Head and neck tumors

Katalin Hideghéty
Incidence of malignant tumors

- Breast + prostate cancer ca. 20-30%
- Lung cancer. 15-20%
- Colorectal cc. 10-12%
- Gynacological tumors. 6-8% (women)
- **Head and neck tumors** kb. 3-10%
- Bladder cancer. 3-4%
- Stomach, pancreas tumors. 2-3%
- Melanoma malignum. 2-3%
- Renal cc. 3%
- Brain tumors 2-3%
Epipharynx
Nasal cavity
Paranasal sinus

Mesopharynx
Oral cavity
Salivary gland

Hypopharynx
Laryngeal tu.
supraglottic, glottic, subglottic.
Epidemiology-Etiology

EU-USA Man : 5%  
Woman: 1-2%

Asia: 13-15%

Squamous cell carcinoma of the head and neck (SCCHN) occurs in 50,000 new cases annually in the US, resulting in over 13,000 deaths each year.
Special features of head and neck cancer

- Immense lymphatic network with cross sections
- Narrow space – tumor invasion to the neighbouring structures (local tissue destruction)
- Few, non-characteristic symptoms
- Late diagnosis
- Alcoholic organopathy
- Multiplex tumors (*identical etiology head and neck, lung, esophagus*)
Risk Factors for Head and Neck Cancer

**Tobacco Products:**
- Smoking Tobacco
- Cigarettes
- Cigars
- Pipes
- Chewing Tobacco
- Snuff

**Ethanol Products**

**Chemicals:**
- Asbestos
- Chromium
- Nickel
- Arsenic
- Formaldehyde

**Other Factors:**
- Ionizing Radiation
- Plummer-Vinson Syndrome
- Epstein-Barr Virus
- Human Papilloma Virus
Human Papillomavirus (HPV)

- **DNA virus**
- Preferentially infect squamous epithelial cells
- >100 genotypes
- ≥40 genital HPV types
Warning Signs of Head and Neck Cancer

- Hoarseness
- Erythroplasia
- Referred otalgia
- Persistent sore throat
- Epistaxis
- Nasal obstruction
- Serous otitis media
- Neck mass
- Non-healing ulcer
- Dysphagia
- Submucosal mass

Frequently symptom-arm at early stages!
Factors Delaying the Diagnosis of Head and Neck Cancers

• Patient procrastination in seeking medical attention

• Physician delay in diagnosis

• Patient remains asymptomatic for a prolonged period
Recognition!

Leukoplakie, erythroplakie - precancerosis

Early, superficial tumours

Symptoms
Pain, swallowing disturbance, hoarsness, snufflessness, weight loss
Diagnostics

Clinical
HNO examination
palpation
panedoscopy
dental status
lab, organ review

Histology
type:squamous cell cancer
lymphom, chemodectom, melanom, sarcom
grading (pTNM, R)

Imaging
USG – neck lymphnodes
CT- locoreg., thorax, liver
MRI- local extent, relationship to the neighbourhood
PET- active tumour, lymph node metastasis
T categories
N categories
Histopathology

histological type: 90% squamous cell cc. (lymphoma, sarcoma)

grade of cell differentiation: G1  G2  G3  G4

proliferation
vascuralisation
perineural or vascular invasion
size and spread pTNM

quality of surgery R0, R1, R2 — resection margin
Prognostic factors

- TNM, pTNM
- Histopathology
- HPV (p16), other molecular factors (PTEN)
- age
- performance status
- treatment – order, technique, quality
- tumour response
- Supportive care (nutrition, management of side effects, late sequelae, pain killing)
• **Mouth-oral cavity**
  • 9,5-13 /100000
  • Smoking, alcohol

• **Mouth: 90% lower lip**
  • Thin submucosa….fast spread to the muscles
  • Met.: I.:subment., retrovasc., submand.
    II.:subdigastr., mid. parajug.
    to both sides from midline

• **Bucca:**
  – The more aboral, the more malignant
  – reg. met.: 10-30% - rare bilateral
    (submand., jugulodigastr., subment.)

