

Indications de la RT dans les cancers thyroïdiens

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Introduction

- Place limitée par rapport à la chirurgie/
Irathérapie
- Absence d'études randomisées
- Quelques «niches » thérapeutiques
- PEC des cancers réfractaires (nouvelle entité)

Cancers différenciés



Cancer de la thyroïde

Cancers différenciés

6. La prise en charge thérapeutique des patients ayant un cancer différencié de la thyroïde de souche folliculaire est adaptée au niveau du risque, défini par la classification TNM et par le type histologique de la tumeur :

- elle repose sur la thyroïdectomie totale dans la majorité des cas ;
- l'irathérapie (radiothérapie interne vectorisée par l'iode-131) n'est indiquée systématiquement que chez les patients à haut risque et dans les formes métastatiques ;
- la place de la radiothérapie externe est limitée, et son indication, si elle se pose, doit être discutée en réunion de concertation pluridisciplinaire (RCP).
- il n'y a pas d'indication de la chimiothérapie dans le traitement initial.

THE ROLE OF POSTOPERATIVE EXTERNAL-BEAM RADIOTHERAPY IN THE MANAGEMENT OF PATIENTS WITH PAPILLARY THYROID CANCER INVADING THE TRACHEA

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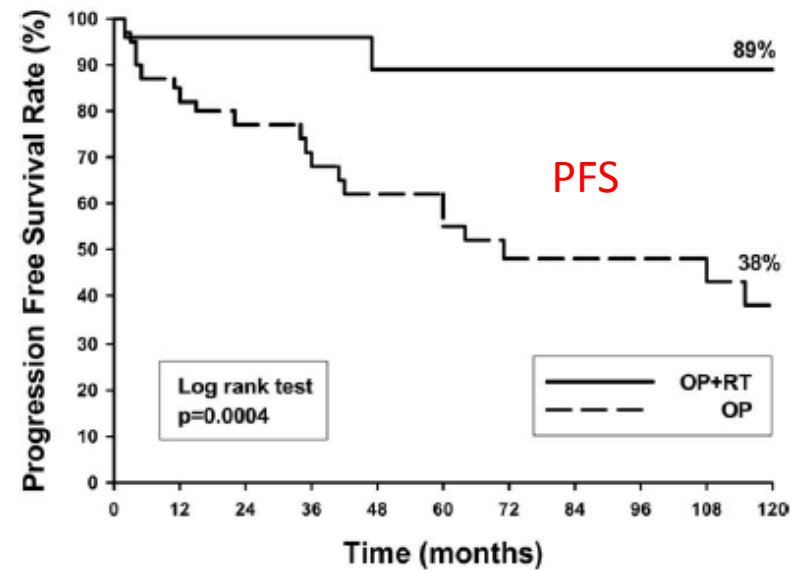
Methods and Materials: Of 1,098 thyroid cancer patients, 68 (6%) were found to have tracheal invasion, and they all received “shave” excision of the tracheal cartilage. Among them, 12 patients had no postoperative residuum, 43 patients had microscopic residuum, and 13 patients had macroscopic residuum. All patients were divided into two groups according to treatment modality with or without EBRT; (1) the control group ($n = 43$) and (2) the EBRT group ($n = 25$).

Résultats

Table 2. Local failure according to radiotherapy for postoperative residual disease status

Postoperative residuum	Treatment modality	Local failure		<i>p</i>
		No. of patients/total no. of patients	%	
No residuum	OP	3/10	30	0.54
	OP + RT	0/2	0	
Microscopic residuum	OP	14/28	50	0.004
	OP + RT	1/15	6.7	
Macroscopic residuum	OP	5/5	100	0.005
	OP + RT	1/8	12.5	

Abbreviations as in Table 1.



