Actualités en radiothérapie ORL

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Réunion GBCO 19 MAI 2017

Cetuximab versus platinum-based chemoradiation in Locally advanced p16 Positive oropharyngeal cancer

C. Barney, Ohio State University, ESTRO 2017,

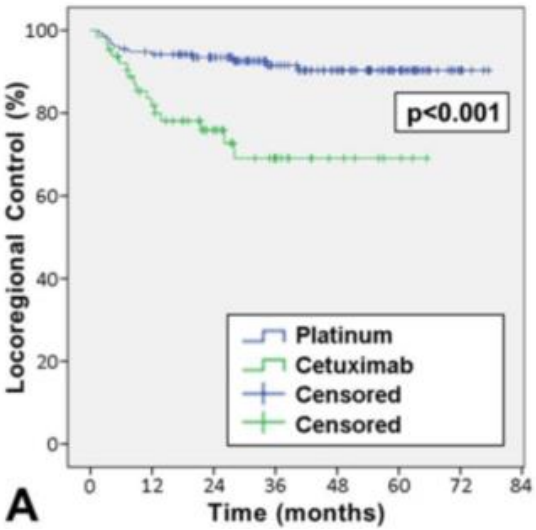
- Etude rétrospective

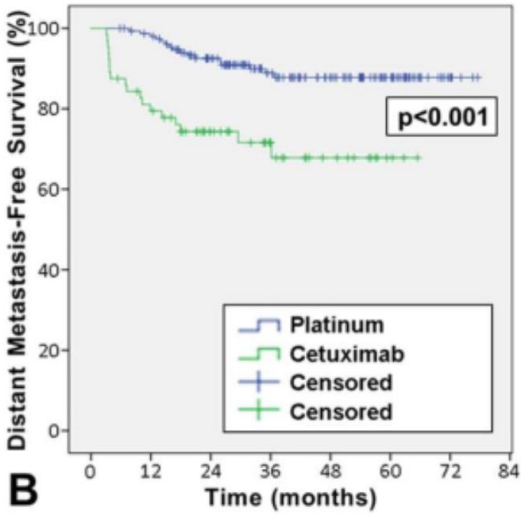
2010-2014:
219 Oropharyngeal cancers AJCC III-IV p16+

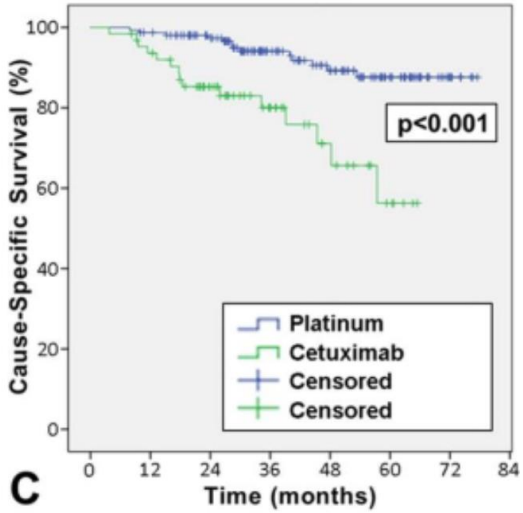
- Groupes équilibrés

155: RT- platine
(136 CDDP; 19 CB)