• **Gingiva:**
  – Spread: base of mouth, bucca
  – Mandible
  – Reg.met.: lower neck: 15-50%  upper: 15-20%
• **Base of mouth:**
  - Loose mucosa-muscle relationship, slower spread as the tongue tu.
  - Can spread to the salivary gland via ductus
  - Submand. lgl
  - 30-50% bilateral met. (submand., subdigastr.)

**Tongue**
  - Two third of the tongue differs from the base of tongue
  - Submucosa (aponeurosis like)
  - Midline: raphe..
  - High probability of lgl met..: 35-65%
  - 10% bilateral

- Side of tongue: submand, subdigastr.
- Apex of tongue: submand., subment., parajug.
– **Hard palate:**
  
  - 2-5% of oral cavity tumors
  - Small salivary gland origin by youngs
  - Osseal spread
  - Low metast.potential
Epipharynx

Etiology, epidemiology:

Relative frequent in India, Iceland and China 20-50 /100000/ man while in EU-USA: 0,3-08

- Genetical predisposition (H2; BW 46)
- Environmental factors
- Ionization radiation
- EBV
Nasopharyngeal cancer

Clinical presentation
Nasal stuffiness, discharge, epitaxis, loss of normal nasal resonance, ear pain, headache, syndromes due to cranial nerve involvement

Lymphnode metastasis
Origin, spread

Nasal cavity 20%
Oropharynx 15%
Parapharyngeal space 80%
Base of skull (lesion of the central nerves) 25-35%
Intracranial 3-12%
Sinus maxillaris 5%

- 60-85% lymphnode metast.
  - 40-50% bilateral
  - Along the V.jug. Int.
  - Retropharing., n.accessorius
  - Jugulodigastr.
  - Mid, dorsal cervicalis lymphatic chain
Signs

• 60-85% cervical lesion
• 27-38% snuffles
• 30% epistaxis
• 17-41 % Ear complaints (pain) hypoacusis, obstruc. of the tube Eustachi + otitis media

• Trotter-trias:
  • Hypoacusis
  • Mandibular neuralgia
  • Paresis of the soft palate

• 26% invasion of the central nerves

• Horner-trias ptosis, enophthalmus, miosis
<table>
<thead>
<tr>
<th>Foramen</th>
<th>Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cribiform plate (ethmoid)</td>
<td>Olfactory nerve and anterior ethmoidal nerve</td>
</tr>
<tr>
<td>Optic foramen</td>
<td>Optic nerve and ophthalmic artery</td>
</tr>
<tr>
<td>Superior orbital fissure</td>
<td>Third (oculomotor), fourth (trochlear), and sixth (abducent) nerves, and</td>
</tr>
<tr>
<td></td>
<td>ophthalmic division of the fifth (trigeminal) nerve; ophthalmic vein;</td>
</tr>
<tr>
<td></td>
<td>orbital branch of middle meningeal and recurrent branch of lacrimal</td>
</tr>
<tr>
<td></td>
<td>arteries; sympathetic plexus; some filaments from carotid plexus</td>
</tr>
<tr>
<td>Foramen rotundum</td>
<td>Maxillary division of trigeminal nerve to pterygopalatine fossa</td>
</tr>
<tr>
<td>Foramen ovale</td>
<td>Mandibular division of trigeminal nerve; accessory meningeal artery;</td>
</tr>
<tr>
<td></td>
<td>lesser superficial petrosal nerve</td>
</tr>
<tr>
<td>Foramen lacerum</td>
<td>Upper portion: internal carotid; sympathetic carotid plexus</td>
</tr>
<tr>
<td></td>
<td>Lower portion: Vidian nerve; meningeal branch of ascending pharyngeal</td>
</tr>
<tr>
<td></td>
<td>artery; emissary vein</td>
</tr>
<tr>
<td>Foramen spinosum</td>
<td>Middle meningeal artery and vein; recurrent branch of mandibular nerve</td>
</tr>
<tr>
<td>Internal acoustic meatus</td>
<td>Seventh (facial) and eighth (auditory) nerves; internal auditory artery</td>
</tr>
<tr>
<td></td>
<td>from basilar artery</td>
</tr>
<tr>
<td>Jugular foramen</td>
<td>Anterior portion: Inferior petrosal sinus</td>
</tr>
<tr>
<td></td>
<td>Posterior portion: Transverse sinus; meningeal branches from occipital</td>
</tr>
<tr>
<td></td>
<td>and ascending pharyngeal arteries</td>
</tr>
<tr>
<td></td>
<td>Intermediate portion: ninth (glossopharyngeal), tenth (vagus), and</td>
</tr>
<tr>
<td></td>
<td>eleventh (spinal accessory) nerves</td>
</tr>
<tr>
<td>Hypoglossal canal</td>
<td>Hypoglossal nerve; meningeal branch of ascending pharyngeal artery</td>
</tr>
<tr>
<td>Foramen magnum</td>
<td>Spinal cord; spinal accessory nerve; vertebral vessels; anterior and</td>
</tr>
<tr>
<td></td>
<td>posterior spinal vessels</td>
</tr>
</tbody>
</table>
Mesopharynx
Anatomy