SG

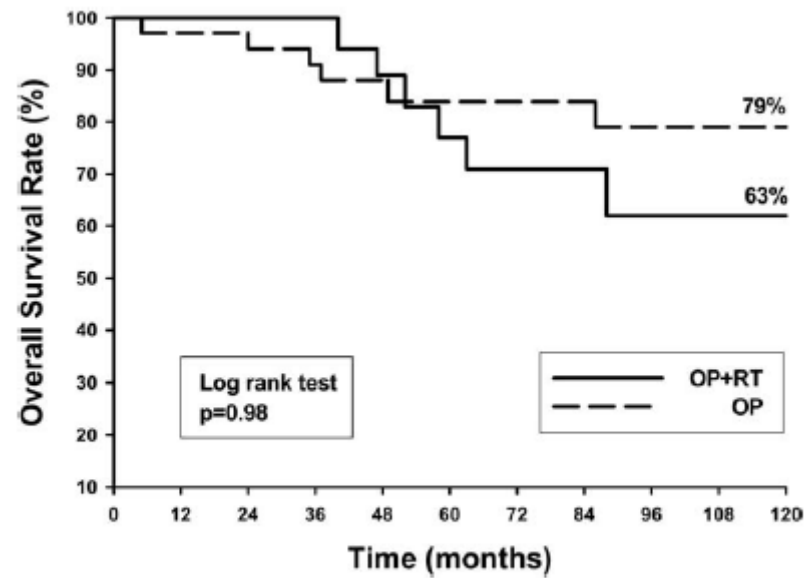


Fig. 3. Overall 10-year actuarial survival rate. OP = operation; RT = radiotherapy.

