

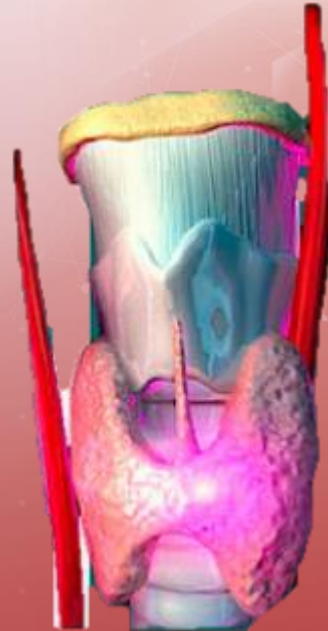


# **NET-TIR CAMPUS 2022**

## **CÁNCER DE TIROIDES**

# Introducción al cáncer de tiroides y refractariedad al yodo radiactivo

Maribel del Olmo García  
Endocrinología y Nutrición  
Hospital La Fe (Valencia)

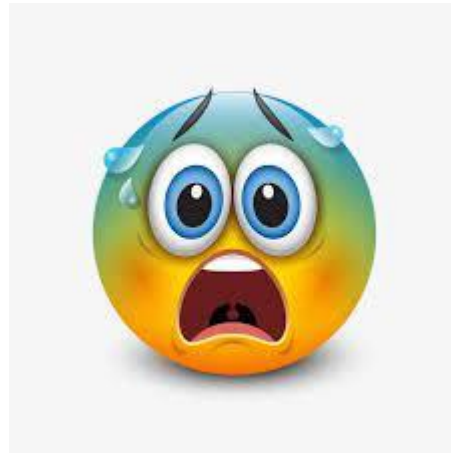




# INTRODUCCIÓN



¿Doctor qué es lo que tengo?



No se preocupe, sólo es un cáncer de tiroides.....





# EPIDEMIOLOGÍA

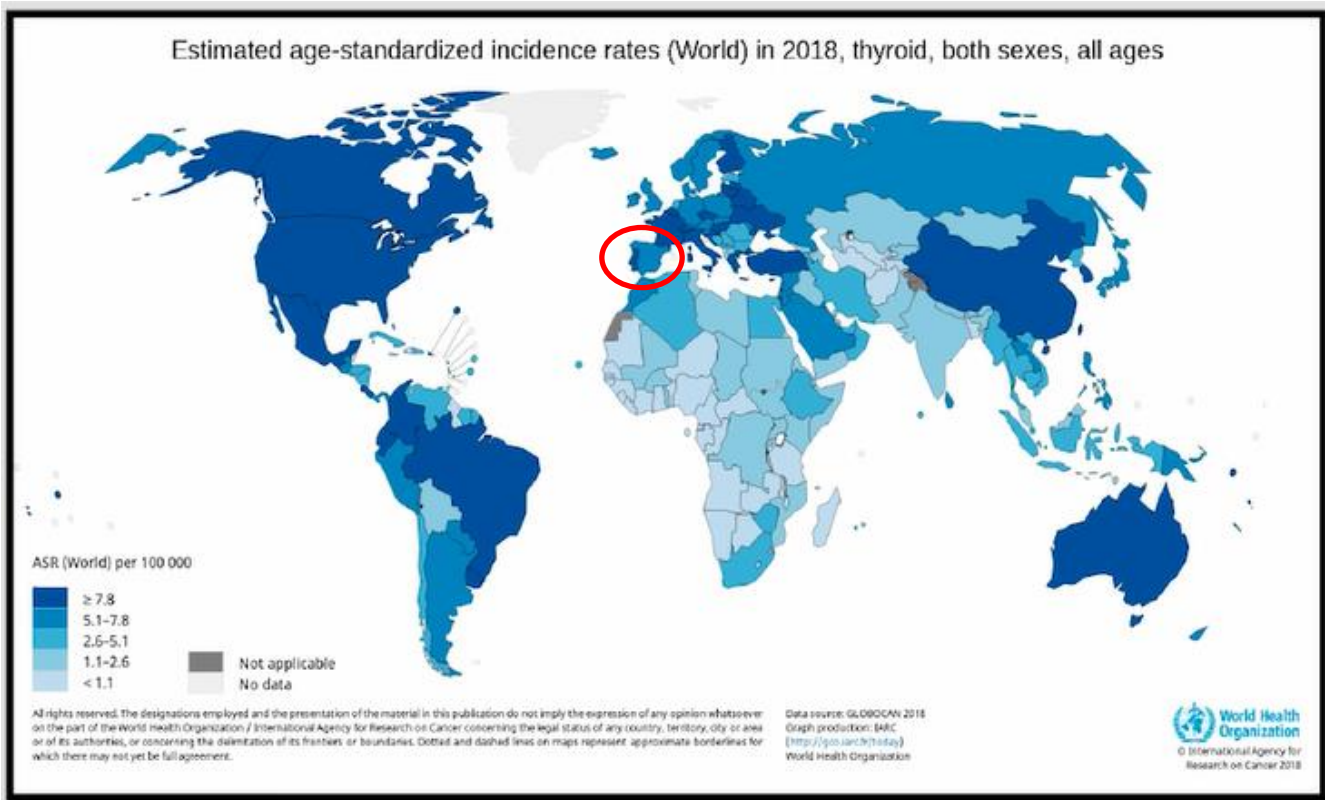
# ¿Es frecuente tener un cáncer de tiroides?

El 50% de la población tiene nódulos tiroideos



El 5-10% serán un ca de tiroides

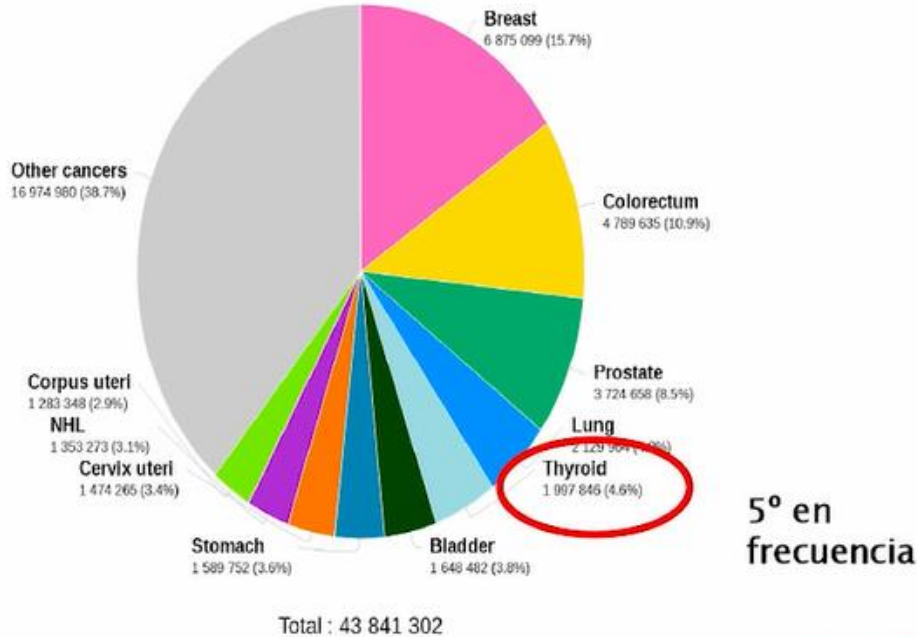
**EL CÁNCER DE TIROIDES ES EL TUMOR ENDOCRINO MÁS FRECUENTE**



WHO 2018



Estimated number of prevalent cases (5-year) in 2018, worldwide, all cancers, both sexes, all ages