The oropharynx or mesopharynx lies behind the oral cavity, extending from the uvula to the level of the hyoid bone.

Anterior wall: base of the tongue and the epiglottic vallecula;

Lateral wall: tonsil, tonsillar fossa, and tonsillar (faucial) pillars;

Superior wall: inferior surface of the soft palate and the uvula.

Lymphytics:

• Jugulodigastr.
• Retro-, és parapharingeal
• N. accessorius
• 0.5% of all malignant tumors
  – Tosill. reg.: 40%
  – Base of tongue: 30%
  – Fauceal pillars: 20%
  – Wall of the pharynx: 10%
• Mortality due to locoregional progression
Hypopharynx
• 0,5-3 % of all malignant tumors
• More frequent by man
• 80%-from the sinus piriformis
• most frequent at age of 60-65 years

**Symptoms:**
– pain,
– Swallowing problems
– hoarsness
– Otalga
– dyspnoe
- submucosus spread
- Late symptoms

**sinus piriformis:**
- To the paraglotticus region, infiltrating
  - Muscles of the larynx
  - Ary cartilage
  - n.recurrens paresis
  - glottis
  - Thyroid

**Dorsal wall tumors**
- mesopharynx
- trachea
- paravert. fascia - irresecability
- **LN:**
  - 75% at dg. (14% bilateral.)
  - parajug, parapharing., trachealis, mediastinalis

**postcrycoid region:** cartilages hoarsness
- Spread toward the sysnus piriformis, oesophagus
Larynx
Glottic cancer
• Most frequent tumor between the head and neck cancer 25-50% and 1-2% of all tumors

• **Epidemiology:**
  – Dominant male
  – Smoking, chemical agents
  – 10 years after stopping the smoking the risk equal with the risk of nonsmokers
  – High degree of marihuane consum.
  – Age peak between 50-70 years
  – Mainly locally growing (met: 20%)

**Anatomy:**
– *supraglottic* rich lymphatic network
– *glottic* practically no lymphocapillary system (barrier)
– *subglottic region* prelaryngeal (Delphian), pretrachealis, lat. paratrachealis, and upper mediastinal lymphonods

**Pathology:**
– 94% *squamous cell cc.* (G1-4)
– verrucous cc. 1-2% generally non metastatic
– anaplasticus 5%
Clinics:

- **supraglottic**:
  - symptom arm
  - Neck mass.
  - Strange feeling

- **glottic**:
  - intermittent hoarsness

- **subglottis**:
  - In early stage symptom arm
  - Breathing with stridor

Supraglottic cc

mainly on the epiglottis, with cartilage infiltr.

- Morgani space to.
  spread toward the corda vocale

Glottic cc.

