Dosage de Tg après stimulation par Thyrogen

Marie-Hélène Schlageter

Pour les patients avec une b-Tg < 0,1 µg/L, un test rhTSH est généralement considéré comme inutile

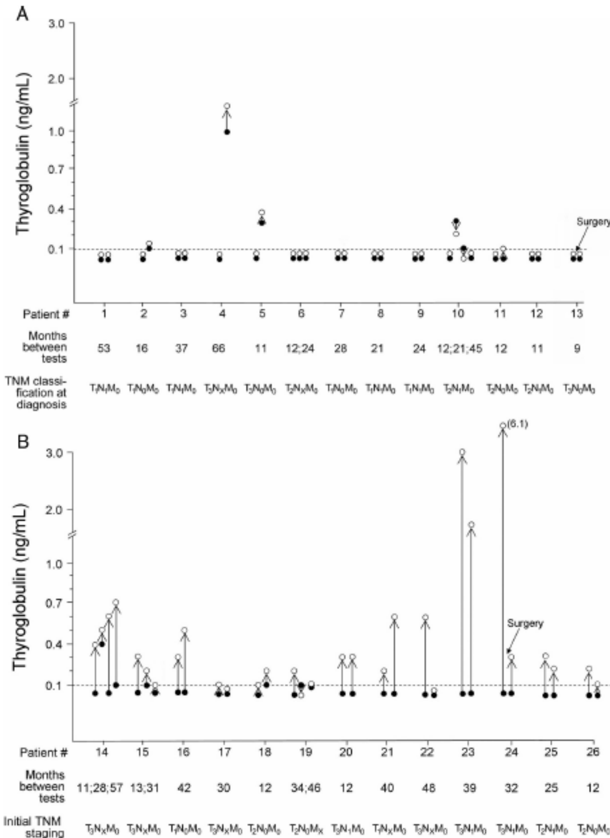


FIG. 2. A, Sequential rhTSH stimulation tests in 13 patients with initial Tg-stim below 0.1 ng/ml followed up to 66 months. In patient no. 10, the second and third Tg-stim values were less than the preceding Tg-supp. Patient no. 13 died from metastatic disease 18 months after the second Tg-stim. B, Sequential rhTSH stimulation tests in 13 patients with initial Tg-stim of at least 0.1 ng/ml followed up to 57 months. Patient no. 24 had recurrent disease and surgery before the second Tg-stim. *Solid symbols* represent Tg-supp; *open symbols* represent Tg-stim.