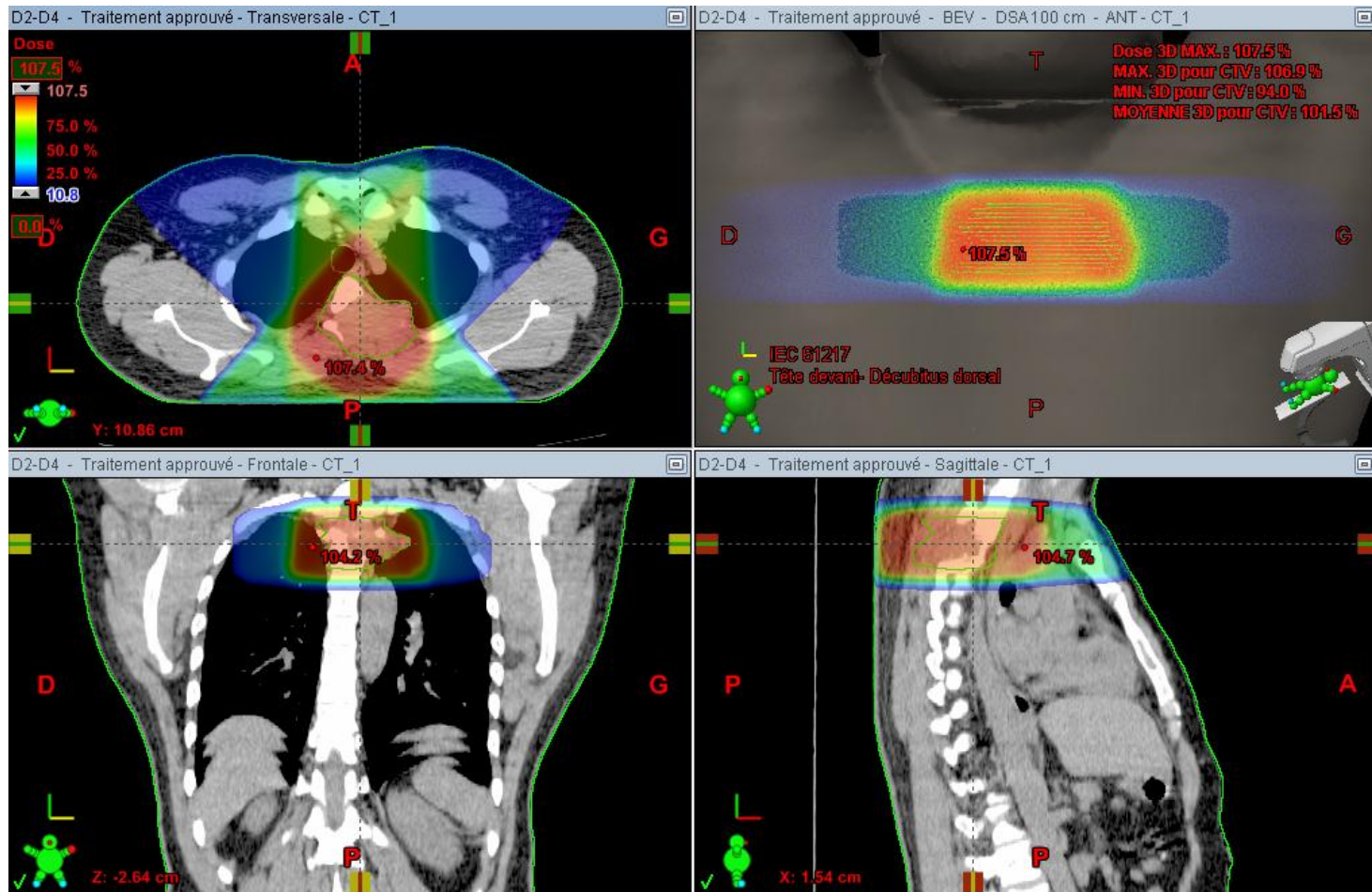
Rôle palliatif majeur

- Antalgique (métastases osseuses).
- Décompressif
 - Moelle
 - Médiastin
- Qualité de vie (long survivants)