Spread along the mucosa
2/3 restricted on the corda vocale
Spread toward the neighbouring glottic region
And neighbouring tissues (fasciae, spaces)
Salivary gland tumors

5-7% of all head and neck cancer
Histology
adenomas, pleomorph adenoma, ductal papilloma, acinic cell carcinoma, mucoepidermoid cc., adenoid cystic cc., papillary cystadenoccc. mucosus adenoccc.,
Nasal cavity and paranasal sinus tumors
Nasal, paranasal sinus cc.
Usually diagnosed at advantaged stage — bad prognosis (5 years 30%)
Radical operation is hardly possible .......... RT is important

**Etiology, epidemiology:**
- 0.3 - 1% of all tumours
- Most frequent around the age of 70
- smoking, alcohol
- occupational inhaled carcinogens

1. lower storey: s.maxill base, proc. alveolaris, hard palatinum 15%
2. mid. storey: s. maxill., lateral wall of the nose 45%
3. upper storey: s. frontális, s.sphenoid., s.ethmoid., ethmoido-orb.cornerl., upper concha 40%

**Clinical:**
- No symptoms for a long time

**Anatomic regions**
- r.olfactoria
- r.respiratorica
- r.vestibularis
- s.frontalis, - sphenoidalis rare

- **lower storey** symptoms: loosening of the teeth, swelling of hard palatinum, fistula, ulcer, inconvenient dental prosthesis
- **mid. storey:** swelling of the face, pain, bleeding of the nose, snuffles
- **upper storey:** Ethmoido-orbitali corner swelling, tears, disturbed vision, double vision,
**Lymphatic system:**

Defector lymph. pathways:

1. retromaxillar
2. parapharigeal
3. retropharingeal
4. subarachnoideal

choanas lymph. path.

1. submandibular
2. Upper cervical lym.n.

- At the first dg. 15-22% positive lymphatic nodes
- local tu. progression is crucial for prog.

**Histology:**

- 70-90% G1-4 **epithelial cc.**
- rarely: basal cell-, taransitional cell cc.
- lymphoepithel. tu.-s, adenocc.-s rare
- 20% sarcoma, lymphoma (high malign.)
- melanoma mal. 4%

**Diagnostics:**

- laryngology
- ophthalmology
- CT, MR (70% bone-destruction)
Complex tumor therapy

- Surgery
- Radiotherapy
- Chemotherapy

Specific therapy:
- Molecular targeted agents
- Immunotherapy
- Vaccination
Preconditions of successful primer agressive-curative treatment

Quick diagnosis - staging
Good performance status
Prevention of the side effects
Intenzíve supportative care
Treatment of early tumors

T1-2, N0-1 M0

• Surgery
• Larynx and function preservation
• Postoperative irradiation if needed
Surgery

Primery - in the komplex management - salvage

- LMC + biopsy
- LASER chordectomy, tonsillectomy
- partial laryngectomy + en block neck dissection (radikal RND vagy mRND)
- Total laryngectomy + RDN l.u.
Partial laryngectomy
Locoregionally advanced H&N CC (LAHNC)

Induction chemotherapy: 2-3 cycles

**Basis cytostatics:**
- 5 fluorouracil
- Cisplatin/Carboplatin
- Docetaxel/Paclitaxel
Long-term results from EORTC24971/TAX323: Comparing TPF to PF in patients with unresectable squamous cell carcinoma of the head and neck

J. B. Vermorken, E. Remenar, C. Van Herpen, M. Degardin, J. S. Stewart, R. Karra Gurunath, C. Fortpied;

308 (86%) / 358 randomized patients

156 TPF 152 PF

PFS 12.7 8.6 months
5-yearsPFS 22.9% 13.5%

PFS remained significantly better with TPF compared with PF (hazard ratio [HR] unadjusted 0.71 (95% CI, 0.57-0.89),

OS 18.8 vs 14.5 months, 5-years OS 27.5% vs 18.6%.