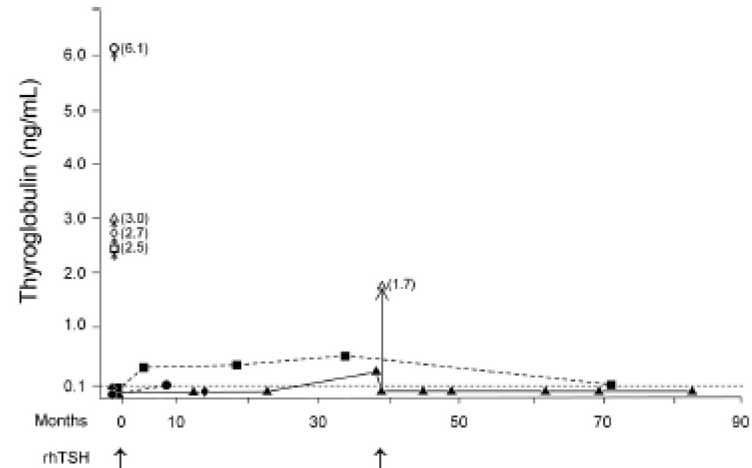


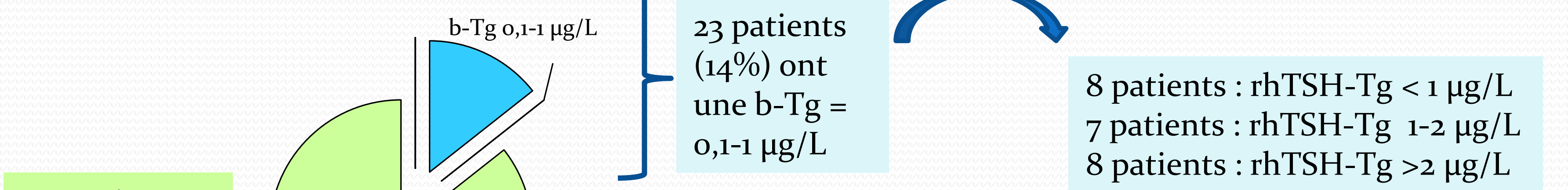
FIG. 1. Longitudinal follow-up on four patients with initial Tg stim over 2.0 ng/ml. One patient (*triangle*, no. 23) had two Tg-stim tests. One patient (*circle*, no. 24) had recurrence detected by ultrasound and subsequent surgery. In one patient (*diamond*, no. 27, TNM classification T2NxM0), Tg-supp remained below 0.1 ng/ml after initial stimulation test. One patient (*square*, no. 28, T1N1M0) had a rise in Tg-supp over the first 34 months of follow-up, followed by a Tg-supp of 0.1 more than 70 months after the initial testing. *Solid symbols* represent Tg-supp; *open symbols* represent Tg-stim.

Conclusion: In patients with DTC whose T_4-suppressed serum Tg is below 0.1 ng/ml, long-term monitoring with annual Tg-supp and periodic neck US are adequate to detect recurrences. In our experience, rhTSH testing does not change management and is not needed in this group of patients. (*J Clin Endocrinol Metab* **97: 2714–2723, 2012**)

Chindris 2012

Patients pour lesquels un test rhTSH est utile : b-Tg (us) faiblement détectable 0,1-1 µg/L

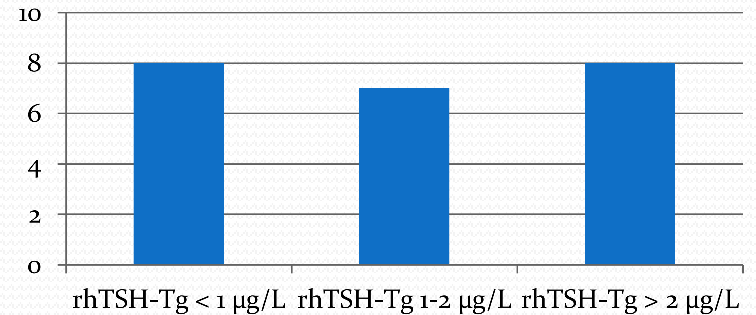
Taux de b-Tg chez 160 Patients



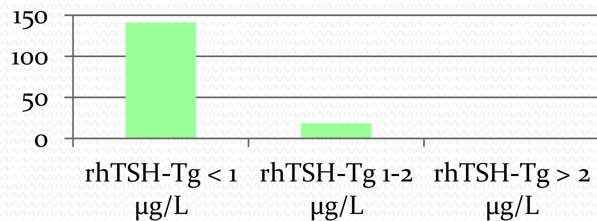
137 patients ont une b-Tg < 0,1 µg/L

23 patients (14%) ont une b-Tg = 0,1-1 µg/L

8 patients : rhTSH-Tg < 1 µg/L
7 patients : rhTSH-Tg 1-2 µg/L
8 patients : rhTSH-Tg >2 µg/L



100% de ces patients : rhTSH-Tg < 2 µg/L
88% de ces patients : rhTSH-Tg < 1 µg/L

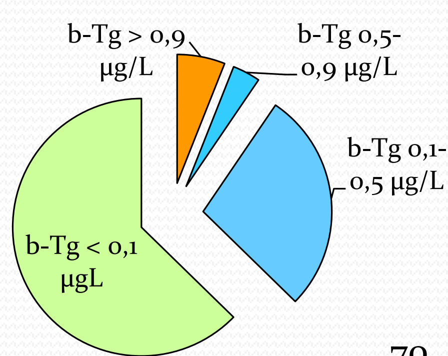


Iervasi 2007

b-Tg et rhTSH-Tg 6-12 mois après traitement initial

Patients pour lesquels un test rhTSH est utile : b-Tg (us) faiblement détectable 0,1-1 µg/L