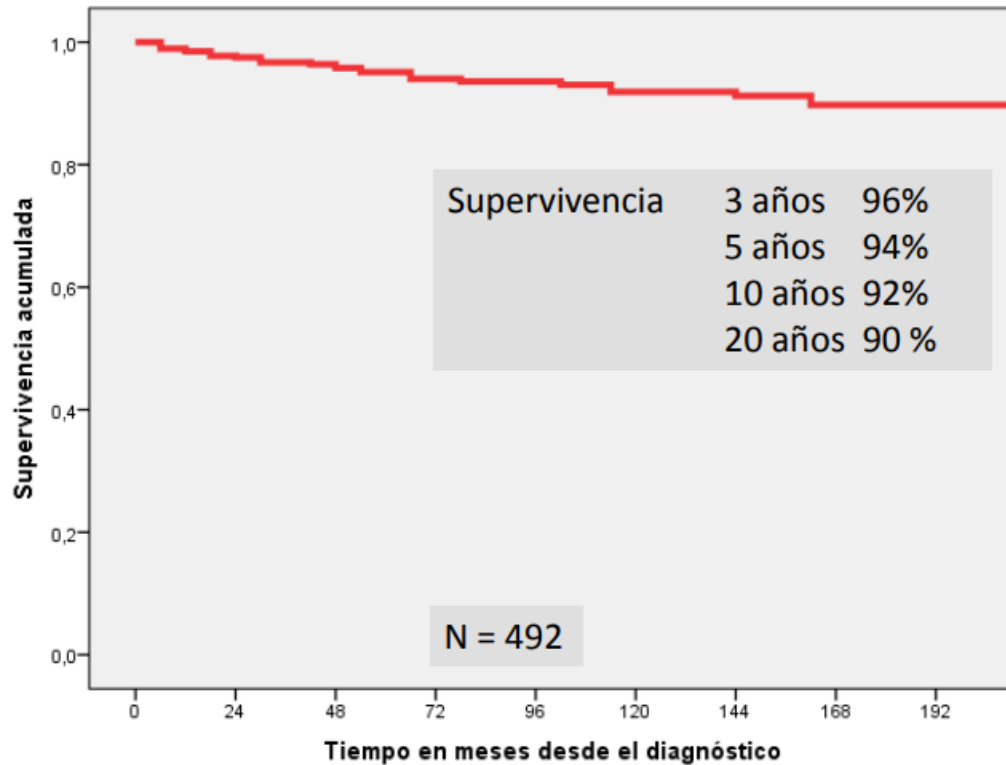


Es más prevalente en mujeres convirtiéndose el 4º en frecuencia

5º en frecuencia

Data source: GLOBOCAN 2018  
Graph production: Global Cancer Observatory (<http://gco.iarc.fr>)





No todos los CDT llevan un curso indolente

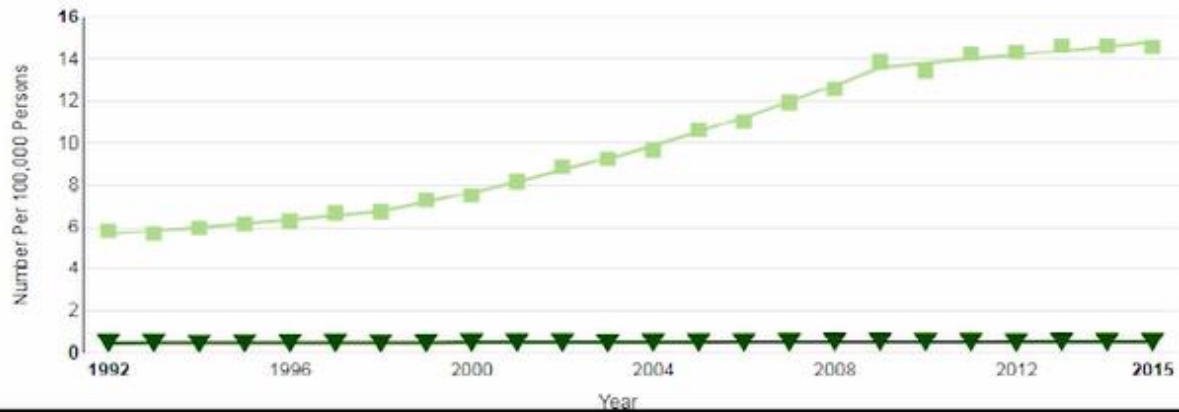
¿Cuál es la probabilidad de morir por un ca de tiroides?

1/200,000 pacientes

Estimated New Cases in 2018	53,990
% of All New Cancer Cases	3.1%

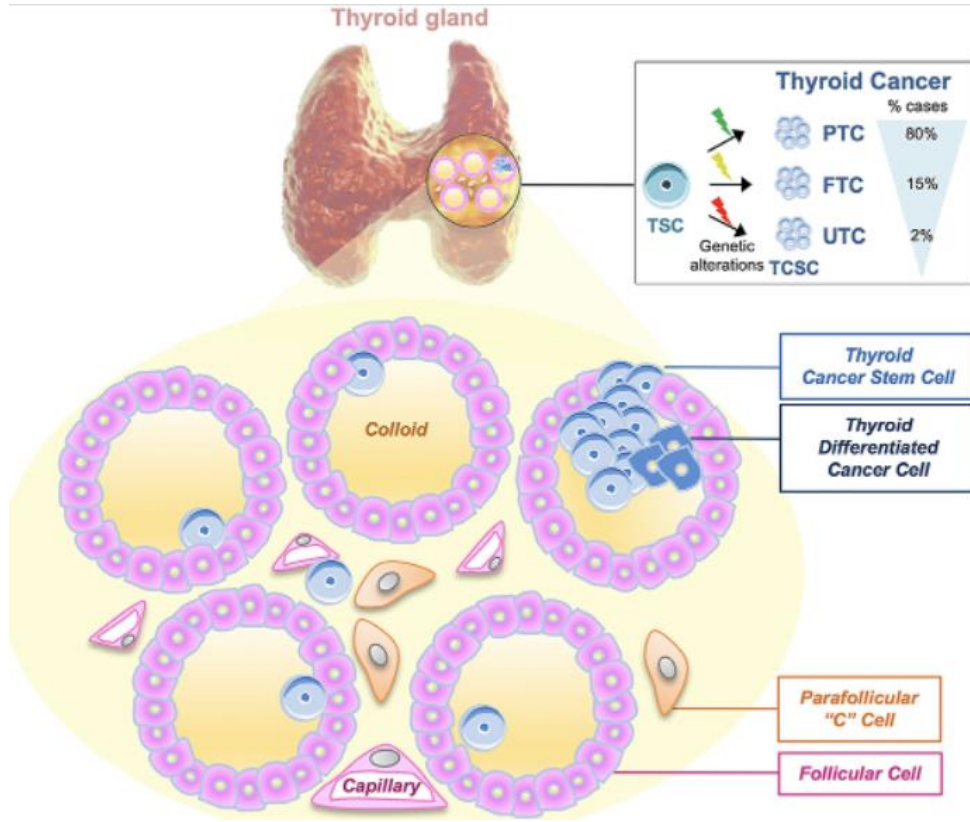
Percent Surviving 5 Years
<b>98.1%</b>
2008-2014