Métastase rachidienne compressive



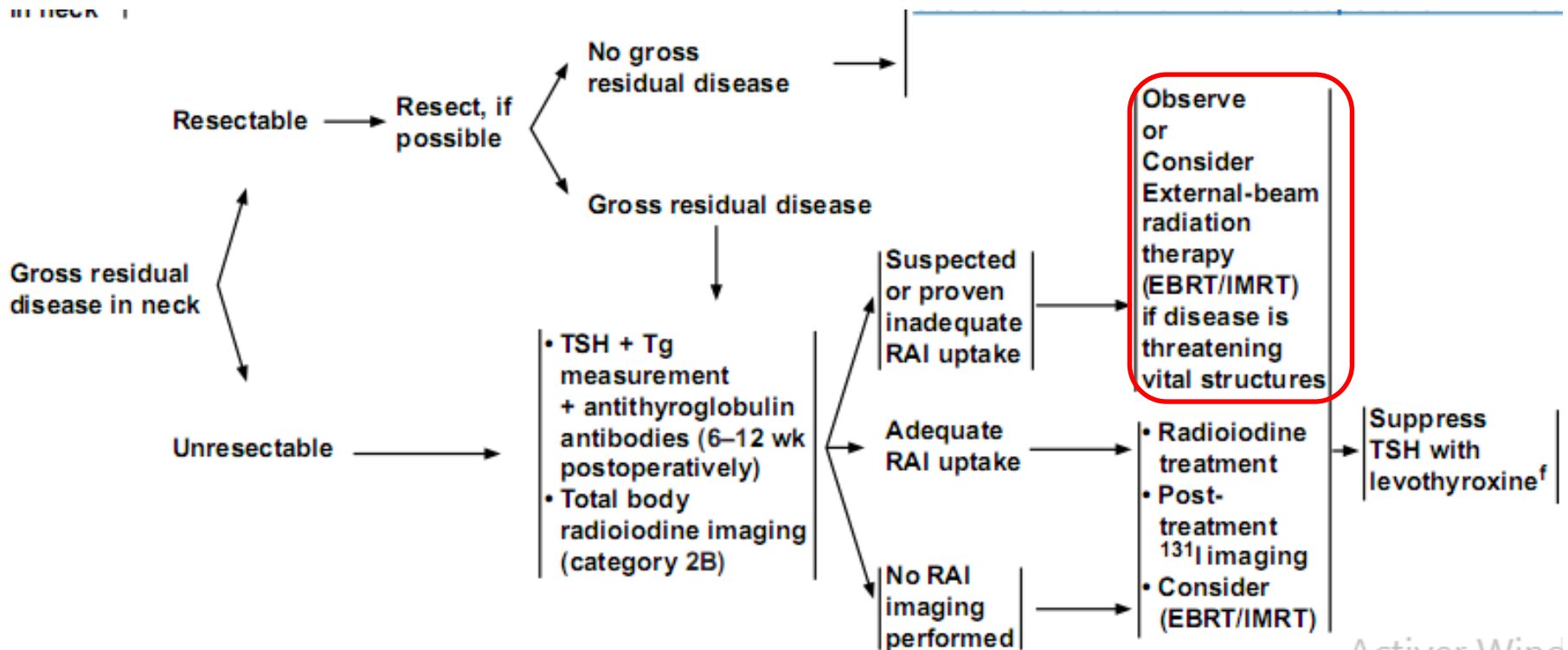
RT décompressive



ATA Guidelines

The ATA states that: “The use of external beam irradiation to treat the primary tumor should be considered in patients over age 45 with grossly visible extrathyroidal extension at the time of surgery and a high likelihood of microscopic residual disease.”

NCCN 2015



CDT: indications de RT à retenir...

- Résidu post opératoire (après chirurgie « experte »)
- Peu ou pas de fixation d'Iode
- Pas de réponse à l'Iode (Bulky)
- Métastase menaçante (fracture, compression)
- ...Préopératoire??

Cancers médullaires: Série ISA

(C Nasr Ben Ammar, L Kochbati & al Cancer Radiothérapie sept2012)

L'objectif de cette étude est d'évaluer les résultats thérapeutiques d'une radiothérapie postopératoire des CMT et l'impact des facteurs pronostiques clinico-pathologiques sur le contrôle locorégional et la survie globale.

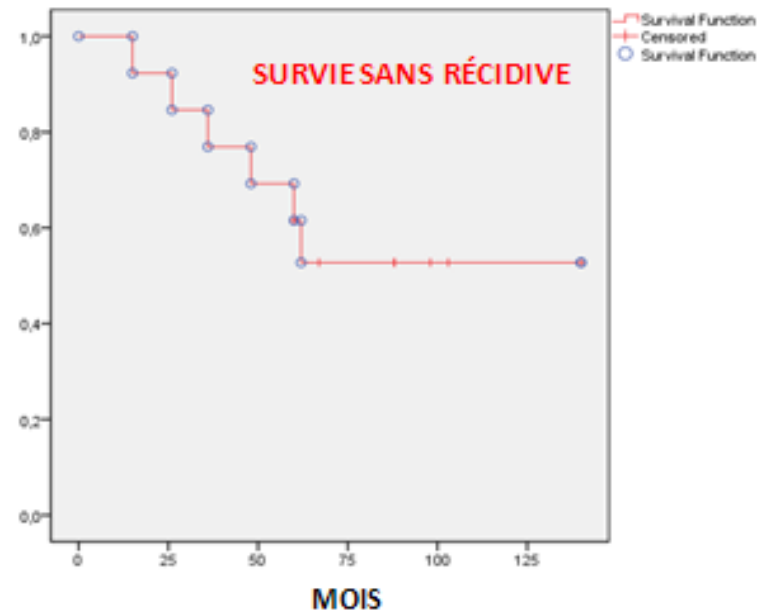
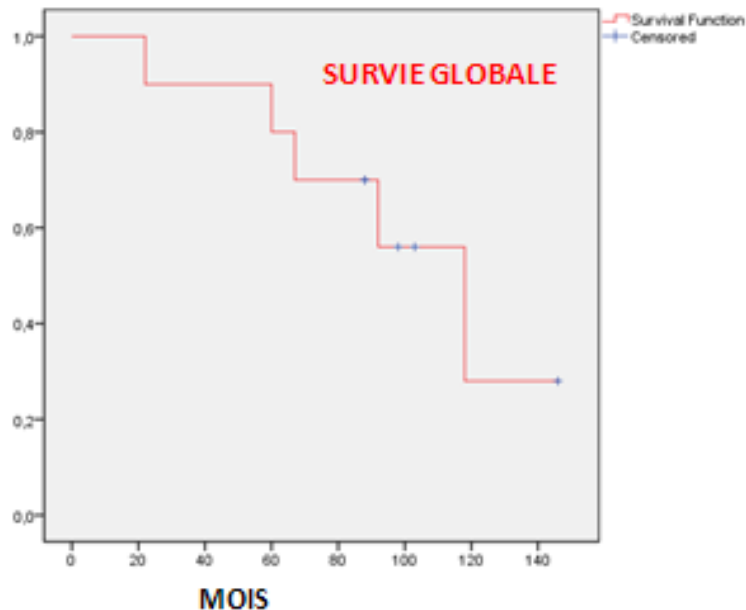
Série ISA: 13 cas (1996- 2005)