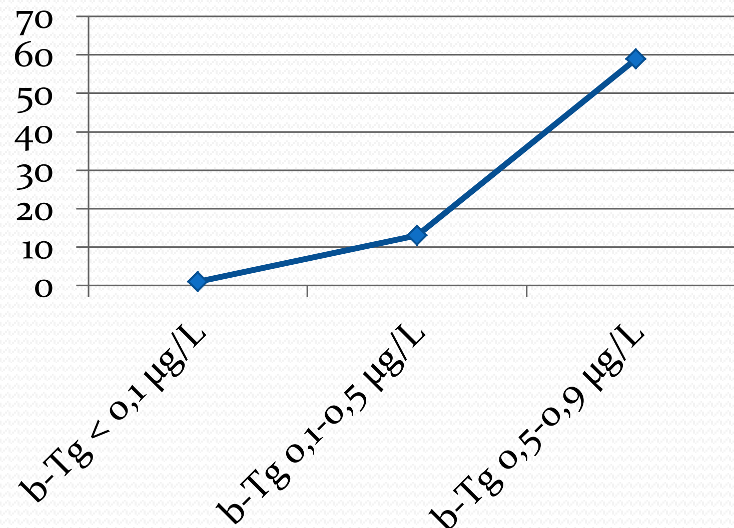
Taux de b-Tg chez 831 patients



31% des patients ont une b-Tg = 0,1-0,9 µg/L

Chez ces patients, la probabilité d'avoir un rhTSH-Tg > 2 µg/L est très variable

% de patients avec rhTSH-Tg > 2 µg/L

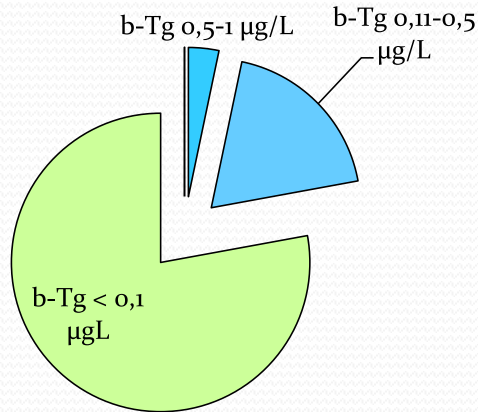


b-Tg et rhTSH-Tg 6-12 mois après traitement initial

Schlumberger, 2007

Patients pour lesquels un test rhTSH est utile : b-Tg (us) faiblement détectable 0,1-1 µg/L