Estimated Deaths in 2018	2,060
% of All Cancer Deaths	0.3%



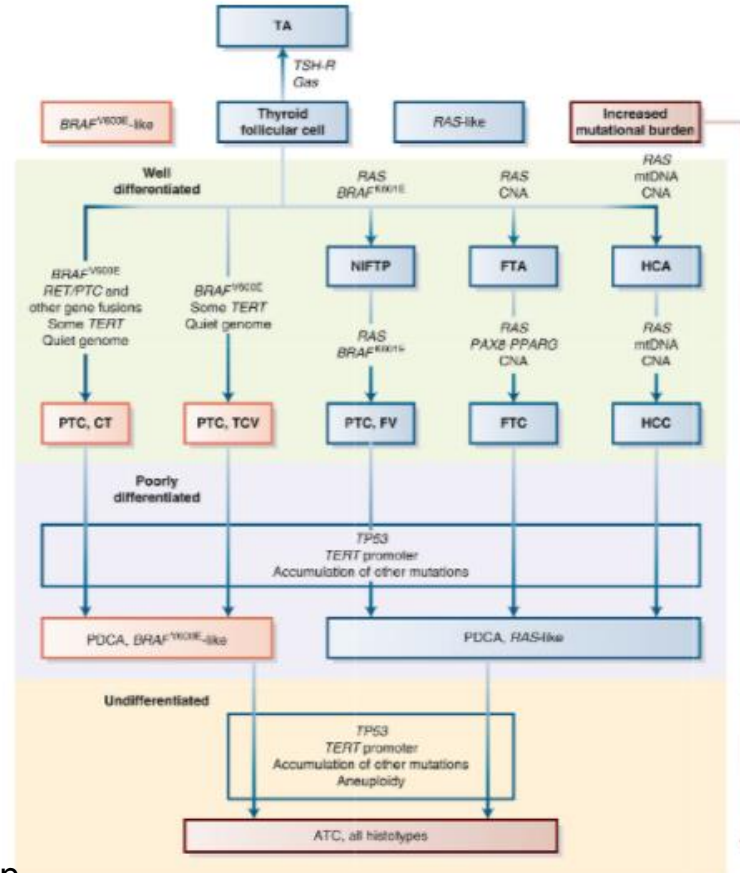


# FISIOPATOLOGÍA



Veschi V, Verona F, Lo Iacono M, D'Accardo C, Porcelli G, Turdo A, Gaggianesi M, Forte S, Giuffrida D, Memeo L, Todaro M. Cancer Stem Cells in Thyroid Tumors: From the Origin to Metastasis. *Front Endocrinol (Lausanne)*. 2020 Aug 25;11:566.

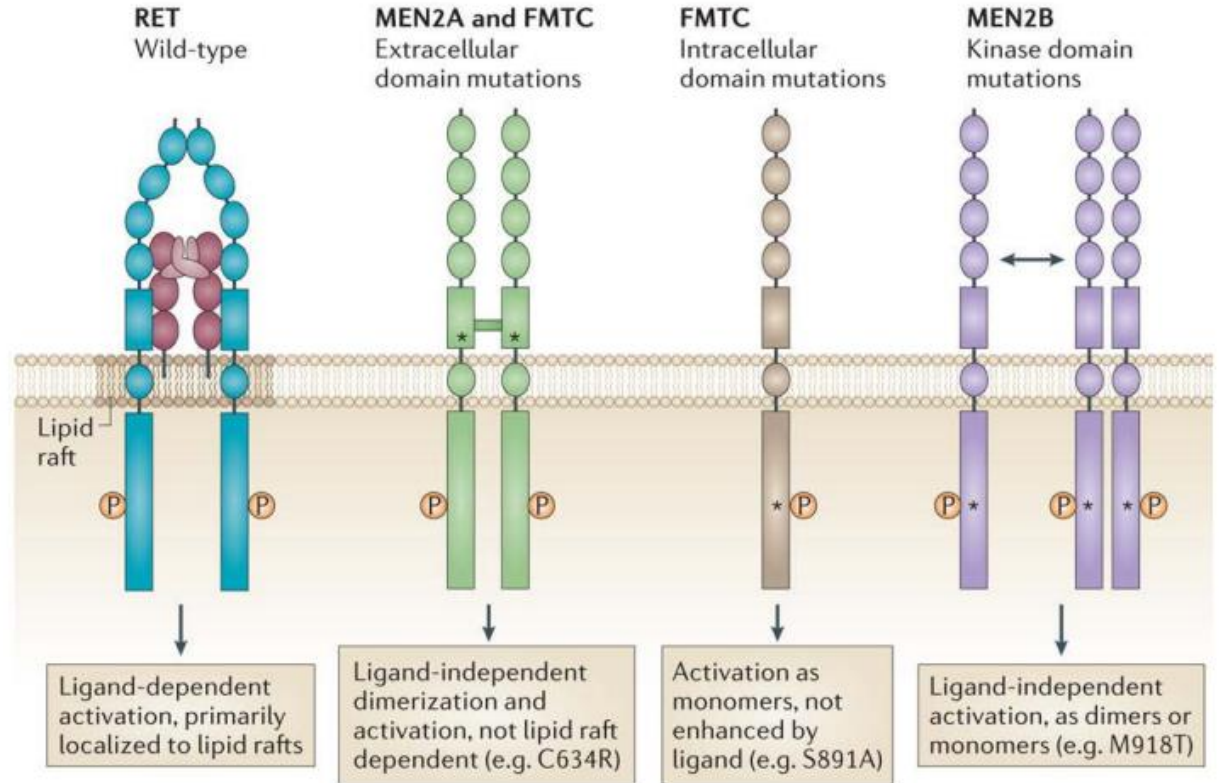
Modelo de carcinoma de tiroides en cuanto a iniciación y progresión de alteraciones genéticas primarias



CA MEDULAR  
DE TIROIDES

FAMILIAR 20-30%

ESPORÁDICO

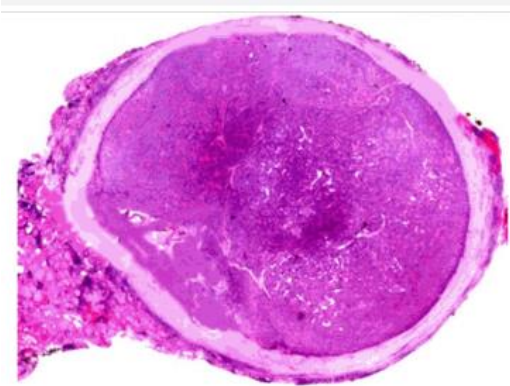


# CLASIFICACION HISTOLÓGICA

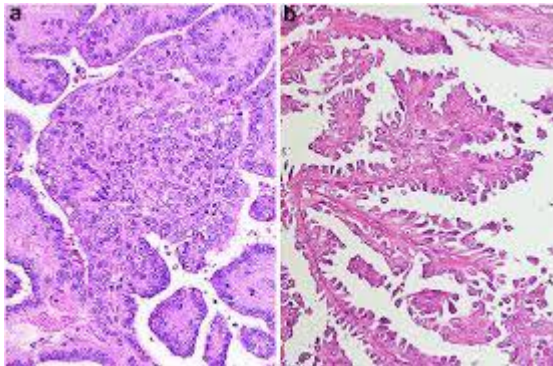
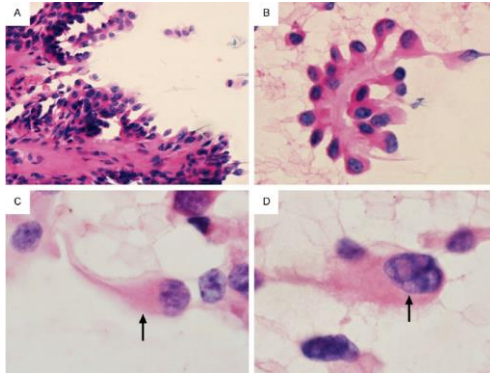