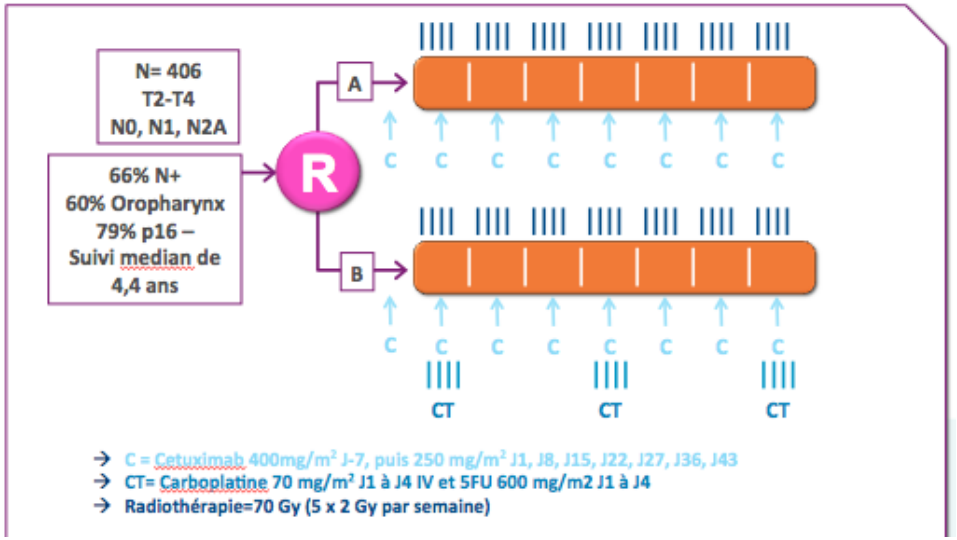
64 cetuximab



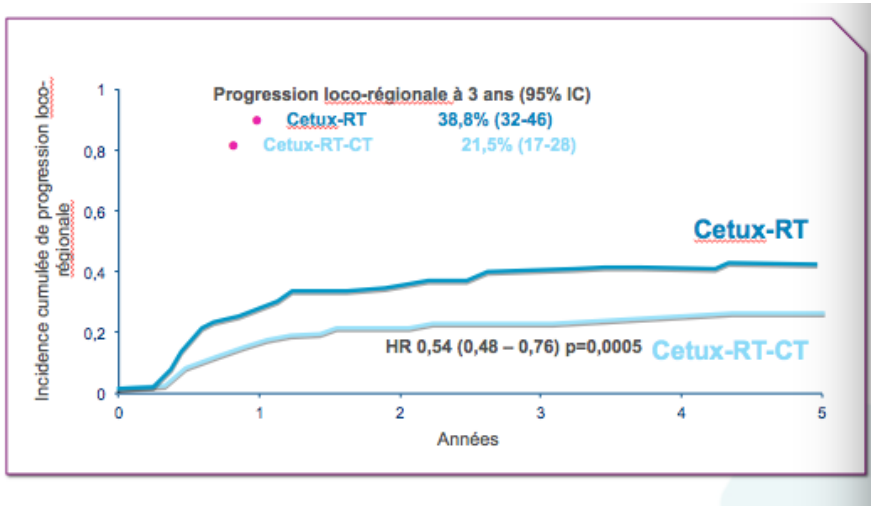


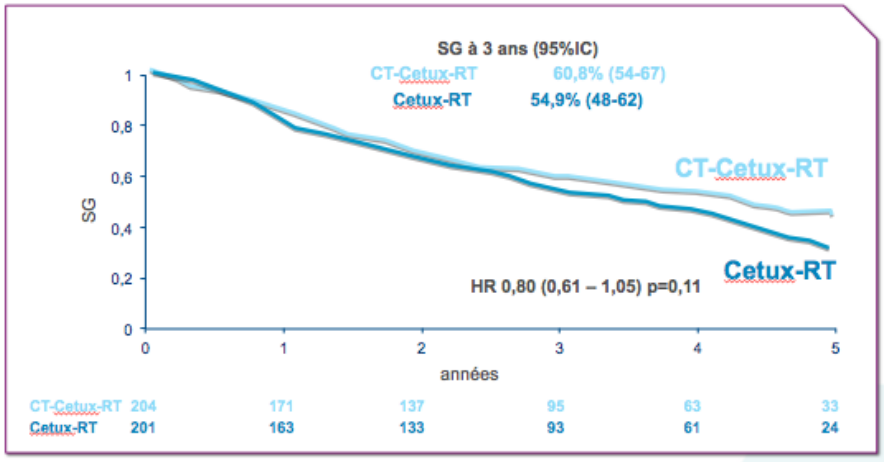


Impact of HPV in effect of Chemotherapy in SCCHN: results of the GORTEC 2007-01 randomized trial