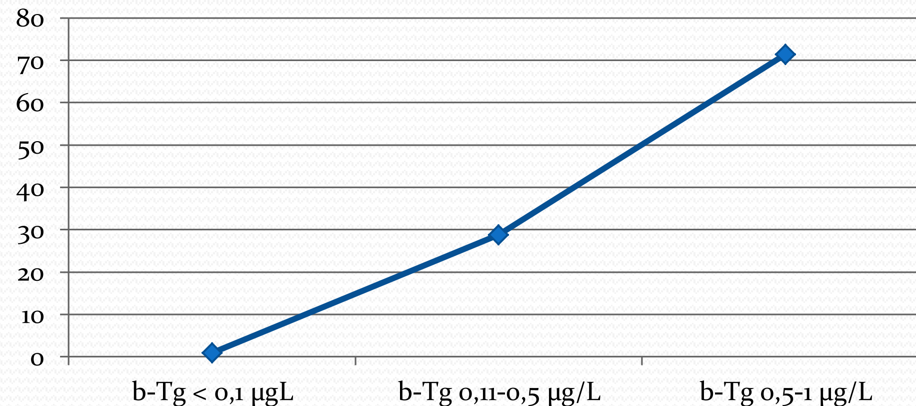
Taux de b-Tg chez 425 patients



22% des patients ont une b-Tg = 0,1-1 µg/L

Chez ces patients, la probabilité d'avoir un rhTSH-Tg > 2 µg/L est très variable

% de patients avec rhTSH-Tg > 2µg/L

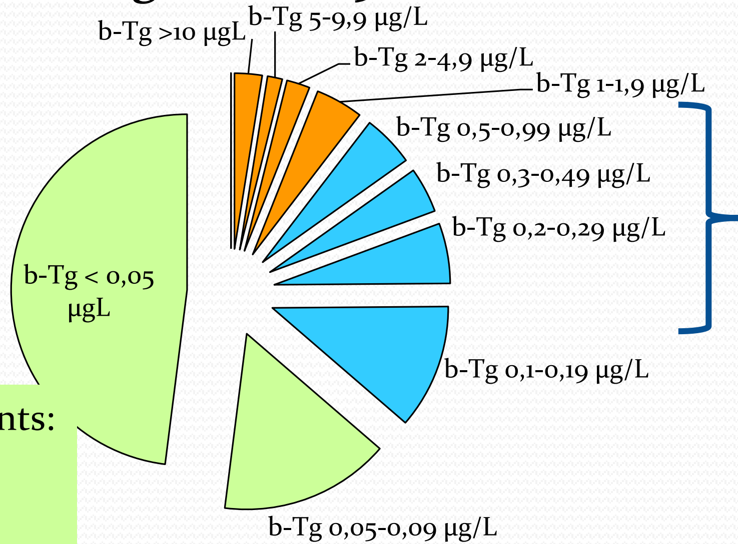


b-Tg et rhTSH-Tg 6-12 mois après traitement initial

Malandrino, 2011

Patients pour lesquels un test rhTSH est utile : b-Tg (us) faiblement détectable 0,1-1 µg/L

Taux de b-Tg chez 1029 Patients

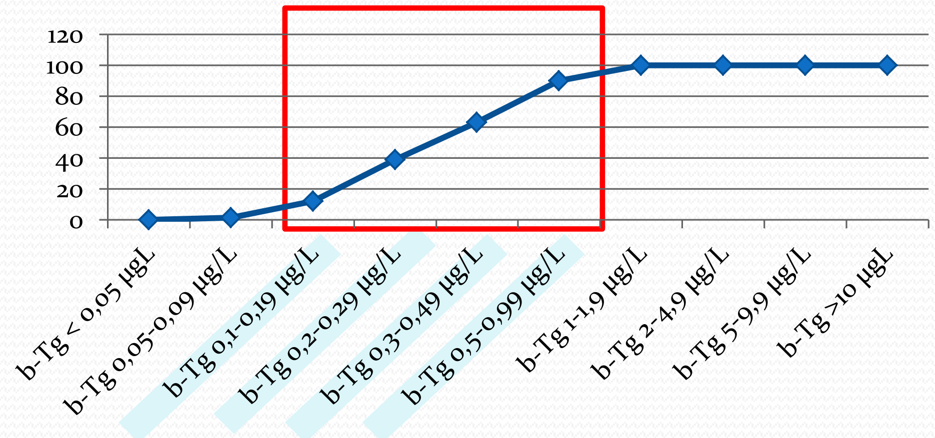


64% patients: b-Tg < 0,1 µg/L

26% des patients ont une b-Tg = 0,1-1 µg/L

Chez ces patients, la probabilité d'avoir un rhTSH-Tg > 2 µg/L est très variable

% de patients avec rhTSH-Tg > 2µg/L



b-Tg et rhTSH-Tg au cours du suivi

Spencer, 2010

Qu'apporte le test au Thyrogen chez ces patients? VPP, sensibilité, spécificité, pronostic