**CLASIFICACION  
HISTOLÓGICA DE LA  
OMS 2017**

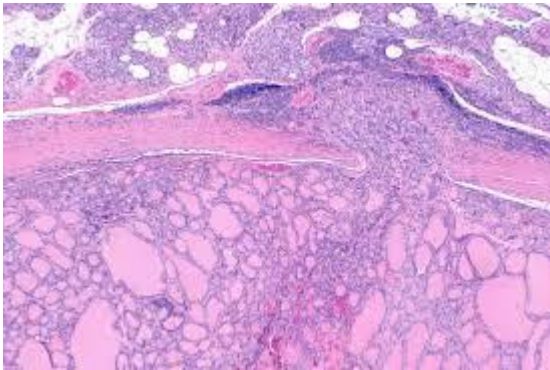
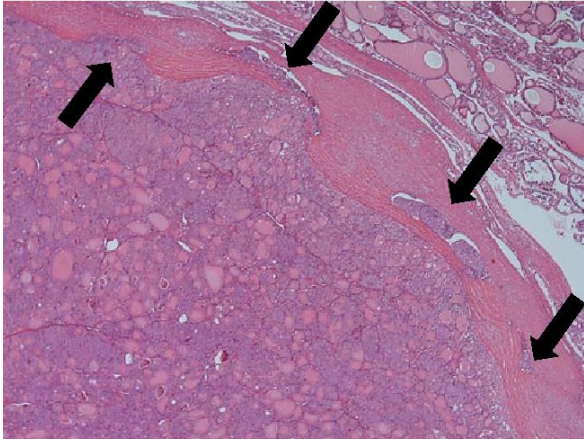
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<b>Spindle epithelial tumour with thymus-like differentiation</b>	8588/3
<b>Intrathyroid thymic carcinoma</b>	8589/3



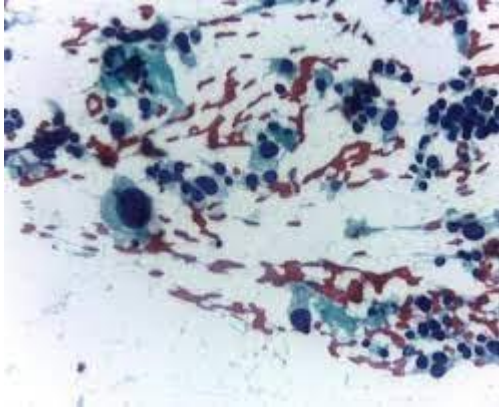
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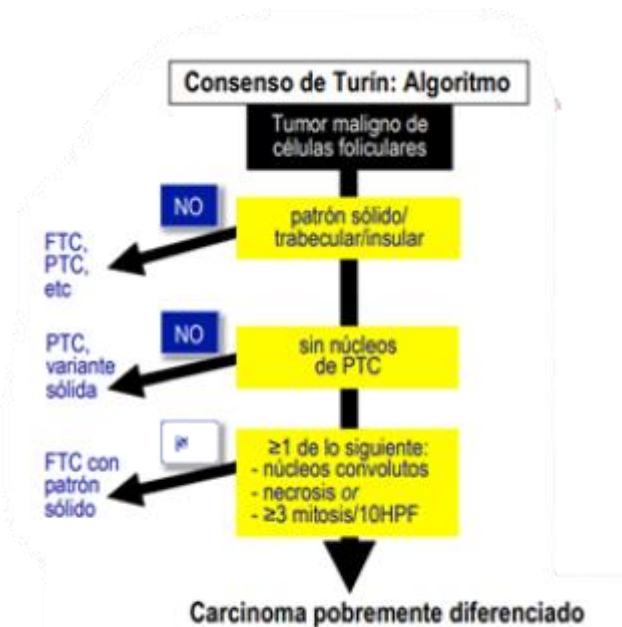
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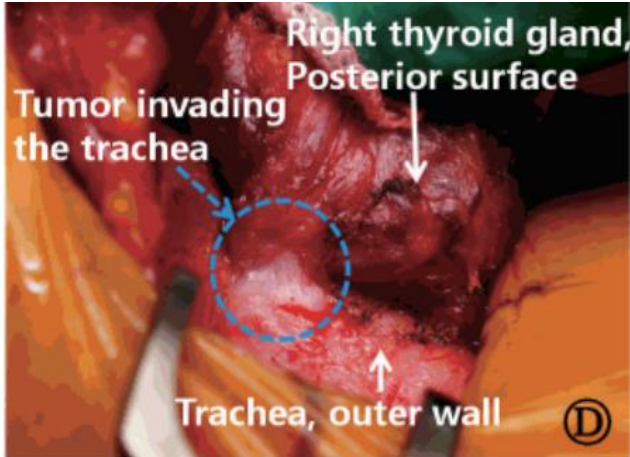
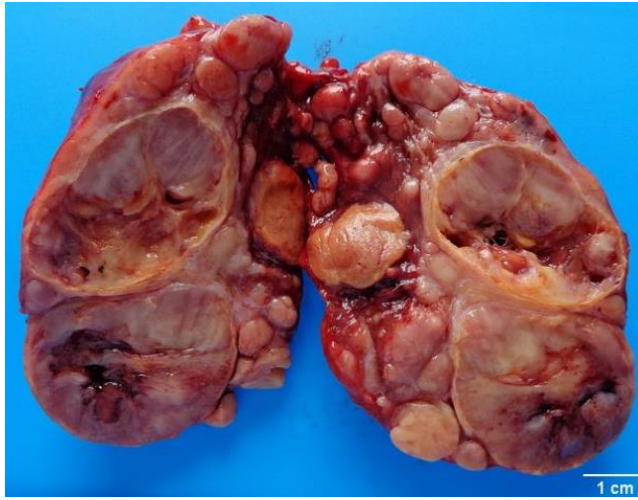