No significant difference in toxicity
Binary system

Chemo

Concomittant CRT

CRT + mol. Targeted agents

Adjuvant chemotherapy

Radiotherapy

IMRT, IGRT

BGRT

Dose-escalation

Fractionation
Quality of radiation

RT delivery prolongation adversely affects outcomes

Impact of radiation therapy deviations on outcome

- \( \text{HR} = 1.89, \ P < 0.001 \)
- 2-y OS: 69\% & 50\%
- Hazard ratio 95\% CI
Individual radiotherapy
Great LET
*(carbon ion)*
Frequent ionisation

Small LET (indirect effect)

Ionisation - free oxygen radicals

Halmozott károsodás
Great RBE
Low OER

Isolated damages
3DCTR, IMRT, IGRT, Adaptive RT

BGRT, PET-CT based /proliferation, hypoxia/
"dose painting"

Total dose ≥ 70 Gy

Accelerated, hyperfractionated
Concomitant boost
COMPARISON OF CONVENTIONAL AND FOUR PROTOTYPES OF ACCELERATED FRACTIONATION SCHEDULES

Conventional: ~70 Gy / 35-38 fx / 7-7.5 wks

Type A: 54 Gy/36 fx / 12 days (CHART)

Type C: 72 Gy/42 fx / 6 wks (Concomitant Boost)

Type D: 76 Gy/54 fx / 5 wks (Escalating Dose)
Immobilization
Identical position, immobilization

Defined parameters of the examination

Patient

Mask with landmarks

photo
dokumentation

Planning CT

Szeged

Images, report

PET/CT

Budapest
Oncentra Masterplan TPS
XIO/FOCAL

GTV_{CT}

Risk organs
OTP

GTV_{PET}
Final definition on the basis of common evaluation of PET and CT

Radiological and nuclear med. consultation/control
Dose prescription

• Aim of the treatment
• Tumour type and characteristics
• Malignant cell amount (tumour size)
• Other therapy modalities
• Tolerance of surrounding normal tissues
3-D plan 2 non-coplanar fields
COMPASS technique
Base of tongue interstitial brachytherapy
CRT
+ molecular targeted agents

• LASCHNC (in stad: III/IV )
• Concept of laryngs preservation
H&N concomitant radio-chemotherapy

↓ 100 mg/m² cisplatin
↓ 750 mg/m² 5FU
↓ radiation

↓ 100 mg/m² cisplatin
↓ 750 mg/m² 5FU
Head and neck squamous cc. concomittant radio-chemotherapy

30 mg/m² cisplatin

irradiation
Concurrent CRT with **weekly platinum** for patients with unresectable/locally advanced SCCHN and comorbidities

S. A. Limaye, S. N. Horowitz, A. Thomas, N. Kohn, B. Mehrotra


Carboplatin AUC 2 (n=11) or cisplatin 35mg/m2 (n=20) or both alternately (n=2) weekly, concurrently with RT.

DFS at 1 yr: 86.4% DFS at 2 yrs: 67.9%
OS at 1 yr: 92.6% OS at 2 yrs: 66.7%

**Conclusions:** The results are provocative. DFS and OS rates are comparable with previously reported in good PS, (RTOG 91-11, and by Adelstein et al (JCO 2003 Jan 1;21(1):92-8) and Bonner et al (NEJM 2006 Feb 9;354(6):567-78). In addition to comparable and sustained survival rates in pts with poor PS and comorbidities, it is a regimen with excellent tolerability and may be considered as a reasonable option in this group of pts.
H&N concomittant radiochemotherapy

50 mg/m² Paclitaxel  200 mg/m² Carboplatin (AUC)

irradiation
Erbitux in locally advanced SCCHN - phase III

N=424

- RT + Erbitux: N=211
- RT: N=213

Overall survival (%)

- 29.3 months
- 49.0 months
- 5-year survival rate: 46%
- 36%

p=0.018

Bonner et al. Lancet Oncol 2010
Head and neck concomittant anti-EGFr-radiotherapy

Loading dose

Cetuximab

radiation
Erbitux usage in locally advanced SCCHN

Treatment patterns in Europe*
(incl. RT only, excluding surgery)

- 2006 (927 pts): 20% RT only, 17% CT only, 55% CRT, 9% Erbitux
- 2007 (923 pts): 21% RT only, 17% CT only, 43% CRT, 18% Erbitux
- 2008 (1239 pts): 19% RT only, 19% CT only, 37% CRT, 26% Erbitux
- 2009 (1220 pts): 12% RT only, 17% CT only, 36% CRT, 36% Erbitux

*Europe: France, Germany, Italy, Spain
Budach et al. ESMO 2010, Abstract No.1033P
Patients

2007. 06- 2011.06.

