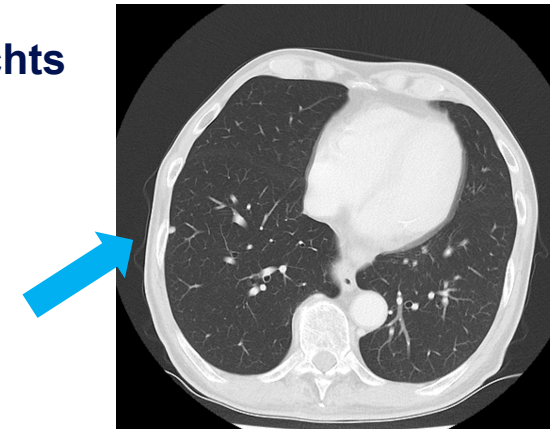

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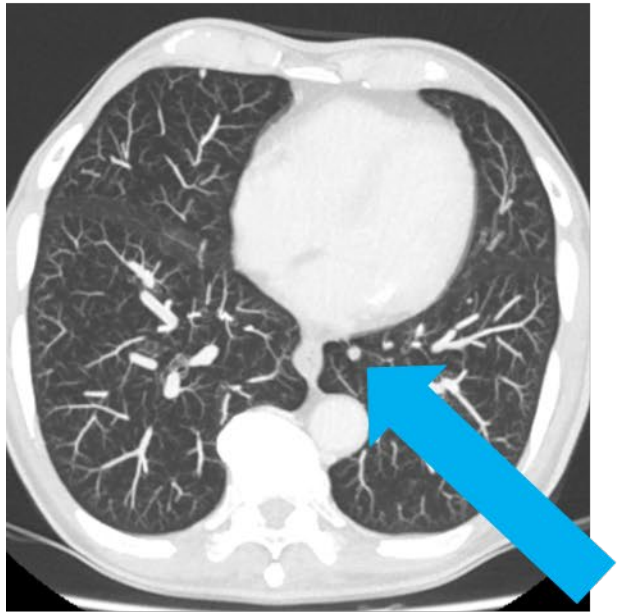

04/22
Beurteilung:
Kein Nachweis eines Lokalrezidivs.
Metastasenresiduum im Zervikallevel III rechts. Kein Nachweis neuer Lymphknotenmetastasen.

Minimal größenprogredienter, daher malignitätssuspekter pulmonaler Rundherd im rechten Unterlappen. Multiple weitere größenprogrediente (Mikro-)Noduli bipulmonal, z. B. parakardial im linken Unterlappen (6 mm, zuvor 3 mm): formal unspezifisch, jedoch in Zusammenschau mit dem übrigen Befund auch als metastasensuspekt wertbar.

CPS 6 – Einleitung Pembrolizumab mono 04/2022 -> im Verlauf von 6 Monaten komplette Remission.