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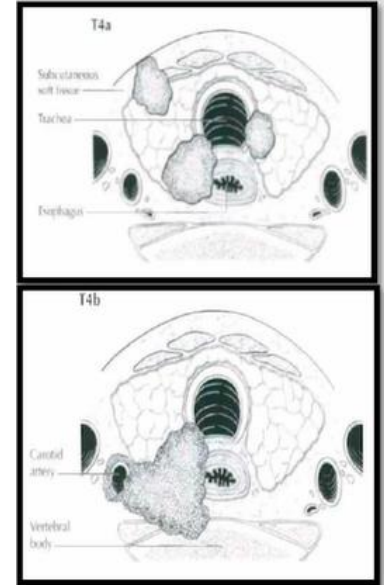
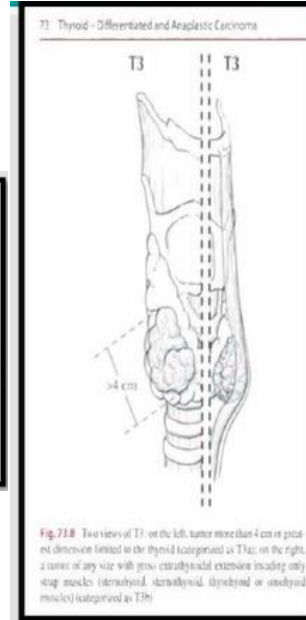
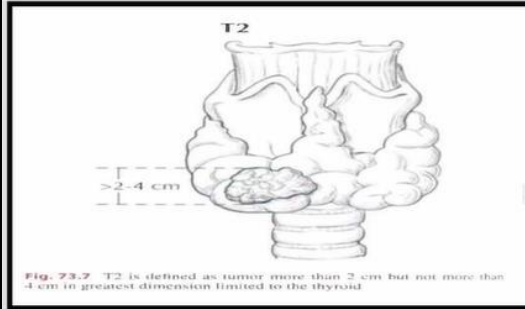
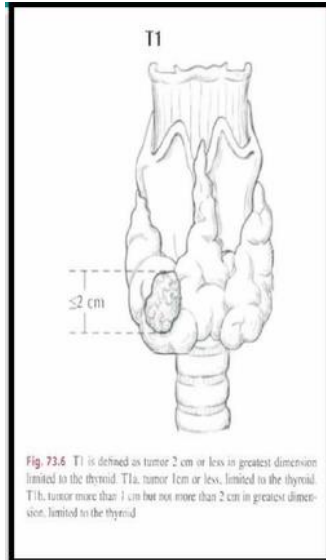
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# MANEJO: CONCEPTOS GENERALES

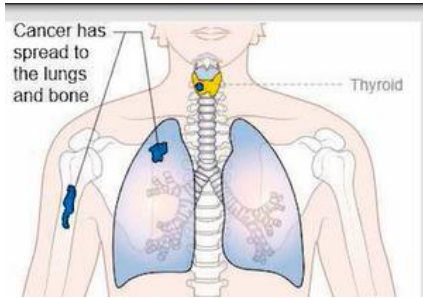




ESTADIAJE  
TNM



ESTADIAJE  
TNM

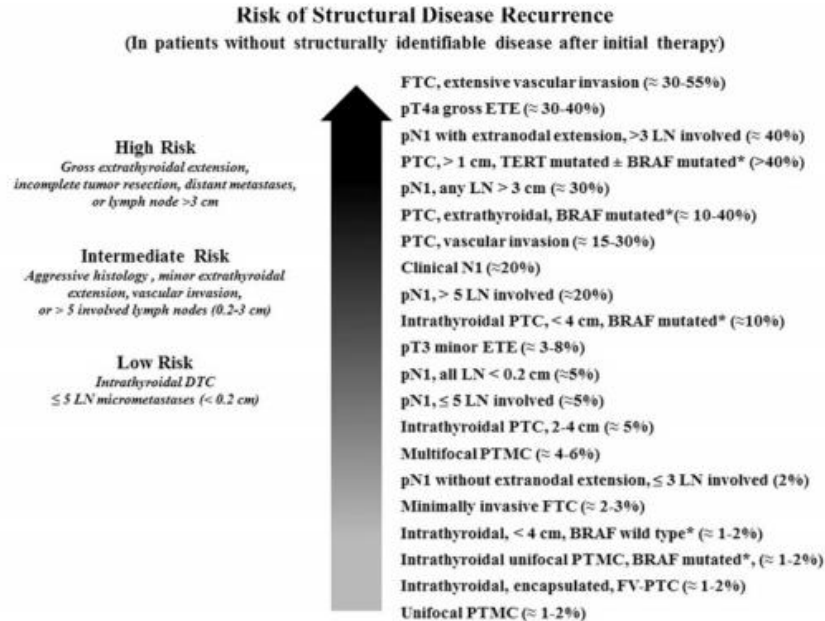


N0	a. Confirmado histológicammente b. Radiológicamente
N1	a. Compartimento central VI y VII b. Compartimentos laterales I-V

M0	No metástasis
M1	Metástasis

ESTADIAJE  
TNM

Stage grouping		Age < 45 years old	Age < 55 years old
Stage I	Any TAny NM0		Any TAny NM0
Stage II	Any TAny NM1		Any TAny NM1
		Age ≥ 45 years old	Age ≥ 55 years old
Stage I	T1NM0		T1-T2NM0
Stage II	T2NM0		T1-T2N1M0
Stage III	T1-T2N1aN0 T3NM0		T3Any NM0 T4aAny NM0
Stage IVA	T4aAny NM0 Any TN1bM0		T4bAny NM0
Stage IVB	T4bAny NM0		Any TAny NM1
Stage IVC	Any TAny NM1		



ERAPÉUTICA O  
CA

**FIG. 4.** Risk of structural disease recurrence in patients without structurally identifiable disease after initial therapy. The risk of structural disease recurrence associated with selected clinico-pathological features are shown as a continuum of risk with percentages (ranges, approximate values) presented to reflect our best estimates based on the published literature reviewed in the text. In the left hand column, the three-tiered risk system proposed as the Modified Initial Risk Stratification System is also presented to demonstrate how the continuum of risk estimates informed our modifications of the 2009 ATA Initial Risk System (see Recommendation 48). \*While analysis of *BRAF* and/or *TERT* status is not routinely recommended for initial risk stratification, we have included these findings to assist clinicians in proper risk stratification in cases where this information is available. FTC, follicular thyroid cancer; FV, follicular variant; LN, lymph node; PTMC, papillary thyroid microcarcinoma; PTC, papillary thyroid cancer.

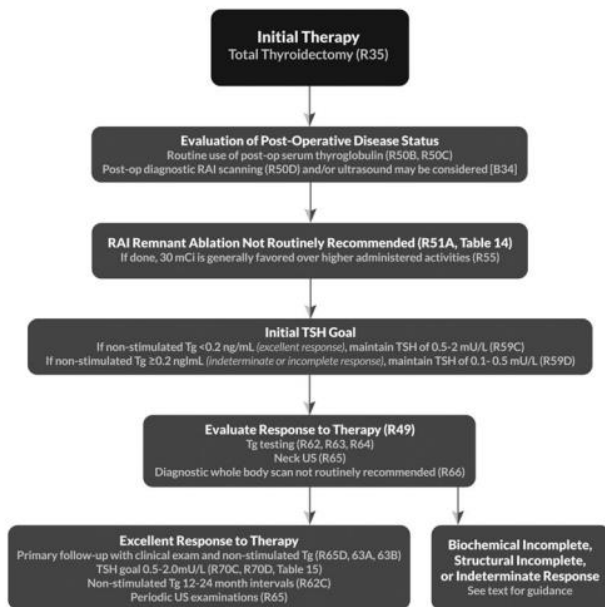


FIG. 5. Clinical decision-making and management recommendations in ATA low-risk DTC patients that have undergone total thyroidectomy. R, recommendation in text.