N= 46  T3-4  N1-3  M0-1  head-neck epithel cc.

Mean age  59.6 years (38-77)

Karnofsky: 8≤ 60%; 31≥70%

E-RT indikation

SD or PD after induction CT  n=18

CT contraindicated because of comorbidity/poor PS  n=21

Re-irrad because of recid.  n= 9
Follow-up: regular laryngeal examination/LMC, MR, PET/CT, biopsy
At the 2/3 of the radiotherapy topoCT-reCT fusion → 39% average tumour volume decrease
Side effects

RT fields dermatitis/mucositis (≥grade3) n= 33/38
Mean.: 19.9 mth

4 year surv.: 25%
Treatment response and HPV

- Favorable prognostic factors account for ~10% of relative survival benefit.
- Increased response to radiation therapy
- Accelerated radiotherapy (6 fx/week) beneficial.
- Increase response to platinum induction chemotherapy
- Possible enhanced benefit from addition of cisplatin to XRT.
- Improved local-regional control
- Cetuximab benefit observed in patients with "HPV profile."
- Reduced second primary cancers
- Smoking reduces response to therapy
Clinical significance

- National Comprehensive Cancer Network (NCCN) Guidelines- 2011
  “HPV testing recommended for all oropharynx tumors”
- National Cancer Institute, US, CTEP
  “HPV status must be used as stratification factor for trials including oropharynx cancer patients”
- U.S Cooperative groups
  “HPV-positive oropharynx cancer is a distinct entity”

Phase II study of induction chemotherapy with TPF followed by radioimmunotherapy with Cetuximab and intensity-modulated radiotherapy (IMRT) in combination with a carbon ion boost for locally advanced tumours of the oro-, hypopharynx and larynx--TPF-C-HIT.

*BMC Cancer. 2011 May*
Side effects of RT

**Acute reaction** (reversibile)

- **General** (nausea, fatigue, loss of appetite, decrease of blood count)
- **Acute local:** mucositis, dermatitis, face-neck oedema, nutritional difficulties weight loss
- **Late sequales:** xerostomy, dental problems, trismus, neck fibrosis, ulceration (skin, mucosa), cartillage-, bone necrosis

if in the treatment volume- vision, hearing, impairment, brain necrosis
• **Side effects- complications:**
  – Mucositis
    • Mouth-hygiene, Mycosis treatment
  – Larynx oedema
    • steroid, tracheostoma
  – Disturbed taste
    • Chemoreceptors transient loss-of-function (recovery after 4-6 months)
  – Xerostomia
    • Th.: artificial saliva, pilocarpin
  – Osteoradionecrosis
    • Rarely aseptic
    • Usually infection through gingiva injury
    • Closure of the gingiva after tooth extraction!!! + AB.
  – Nerve injury
    • Spinal cord injury: rare
    • Plexus injury (treatment max. 50 Gy at the neck)
Weight loss connected to the therapy

- Mechanical barrier of ingestion (lack of tumour reaction)
- Loss of appetite
- Acut reactions upon irradiation: mucositis, oesophagitis, gastroenteritis, lack of taste
- Side effects of chemotherapy: mucositis, nausea, vomiting, diarrhoea
- Late complications: xerostomia, loss of teeth, limited movement of the temporo-mandibular joint, lockjaw, mandibula-necrosis, oesophagus ulceration, chronic enteritis
Therapeutical nutrition

• Roboration before the therapy
• Reduce the side effects (mouth hygiene, alcohol, nicotin forbidden, check intolerance, education)
• Adequate supportive therapy (reduction of pain, nausea, vomiting, diarrhea)
• Prepare gastric feeding tube in time (PEG, Gastrostoma)
• Continous control on ingestion, liquid nutritives, if necc.
• Total parental nutrition
Treatment of recidival/metastatic head-and-neck tumours

Mol. Targeted ther. + reirradiation
First-line treatment patterns for recurrent and/or metastatic head and neck cancer (R/M HNC) in Europe.
M. C. Merlano, J. B. Vermorken, H. Wilke, J. Bourhis, R. Mesia, J. Guigay, U. Keilholz, M. Hartmann, J. Lefebvre

256 physicians provided 2065 patient records. 845 records were for patients with R/M disease, of whom 747 (88%) were given first-line treatment.