Age		
Moyenne	49 ans	
Extrême	19 – 80 ans	
Sexe		
Masculin	54 % (7)	
Féminin	46 % (6)	
Marges de résection		
Tumorale	73 % (8)	→ 83%
Economique	10 % (2)	
Saine	17 % (3)	
Envahissement ganglionnaire		
N-	32 % (4)	
N+(1-2)	15 % (2)	→ 68%
N+(≥3)	53 % (7)	

Tableau «1» : Caractéristiques anatomocliniques des 13 patients

Résultats

- Suivi médian: 132 mois
- Taux de contrôle locorégional: 62 %.
- SG à 3 ans: 76 % et à 5 ans de 61%
- FP: qualité d'exérèse et N+





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NCCN Guidelines Version 2.2015

Thyroid Carcinoma – Medullary Carcinoma

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PRESENTATION

Medullary
thyroid
carcinoma
on FNA

- Basal serum calcitonin level
- CEA
- Pheochromocytoma screening^b
- Serum calcium
- Consider genetic counseling
- Screen for RET proto-oncogene mutations^c (exons 10, 11, 13–16)
- Thyroid and neck ultrasound (including central and lateral compartments), if not previously done
- Consider evaluation of vocal cord mobility
- Consider contrast-enhanced CT of chest and abdomen

≥1.0 cm in
diameter
or bilateral
thyroid disease

- Total thyroidectomy with bilateral central neck dissection (level VI)
- Therapeutic ipsilateral or bilateral modified neck dissection for clinically or radiologically identifiable disease (levels II–V)
- Consider prophylactic ipsilateral modified neck dissection for high-volume or gross disease in the adjacent central neck
- Consider therapeutic EBRT/IMRT for grossly incomplete tumor resection when additional attempts at surgical resection have been ruled out
- Consider adjuvant EBRT/IMRT for gross extrathyroidal extension (T4a or T4b) with positive margins after resection of all gross disease and following resection of moderate-to high-volume disease in the central or lateral neck lymph nodes with extra-nodal soft tissue extension

A retenir

Les «Guidelines» de l' ATA (American Thyroid Association) ne proposent une radiothérapie postopératoire que pour un sous-groupe à haut risque défini par une chirurgie type R1 et/ou une effraction extracapsulaire avec un taux de thyrocalcitonine postopératoire qui reste élevé sans métastases documentées.