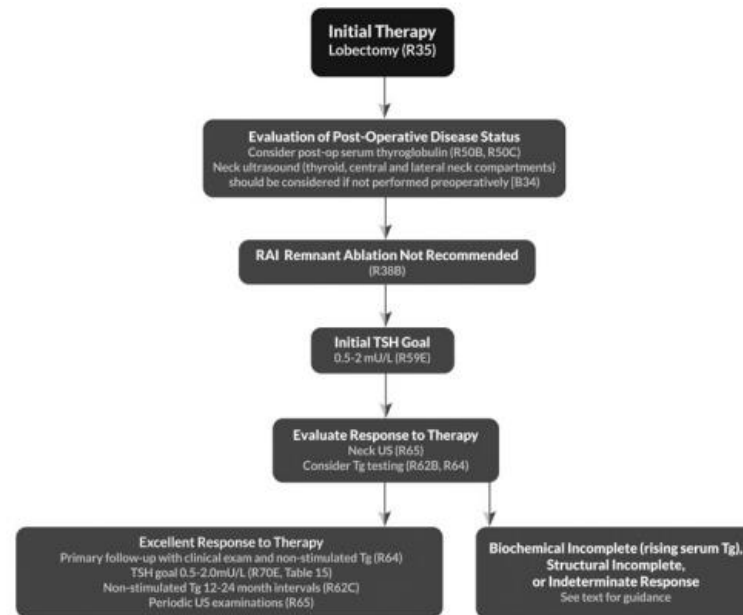
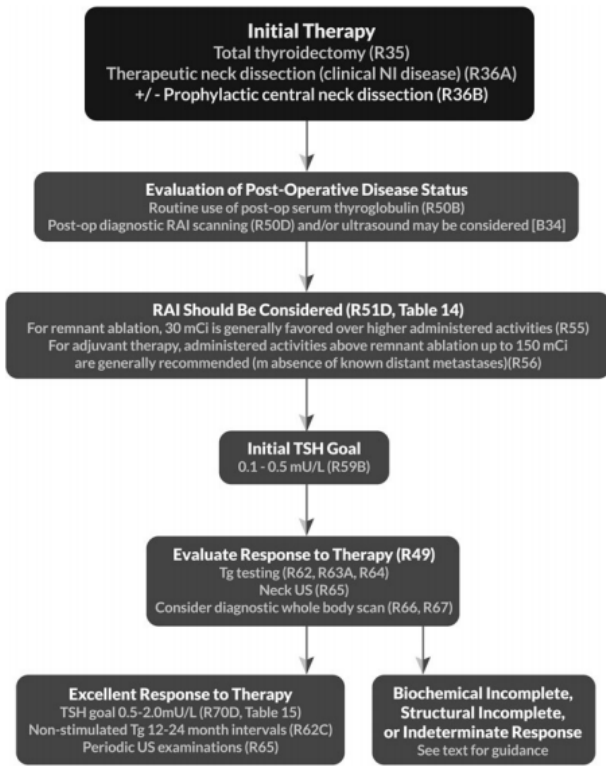
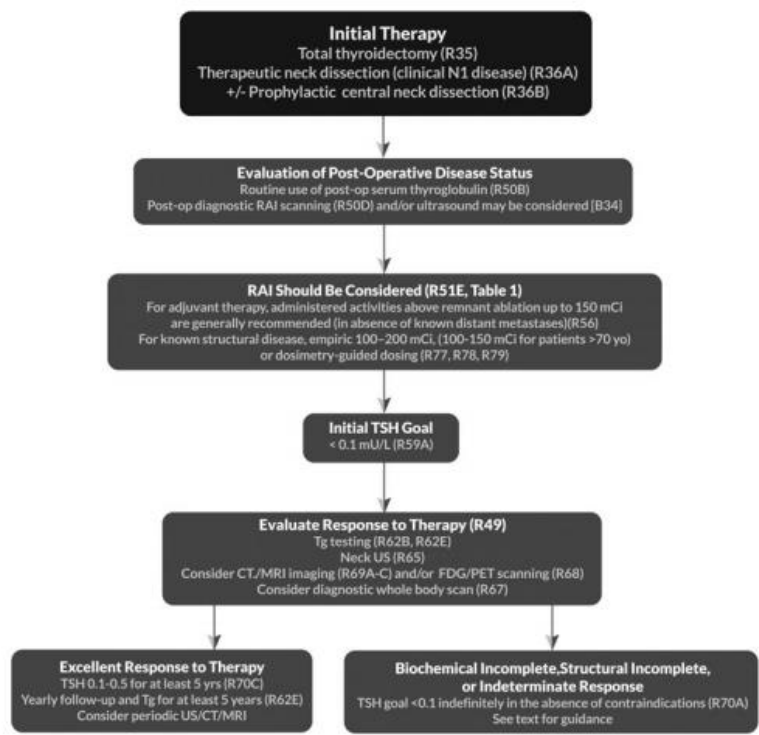


FIG. 6. Clinical decision-making and management recommendations in ATA low-risk DTC patients that have undergone less than total thyroidectomy (lobectomy with isthmus resection). R, recommendation in text.



**FIG. 7.** Clinical decision-making and management recommendations in ATA intermediate risk DTC patients that have undergone total thyroidectomy. R, recommendation in text.



**FIG. 8.** Clinical decision-making and management recommendations in ATA high risk DTC patients that have undergone total thyroidectomy and gross residual disease remaining in the neck. R, recommendation in text.

TABLE 13. CLINICAL IMPLICATIONS OF RESPONSE TO THERAPY RECLASSIFICATION IN PATIENTS WITH DIFFERENTIATED THYROID CANCER TREATED WITH TOTAL THYROIDECTOMY AND RADIOIODINE REMNANT ABLATION




Category	Definitions <sup>a</sup>	Clinical outcomes	Management implications
Excellent response	Negative imaging <b>and either</b> Suppressed Tg <0.2 ng/mL <sup>b</sup> <b>or</b> TSH-stimulated Tg <1 ng/mL <sup>b</sup>	1%–4% recurrence <sup>c</sup> <1% disease specific death <sup>c</sup>	An excellent response to therapy should lead to an early decrease in the intensity and frequency of follow up and the degree of TSH suppression
Biochemical incomplete response	Negative imaging <b>and</b> Suppressed Tg ≥1 ng/mL <sup>b</sup> <b>or</b> Stimulated Tg ≥10 ng/mL <sup>b</sup> <b>or</b> Rising anti-Tg antibody levels	At least 30% spontaneously evolve to NED <sup>d</sup> 20% achieve NED after additional therapy <sup>a</sup> 20% develop structural disease <sup>a</sup> <1% disease specific death <sup>a</sup>	If associated with stable or declining serum Tg values, a biochemical incomplete response should lead to continued observation with ongoing TSH suppression in most patients. Rising Tg or anti-Tg antibody values should prompt additional investigations and potentially additional therapies.
Structural incomplete response	Structural or functional evidence of disease With any Tg level With or without anti-Tg antibodies	50%–85% continue to have persistent disease despite additional therapy <sup>e</sup> Disease specific death rates as high as 11% with loco-regional metastases and 50% with structural distant metastases <sup>a</sup>	A structural incomplete response may lead to additional treatments or ongoing observation depending on multiple clinico-pathologic factors including the size, location, rate of growth, RAI avidity, <sup>13</sup> FDG avidity, and specific pathology of the structural lesions.
Indeterminate response	Nonspecific findings on imaging studies Faint uptake in thyroid bed on RAI scanning Nonstimulated Tg detectable, but <1 ng/mL Stimulated Tg detectable, but <10 ng/mL <b>or</b> Anti-Tg antibodies stable or declining in the absence of structural or functional disease	15%–20% will have structural disease identified during follow-up <sup>a</sup> In the remainder, the nonspecific changes are either stable, or resolve <sup>a</sup> <1% disease specific death <sup>a</sup>	An indeterminate response should lead to continued observation with appropriate serial imaging of the nonspecific lesions and serum Tg monitoring. Nonspecific findings that become suspicious over time can be further evaluated with additional imaging or biopsy.