ASCO 2016
Pas de bénéfice en survie
Bénéfice en CLR
Toxicités augmentées
« Option thérapeutique »





Oropharynx P16- dans le GORTEC 2007 01

- 65% d'oropharynx
- 236 (89%) analysables pour p16 (115 bras A , 121 bras B)
- 21% de p16+ (24 Bras A et 25 bras B)
- 15 des 49 p16+ sont non fumeurs
- Alors que seuls 3% des p16- sont non fumeurs

- Amélioration significative de la PFS et du contrôle loco régional chez les p16+ comparés à P16- (p 0,0002)
- Test d'interaction non significatif (p0,13) entre le statut p16 et le type de traitement

TNM-8

- The TMN 8th edition is being published in December 2016.
  - The UICC TNM Project has published the 8th Edition of the TNM Classification of Malignant Tumours that comes into effect on January 1, 2017. Since some organizations may not be ready to adopt the new classification, we recommend that the edition of the TNM classification be always included in data reporting

  - The following is a summary of the changes between the 7th and 8th editions of TNM.
- Major changes are listed and minor changes are identified.

TNM-8

New classifications:

- Oropharynx p16+ve
- Unknown primary cervical neck lymph nodes
- Skin head and neck cancers
- Thymus
- Neuroendocrine tumors: pancreas
- Osteosarcoma: Pelvic, Spine
- Soft tissue Sarcoma: Head and neck, Retroperitoneal, Thoracic and Abdominal Viscera

cervical nodes

Clinical

N1, N2a, N2b and N2c unchanged other than specify without extranodal extension

• N3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

• N3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

* The presence of skin involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement is classified as clinical extra nodal extension

- **Pathological**
- **N1, N2a, N2b and N2c unchanged other than specify without extranodal extension**
- pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
- pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or, multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

Oropharynx p16 Positive tumours

Clinical and Pathological T categories

- T1 Tumour 2 cm or less in greatest dimension
- T2 Tumour more than 2 cm but not more than 4 cm
- T3 Tumour more than 4 cm in or extension to lingual surface of epiglottis
- T4 Tumour invades any of the following: larynx, deep/ extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), medial pterygoid, hard palate, mandible*, lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encases carotid artery

Oropharynx p16 Positive tumours

Clinical N categories

N0 No regional lymph node metastasis

N1 Unilateral metastasis, in lymph node(s), all 6 cm or less

N2 Contralateral or bilateral metastasis in lymph node(s), all 6 cm or less in greatest dimension

N3 Metastasis in lymph node(s) greater than 6 cm in dimension

Pathological N categories

pN0 No regional lymph node metastasis

pN1 Metastasis in 1 to 4 lymph node(s)

pN2 Metastasis in 5 or more lymph node(s)

Oropharynx p16 Positive tumours

Clinical

Stage I	T1,T2	N0,1	M0
Stage II	T1,T2	N2	M0
	T3	N0,N1,N2	M0
Stage III	T1-T4	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M0

Pathological

Stage I	T1,T2	N0,1	M0
Stage II	T1,T2	N2	M0
	T3	N0,N1	
Stage III	T3,T4	N2	M0
Stage IV	Any T	Any N	M0

Nasopharynx

T categories

T1 Unchanged

T2 Tumour with extension to parapharyngeal space and/or infiltration of the medial pterygoid, lateral pterygoid, and/or prevertebral muscles

T3 Tumour invades bony structures of skull base cervical vertebra, pterygoid structures, and/or paranasal sinuses

T4 Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, parotid gland and/or infiltration beyond the lateral surface of the lateral pterygoid muscle

N Categories

N1 Unilateral metastasis, in cervical lymph node(s), and/or unilateral or bilateral metastasis in retropharyn-geal lymph nodes, 6 cm or less ,above the caudal border of cricoid cartilage

N2 Bilateral metastasis in cervical lymph node(s), 6 cm or less above the caudal border of cricoid cartilage