Of these patients, 557 (75%) received a systemic treatment only, 22% received systemic treatment plus RT and 3% received RT alone.

403/557 (72%) patients treated with first-line systemic treatment received combination therapy.

Between 2008-2009, there was a doubling of combination of platinum-based CT + cetuximab 35% vs 65%
### Single Agent Response Rates of EGFR-targeted mAbs and TKIs in SCCHN

<table>
<thead>
<tr>
<th>Drug</th>
<th>Phase</th>
<th>Reference</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab</td>
<td>II</td>
<td>Vermorken et al, 2007</td>
<td>13%</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>II</td>
<td>Soulières et al, 2004</td>
<td>4%</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>II</td>
<td>Cohen et al, 2003</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Cohen et al, 2005</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Stewart et al, 2009</td>
<td>8%</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>II</td>
<td>Abidoye et al, 2006 (ASCO)</td>
<td>0%</td>
</tr>
<tr>
<td>Zalutumumab</td>
<td>III</td>
<td>Machiels et al, 2010 (ASCO)</td>
<td>6%</td>
</tr>
</tbody>
</table>

References:
- EBSCOhost; Scherf TY, et al. ESMO. 2010;10:10PD.

N=10
IMRT: median dose of 50.4 Gy. + Cetuximab

Median OS after initiation of reirradiation: 7 months
1-year OS: 40%. 1-year LRC: 44%

Severe acute toxicity: 1 fatal infield arterial bleeding, 1 flap necrosis.
Severe late toxicities: 1 fibrosis of the temporomandibular joint
1 stenosis of the cervical esophagus

IMRT reirradiation with concurrent cetuximab in recurrent HNC is feasible with acceptable acute toxicity.
SZTE- onkoteápia  E-Reirradiáció

2008. 01- 2011.06.
N= 9  átl. 62 év (48-77) sokszorosan előkezelt
   Loc-rec:5
   Loc rec+ met: 2
   Duplex tumor: 2

20-25x 1,4-1,6 Gy + Erbitux

PR:7;  Átl. túlélés: 6,5 hó;  Él: 3

Grade 3-4 akut/késői toxicitás: 0
Cetuximab
Panitumumab
Zalutumumab
Lapatinib
Erlotinib
BIBW 2992
PF-00299804
TKI
Multi-I
Anti-EGFr
VEGF inhibitors
Ligand (e.g., EGF, TGF-alpha)
Heterodimer (e.g., EGFR/erbB2)
Pi3K
STAT
Akt
SH2
SH3
SOS
ras-GTP
raf-1
Cell proliferation
Decreased apoptosis
Angiogenesis
Metastasis and radio resistance
Gene transcription, cell cycle progression
Extracellular domain
Intracellular domain
EGFR
HER2
HER3
HER4
No bound ligand
Kinase inactive
Intracellular ligand-binding domain
Proteosoma-I
Bortezomib
Cetuximab
Panitumumab
Nimotuzumab
Sorafenib
BIBW 2992
PF-00299804
TKI
Lapatinib
Erlotinib
c-Raf, b-Raf VEGFR-1/2/3, PDGFR-β
Multi-I
Lokoregionálisan előrehaladott tumorok esetén indukciós KT értékelése alapján konkomittáns KRT/E-RT javasolt, intenzív szupportáció –preventív ellátás mellett

Recidíva esetén E-reirradiáció végezhető

Szisztémás gyógyszer- sugárkezelés optimalizálása (magas szintű standardok)

Individualizált kezelés
- HPV és prediktív molekuláris markerek
- tumorválasz- terápia-váltás
- Rehabilitáció-követés