TABLE 15. THYROTROPIN TARGETS FOR LONG-TERM THYROID HORMONE THERAPY

Increasing Risk of TSH Suppression	Excellent	Indeterminate	Biochemical Incomplete**	Structural Incomplete
No Known Risk				
Menopause		Mild suppression. TSH target 0.1–0.5* mU/L	Moderate or Complete Suppression. TSH target <0.1 mU/L	
Tachycardia				
Osteopenia				
Age > 60		No suppression. TSH target 0.5*–2.0 mU/L		
Osteoporosis				
Atrial Fibrillation				

\* 0.5 mU/L represents the lower limit of the reference range for the TSH assay which can be 0.3–0.5 mU/L depending on the specific assay

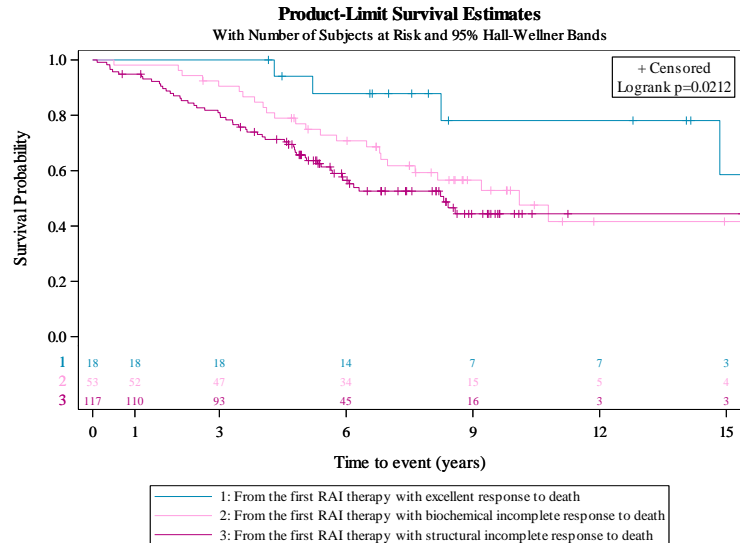
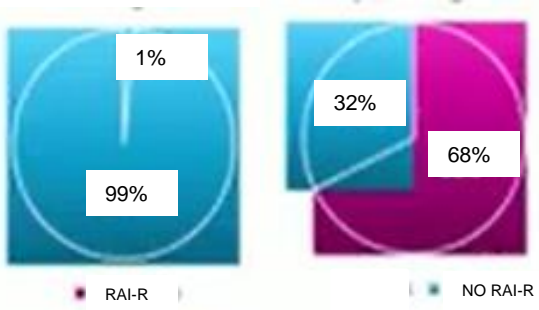
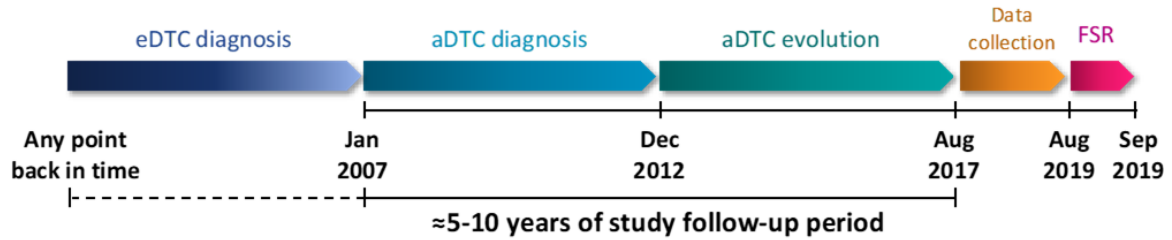
\*\* TSH target for patients with a biochemical incomplete response can be quite different based on original ATA risk, Tg level, Tg trend over time and risk of TSH suppression

-  No suppression. TSH target 0.5\*–2.0 mU/L
-  Mild suppression. TSH target 0.1–0.5\* mU/L
-  Moderate or Complete suppression. TSH target <0.1 mU/L

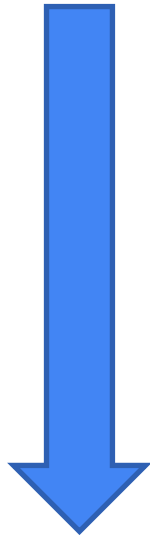
# CARCINOMA DE TIROIDES METASTÁSICO: CONCEPTOS GENERALES



ERUDIT STUDY

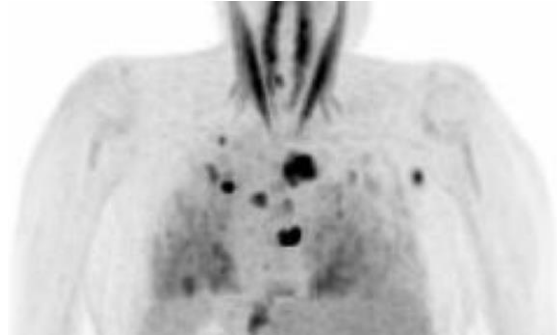


# ORDEN DE JERARQUICO EN EL TRATAMIENTO



Cirugía de enf locorregional  
Tratamiento con I131  
RT o tratamientos locorregionales  
Tratamiento sistémico

TRATAMIENTO  
CON I 131



Treatment of pulmonary metastases

Pulmonary micrometastases should be treated with RAI therapy and RAI therapy should be repeated every 6-12 months as long as disease continues to concentrate RAI and respond clinically because the highest rates of complete remission are reported in these subgroups.

100-200 mCi

TRATAMIENTO  
CON I 131

Treatment of pulmonary metastases

Radioiodine-avid macronodular metastases may be treated with RAI and treatment may be repeated when objective benefit is demonstrated (decrease in the size of the lesions, decreasing Tg), but complete remission is not common and survival remains poor

100-200 mCi



TRATAMIENTO  
CON I 131

*Treatment of bone metastases*

*RAI therapy of iodine-avid bone metastases has been associated with improved survival and should be employed, although RAI is rarely curative.*

*100-200 mCi*

TRATAMIENTO  
CON I 131



*Treatment of bone metastases*

*RAI therapy of iodine-avid bone metastases has been associated with improved survival and should be employed, although RAI is rarely curative.*

*100-200 mCi*

## TRATAMIENTO CON I 131

Treatment of empiric RAI therapy be considered for Tg-positive, RAI diagnostic scan-negative patients

Empiric (100-200 mCi) or dosimetrically determined RAI therapy may be considered in patients with more significantly elevated serum Tg levels, rapidly rising serum Tg levels, or rising ant-Tg antibody levels, in whom imaging (anatomic neck/chest imaging and/or 18FDG-PET/CT) has failed to reveal a tumor source that is amenable to directed therapy. The risk of high cumulative administered activities of RAI must be balanced against uncertain long-term benefits. If empiric RAI therapy is given and the posttherapy scan is negative, the patient should be considered to have RAI-refractory disease and no further RAI therapy should be administered.

# REFRACTARIEDAD AL YODO



# ¿Qué paciente es refractario al yodo?



**PACIENTE A**  
Varón de 20 años  
Ca papilar de tiroides  
Metástasis miliares  
pulmonares  
Tto: 650 mCi  
Tg se ha duplicado en 6m  
EE Rx

**PACIENTE B**  
Mujer de 65 años  
Ca papilar variedad células  
tachuela  
Enf cervical irresecable  
Mtx pulmonares EE  
Tto: 400 mCi  
FDG +, MIBG neg  
Tg 60 ng/mL  
Crecimiento del 20% en 12  
meses de enf cervical



**PACIENTE C**  
Varón de 45 años  
Ca folicular  
Tg 24 ng/mL  
Mtx pulmonares que han  
aumentado de 25 a 29 mm  
en 4 meses tras tto con I131  
(12%)

## ATA GUIDELINES 2015

In most publications, the following categories are proposed:

- (1) the absence of uptake of RAI in all lesions on scintigraphy;
- (2) the absence of RAI uptake in some but not all lesions;
- (3) progression despite uptake of RAI;
- (4) reaching the maximum recommended activity of RAI (=22,2GBq).