A discuter?? Contrôle local>>survie

Cancers anaplasiques

- Aggressivité extrême
- Evolutivité locorégionale et métastatique
- Médiane de survie < 6 mois
- RT souvent palliative

**COMBINED TREATMENT OF ANAPLASTIC THYROID CARCINOMA WITH
SURGERY, CHEMOTHERAPY, AND HYPERFRACTIONATED ACCELERATED
EXTERNAL RADIOTHERAPY**

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Etude prospective non randomisée

Entre 1990 et 2000

N: 30

24 M0 (17 chirurgie première et 3
chirurgies secondaires)

Chirurgie + Chimio + Radiothérapie

[chimio-radiothérapie alternée]

chimiothérapie : 6 cycles

adriamycine 60 mg/m² J1-J28

cisplatine 120 mg/m² J1-J28

radiothérapie

entre les cycles 2 et 3

cou et médiastin supérieur

40 Gy / 3,2 semaines + 10-15 Gy

bifractionnée, accélérée 2X1,25 Gy/J/5j/sem

SG

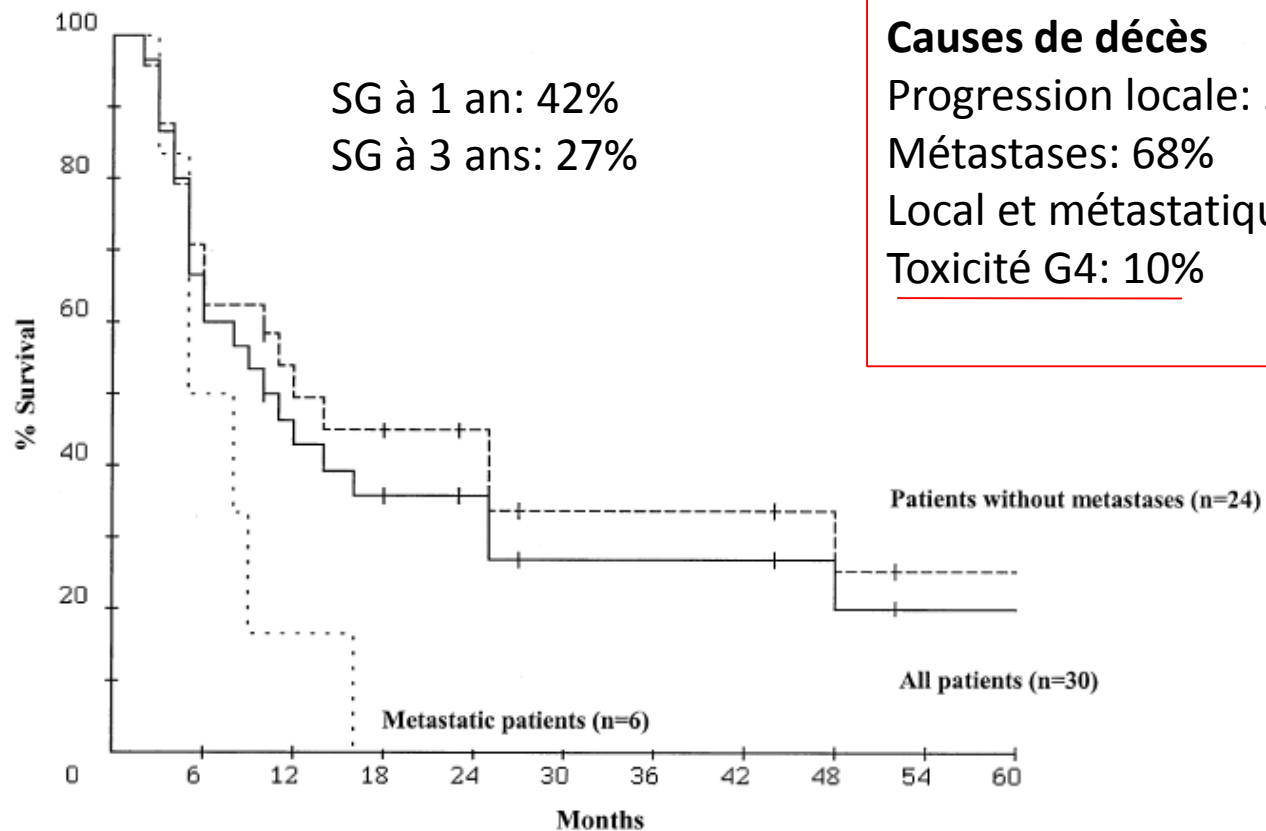


Fig. 1. Overall survival of the 30 anaplastic thyroid cancer patients and survival according to the presence or absence of initial distant metastases.