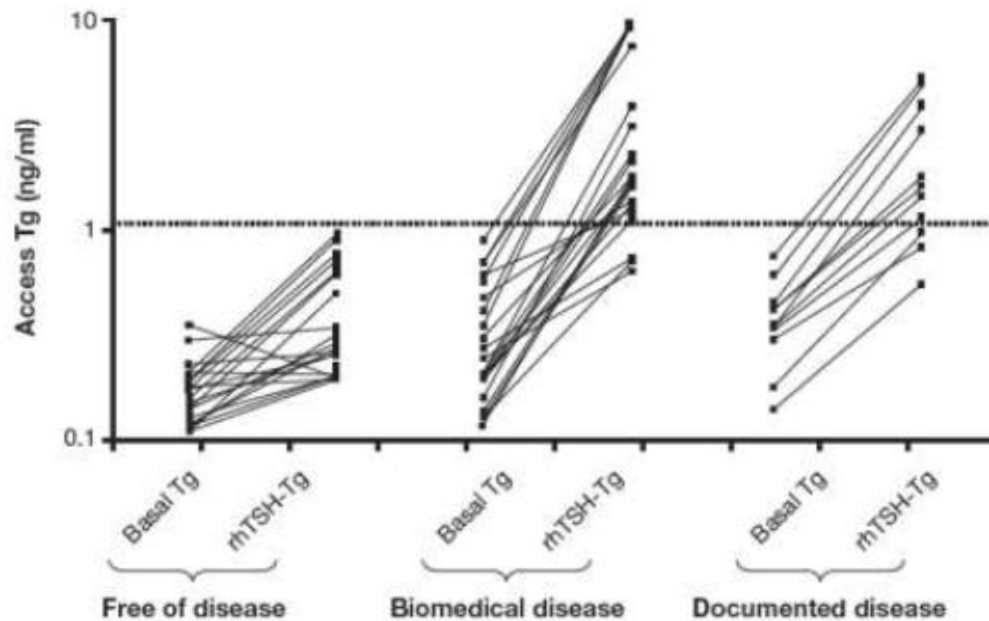


Fig. 2 - rhTSH-stimulated Access Tg in patients free of disease (no.=25), with biochemical disease (no.=21) and with documented disease (no.=14). Tg values in the vertical axis are plotted on a log scale.

VPP b-Tg = 58%
VPP rhTSH-Tg > 1 µg/L : 38% (11/29)

Castagna 2011

Qu'apporte le test au Thyrogen chez ces patients? VPP, sensibilité, spécificité, pronostic

- Iervasi 2007

	b-Tg 0,1-1 µg/l	rh-TSH-Tg > 1 µg/L	rh-TSH-Tg > 2 µg/L
VPP	78% (18/23)	80% (12/15)	75% (6/8)

- Malandrino 2011
  - VPP rhTSH-Tg 1-2 µg/L = **9%** (2/23)
  - VPP rhTSH-Tg >2 µg/L = **10%** (3/31)

- Chindris 2012 : b-Tg < 0,1 µg/L

TABLE 4. Sensitivity, specificity, PPV, and NPV values for Tg-stim cutoffs of more than 2.0 and 1.4, respectively, for US and ^{131}I using biopsy-proven disease as gold standard for recurrence among patients with Tg-supp below 0.1 ng/ml

Test	Tg stim >2.0 ng/ml (%)	Tg-stim ≥1.4 ng/ml (%)	US (%)	^{131}I scan (%)
Sensitivity	14 (1/7)	14 (1/8)	86 (6/7)	28 (2/7)
Specificity	98 (153/156)	97 (152/156)	92 (134/146)	93 (122/131)
PPV	25 (1/4)	20 (1/5)	33 (6/18)	18 (2/11)
NPV	96 (153/159)	96 (152/158)	99 (134/135)	96 (122/127)

Qu'apporte le test au Thyrogen chez ces patients? VPP, sensibilité, spécificité, pronostic

Inclusion :
107 patients
b-Tg < 1µg/L (<0,5 ou 0,6-0,9 µg/l)
rhTSH-Tg : 10 mois à 35 ans, médiane 3,3 ans après traitement initial

Groupe 1 rhTSH-Tg < 0,5 µg/L
Groupe 2 rhTSH-Tg 0,6-2 µg/L
Groupe 3 rhTSH-Tg >2µg/L
Courbe ROC : seuil 2,6 µg/L

Sensibilité 80% (rhTSH-TG>2µg/L)