N3 Metastasis in cervical lymph node(s) greater than 6 cm in dimension and/or extension below the caudal border of cricoid cartilage

Nasopharynx

Stage Groups

Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0, N1	M0
Stage III	T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage IVA	T4	N0, N1, N2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

Stage IV compressed previous stage IVB now IVA

Cervical Node
Unknown Primary

- If EBV positive stage as per nasopharyngeal carcinomas
- If p16 positive stage as per p16 positive oropharynx carcinomas

- If EBV and p16 negative clinical and
- pathological node definitions are as
- above

Stage III	T0	N1	M0
Stage IVA	T0	N2	M0
Stage IVB	T0	N3	M0
Stage IVC	T0	N1, N2, N3	M1

Thyroid Carcinoma
Papillary and Follicular

The definition of T3 has been revised for papillary and follicular and medullary carcinomas

T3a Tumour more than 4 cm in greatest dimension, limited to the thyroid

T3b Tumor of any size with gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, or omohyoid muscles)

The age for a poor prognosis has changed from 45 years to 55 years

Stage < 55 years old

Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1

Stage ≥55 years old

Stage I	T1a,T1b,T2	N0	M0
Stage II	T3	N0	M0
	T1, T2, T3	N1	M0
Stage III	T4a	Any N	M0
Stage IVA	T4b	Any N	M0
Stage IVB	Any T	Any N	M1