Importance de la chirurgie la plus complète possible

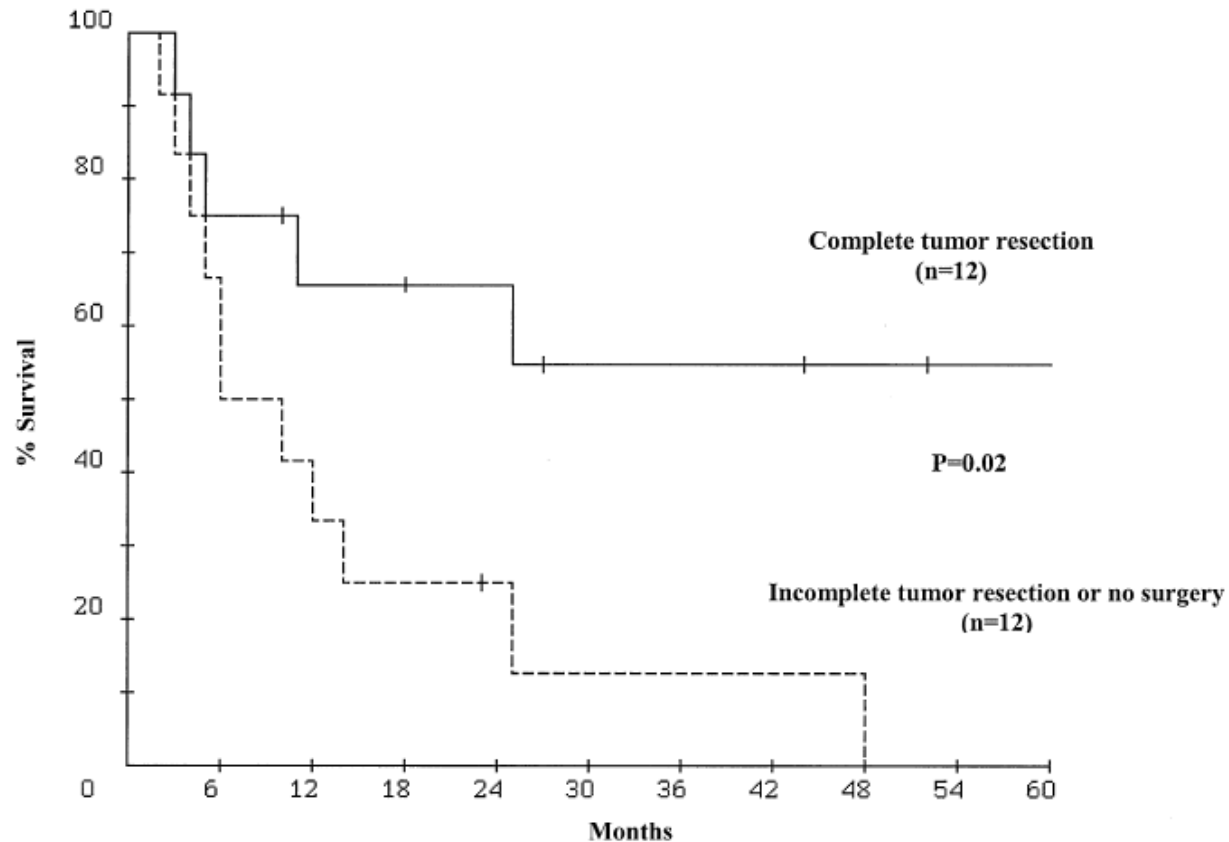


Fig. 2. Overall survival according to the completeness of surgery in the 24 nonmetastatic patients.