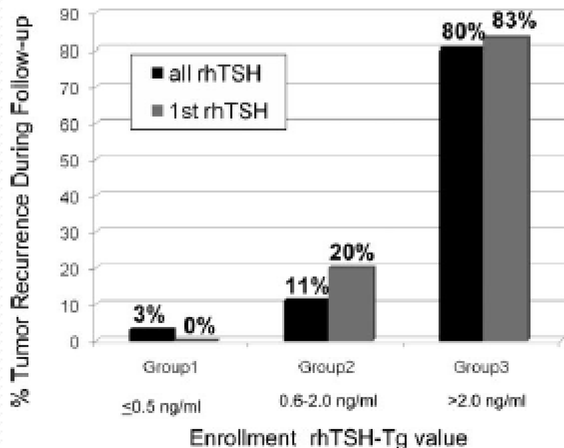


FIG. 1. Percentage of patients after thyroidectomy and radioiodine therapy with tumor recurrence during follow-up after an enrollment rhTSH stimulated Tg value was 0.5 ng/ml or less (group 1), 0.6–2.0 ng/ml (group 2), and greater than 2.0 ng/ml (group 3). *Gray bars*, Patients whose enrollment rhTSH testing was their first stimulation after remnant ablation, and the testing was within 2 yr (730 d) of their first thyroid cancer surgery; *black bars*, all patients.

VPP 80% (rhTSH-TG>2µg/L)
VPP 84% (rhTSH-TG>2,5µg/L)

TABLE 1. Performance of basal and stim-Tg cutoffs to predict tumor detection

	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Basal Tg 0.6–1.0 ng/ml (n = 8)[a]	30	98	85	75
rhTSH-Tg >2.0 ng/ml (n = 20)	80	95	95	80
rhTSH-Tg ≥2.5 ng/ml (n = 18)	80	97	95	84

NPV, Negative predictive value; PPV, positive predictive value.

[a] TSH 0.2 mIU/liter or less in all patients with basal Tg greater than 0.5 ng/ml except patient 19 described in the text with TSH 4.54 mIU/liter and Tg 0.6 ng/ml without definitive tumor recurrence, and patient 89 with TSH 2.21 mIU/liter and Tg 1.0 ng/ml with tumor recurrence.

Valeur pronostique

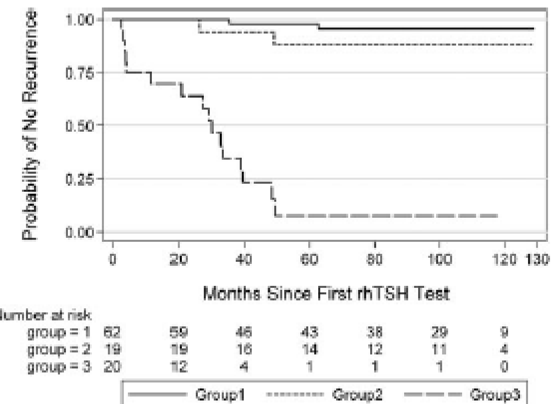


FIG. 2. Kaplan-Meier estimate of the probability of patients in each group not immediately lost to follow-up without tumor recurrence as a function of time since stratification rhTSH test. Patients at risk are patients evaluated at each time point after their enrollment rhTSH test and found to be without tumor recurrence since their stratification. Decrements in at risk patients are due to tumor recurrence or lack of follow-up.

Kloos 2010

Quelques observations

- Les études de performance de Tg us ou 2g et des tests au Thyrogen ont été réalisées chez des patients sans anticorps anti-Tg.
- Ces études sont presque toutes basées sur la méthode de dosage de Tg Beckman Access ou Dxi, certaines sur la méthode Immulite. Les performances des nouvelles techniques de Tg us ou 2g (Roche ou Kryptor), restent à établir.
- L'observation d'une réponse « paradoxale » de Tg sous Thyrogen (par exemple une Tg basale autour de 1-2 µg/L qui n'augmente pas sous Thyrogen) peuvent refléter une interférence due à des anticorps hétérophiles ou à des HAMA.

Conclusion

- Pour les patients avec un taux de Tg sous LT4 faiblement détectable (0,1-1 µg/L), le test au Thyrogen garde son intérêt pour détecter une maladie résiduelle.
- Les performances diagnostiques d'un taux de Tg sous LT4 faiblement détectable (0,1-1 µg/L) restent à établir et à comparer au test au thyrogen.