Immunothérapies et cancers ORL

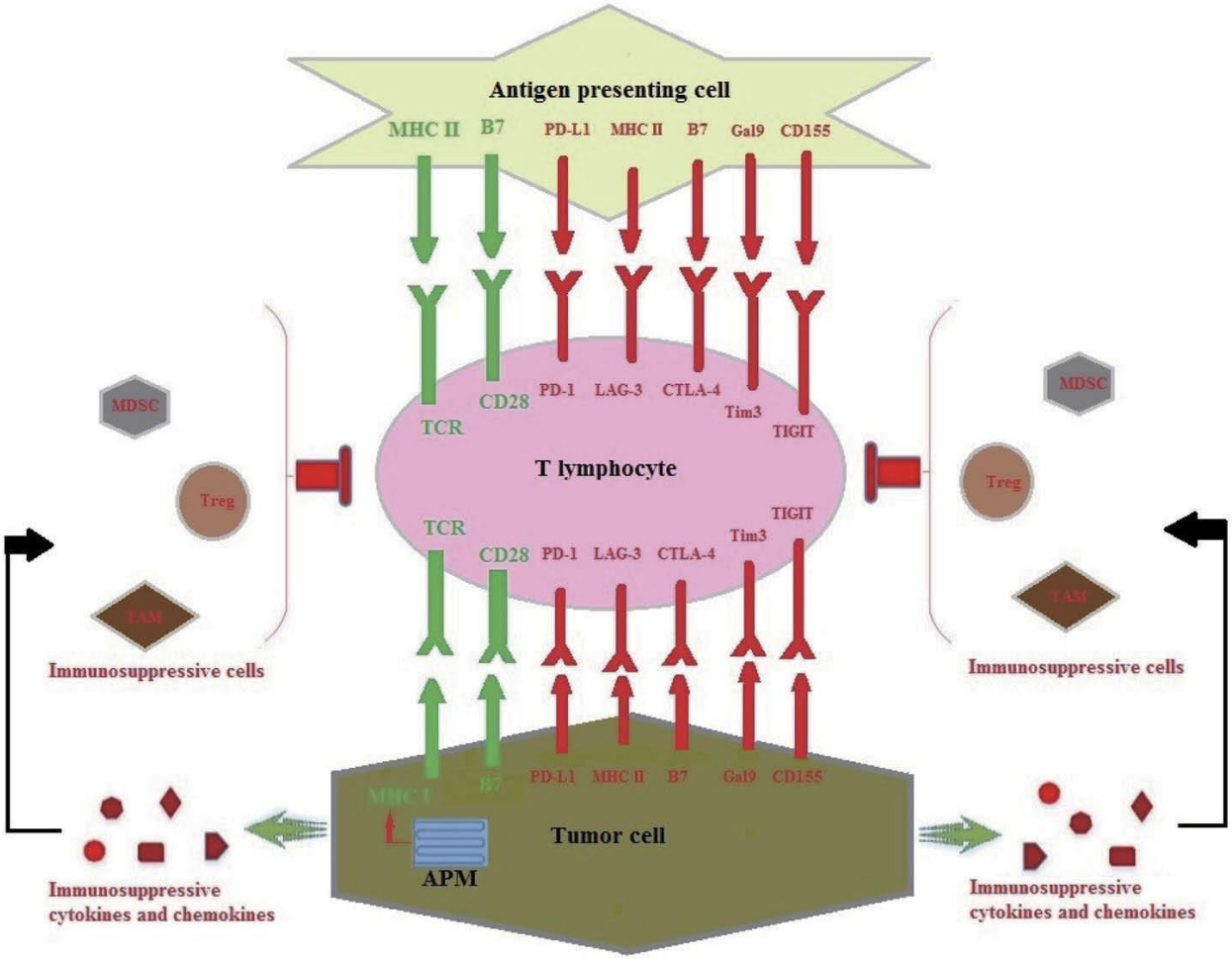


Table 1. Summary of clinical trials of immune checkpoint inhibitors in HNSCC.

	Checkpoint blockade					
Target	Drug name	NCT/trial	Phase	Combination	No. of patients	Status
PD-1	Pembrolizumab	KEYNOTE-012	I	Single	192	Platinum-refractory R/M HNSCC
PD-1	Pembrolizumab	KEYNOTE-040	III	Single	466	Platinum-refractory HNSCC
PD-1	Pembrolizumab	KEYNOTE-048	III	Platinum/5-FU	780	R/M HNSCC
PD-1	Pembrolizumab	NCT02289209	II	Reirradiation	48	Second primary HNSCC
PD-1	Pembrolizumab	NCT02318771	I	RT	40	R/M HNSCC
PD-1	Nivolumab	CHECKMATE141	III	Single	506	Platinum-refractory R/M HNSCC
PD-1	Nivolumab	NCT02764593	I/III	R(C)T	120	Advanced HNSCC
PD-L1	Durvalumab	NCT02952586	III	Cisplatin + RT	640	Advanced HNSCC
CTLA-4	Ipilimumab	NCT01935921	Ib	Cetuximab + RT	18	Advanced HNSCC
CTLA-4	Ipilimumab	CheckMate714	II	Nivolumab	315	R/M HNSCC
CTLA-4	Ipilimumab	CheckMate 651	III	Nivolumab	490	HNSCC
CTLA-4	Tremelimumab	NCT02319044	II	Durvalumab	543	PD-L1-negative, platinum-refractory R/M HNSCC
CTLA-4	Tremelimumab	KESTREL	III	Durvalumab	760	R/M HNSCC
CTLA-4	Tremelimumab	EAGLE	III	Durvalumab	720	PD-L1±, platinum-refractory R/M HNSCC

PD-1: programmed cell death 1; HNSCC: head and neck squamous cell carcinoma; CTLA-4: cytotoxic T-lymphocyte protein 4; NCT: Clinical Trial; R/M: Recurrent/Metastatic; FU: Fluorouracil; RT: Radiation Therapy.

- ✓ Taux de réponse 20% revues centralisées (platinum-refractory)
- ✓ Approbation accélérée du pembrolizumab par la FDA
- ✓ Nivolumab: ↘ 30% risque de décès

- ✓ Et beaucoup de questions:
  - ✓ Standardisation de l'évaluation de la réponse
  - ✓ Seuil de Positivité de PDL1 et standardisation de son évaluation
  - ✓ combinaisons

conclusion

- Essais en cours sur la désescalade thérapeutique des Tumeurs P16+
- Place des immunothérapies en stratégie initiale (essai GORTEC)
- Applicabilité autre que pronostique de la nouvelle TNM?