Résultats de la trimodalité

Table 2 Selected Previous Reported Studies in Anaplastic Thyroid Cancer Using Radiation Therapy

Study	Year	#	M1	Study Type	Treatment Variables	CT	OS*	Notes
Kim and Leeper ³⁶	1987	19	0%	Prospective	CT/RT [§]	D	12 months	No standardized chemotherapy, but all doxorubicin based. In 8 pts with curative surgery, median survival 43 months
Haigh et al ³³	2001	33	64%	Retrospective	Surg-curative → CT/RT Surg-palliative ± CT/RT CT/RT alone	Various	3.8 months	
De Crevoisier et al ³⁷	2004	30	20%	Prospective	Surg-R0/R1 + CT/RT (pre or post)	CDDP [‡] + D	10 months	
Wang et al ³⁴	2006	47	17%	Retrospective	Surg → RT	None	5.6vmonths	22/47 pts had total or partial thyroidectomy. Includes subjects who received radical RT (23) and palliative RT(24)
Brignardello et al ³⁸	2007	27	56%	Retrospective	Surg → CT/RT palliative CT	CDDP + D	3.9 months	7 patients received palliative CT with paclitaxel alone
Swaak-Kragten et al ³⁹	2009	30	34%	Prospective	CT/RT → CT	D	5.4 months	Pts could receive surgery before treatment. RT was hyperfractionated

OS, OS (refers to median overall survival); CDDP, cisplatin; CT, chemotherapy; D, doxorubicin; RT, radiation therapy; Surg, surgery, #, number of subjects.

Cancer anaplasique

indications à retenir...

- Souvent palliative
- Efforts pour éviter la mort par suffocation...
- Multimodalité (hyperfractionnée?) : résultats encourageants mais toxicité limitante +++

Cancers réfractaires et perspectives

Nouvelle entité:

- CMT localement avancés non accessibles au traitement ou métastatiques
- CDT localement avancés non accessibles au traitement ou métastatiques et réfractaires à l'Iode
- CAT: impasse thérapeutique??

Thérapie ciblée

Inhibiteurs de la Thyrosine Kinase

Sorafinib, Sunitinib, Gefitinb...

PRINCIPLES OF KINASE INHIBITOR THERAPY IN ADVANCED THYROID CARCINOMA

- Oral kinase inhibitors demonstrate clinically significant activity in randomized, placebo-controlled clinical trials in **locally recurrent unresectable and metastatic medullary thyroid cancer (MTC) and in radio iodine-refractory differentiated thyroid cancer (DTC).**^{1,2,3}
- When considering kinase inhibitor therapy for individual patients, several factors should be considered.
 - ▶ Kinase inhibitor therapy can be associated with **progression-free survival, but is not curative.**
 - ▶ Kinase inhibitor therapy is expected to cause side effects that may have a significant effect on quality of life.
 - ▶ The natural history of MTC and DTC is quite variable with rates of disease progression ranging from a few months to many years.

Pour récapituler...

Table 47.4 Indications for External Irradiation in Thyroid Cancer

1. Primary therapy of thyroid cancer if unresectable locally, particularly if ^{131}I does not concentrate in tumor
2. Bulky tumor (e.g., mediastinal disease) large enough that it is uncontrollable by ^{131}I alone
3. Residual bulky tumor in the central neck, tracheal, and/or esophageal area or cervical nodal regions after thyroid surgery and removal of malignant cervical adenopathy that may not be controlled by ^{131}I alone
4. Skeletal metastases
 - a. Concentration of ^{131}I small or absent
 - b. Concern about a pathologic fracture, regardless of the degree of ^{131}I concentration
5. Brain metastases
6. Hepatic metastases if symptomatic or other treatment methods have been unsuccessful
7. Relief of pressure symptoms occurring in vital areas caused by soft-tissue masses
8. Superior vena cava syndrome
9. Continually recurring thyroid cancer regardless of ^{131}I accumulation
10. Recurrent or metastatic thyroid cancer occurring after maximal ^{131}I therapy
11. In sequence or conjunction with chemotherapy, particularly in anaplastic cancer
12. Preoperative therapy