## PRINCIPIOS DE MARTINICA

1. Necesidad de compromiso en la cooperación multidisciplinar para avanzar en el manejo del CDT.
2. Se debe definir el objetivo de la terapia con I- 131.
- 3-4. Necesaria evaluación del estado de la enfermedad tras la cirugía previo I 131. Estandarización.
5. Consideración de factores para seleccionar a pacientes para tratamiento adyuvante.
6. La dosis óptima de I131 como terapia adyuvante no puede determinarse.
7. Escenarios clínicos de refractariedad a I 131.
8. Los criterios de refractariedad tienen que evolucionar.
9. Necesidad de estudios prospectivos



Controversies, Consensus, and Collaboration in the Use of  $^{131}\text{I}$  Therapy in Differentiated Thyroid Cancer: A Joint Statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association

**PRINCIPIO 7. Utilizar escenarios clínicos de refractariedad a I 131 para conocer la probabilidad de que un tumor responda a I 131, pero no usar el concepto "refractario" taxativamente.**

ESCENARIOS QUE SUGIEREN QUE UN PACIENTE PUEDE TENER UN CT REFRACTARIO

No captación de I131 en rastreo diagnóstico

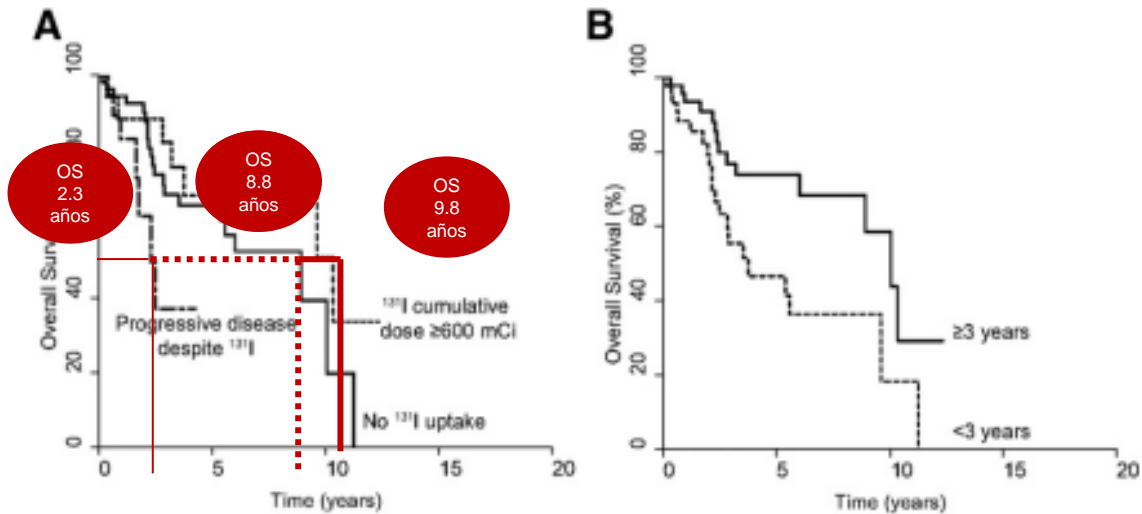
No captación de I131 en rastreo post-tratamiento

Captación de I131 solo en algunos focos tumorales

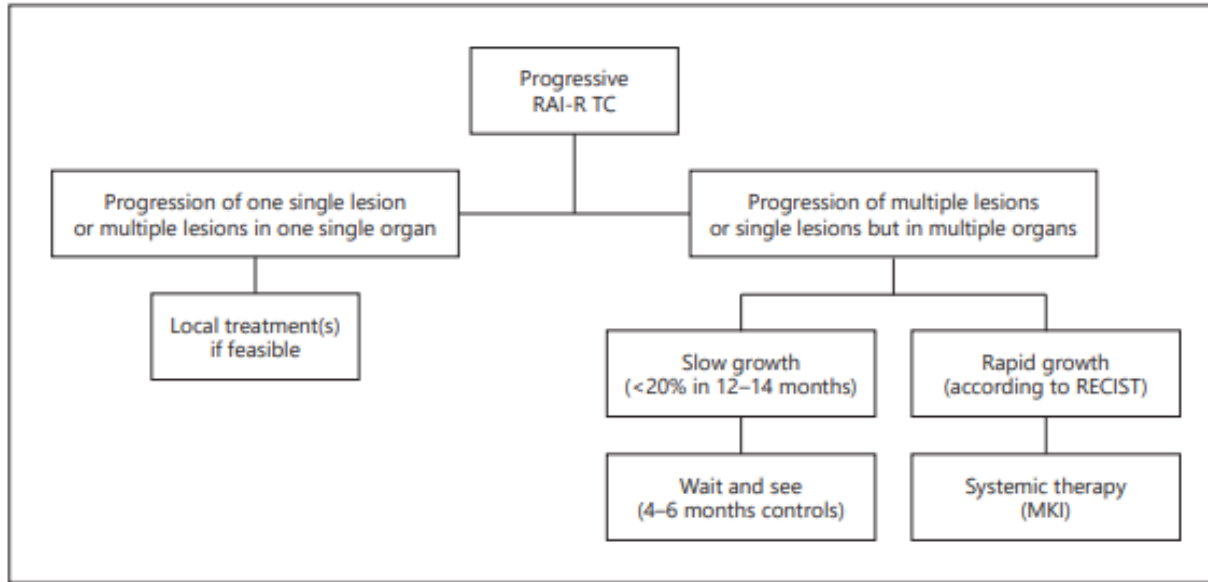
Progresión de las metástasis a pesar de captación de I 131

Progresión de las metástasis a pesar de dosis acumulada > 600 mCi

Controversies, Consensus, and Collaboration in the Use of  $^{131}\text{I}$  Therapy in Differentiated Thyroid Cancer: A Joint Statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association



**Figure 2.** Kaplan-Meier curves of overall survival (OS). **(A):** Criteria for radioiodine refractory (RR) classification (median OS of patients classified as RR because of a lack of <sup>131</sup>I uptake, a cumulative dose of <sup>131</sup>I of ≥600 mCi, and tumor progression within 12 months following <sup>131</sup>I treatment: 9.1 [95% confidence interval (CI) 5.4-NR], 10.3 [95% CI 3.8 NR], and 2.3 [95% CI 1.7 NR] years, respectively,  $p < .007$ ). **(B):** Time from initial diagnosis of differentiated thyroid carcinoma to diagnosis of RR disease (median OS of ≥3 vs. <3 years: 10.0 [95% CI 8.9-NR] vs. 3.7 [95% CI 2.5-NR] years, log-rank test,  $p = .011$ ).



**Fig. 1.** Algorithm for decision making when a radioiodine refractory (RAI-R) thyroid cancer (TC) is progressing.

# ¿A cuál de estos pacientes administrarías tto sistémico?



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Mujer de 65 años  
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Enf cervical irresecable  
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Crecimiento del 20% en 12 meses de enf cervical



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Ca folicular  
Tg 24 ng/mL  
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COMITÉ  
MULTIDISCIPLINAR







**MUCHAS GRACIAS**