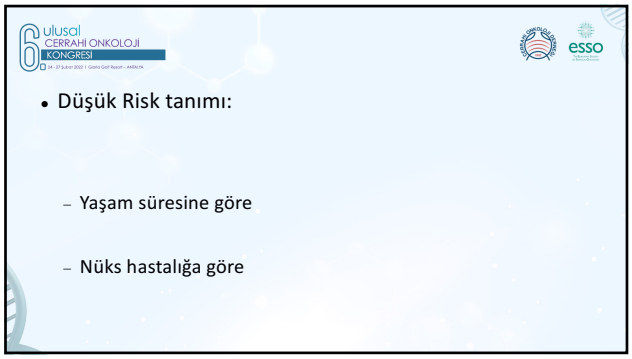


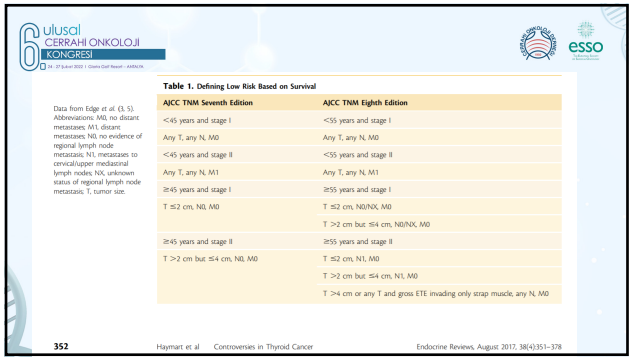


Table 1. Defining Low Risk Based on Survival

AJCC TNM Seventh Edition	AJCC TNM Eighth Edition
<45 years and stage I	<55 years and stage I
Any T, any N, M0	Any T, any N, M0
<45 years and stage II	<55 years and stage II
Any T, any N, M1	Any T, any N, M1
≥45 years and stage I	≥55 years and stage I
T ≤2 cm, N0, M0	T ≤2 cm, N0/NX, M0
	T >2 cm but ≤4 cm, N0/NX, M0
≥45 years and stage II	≥55 years and stage II
T >2 cm but ≤4 cm, N0, M0	T ≤2 cm, N1, M0
	T >2 cm but ≤4 cm, N1, M0
	T >4 cm or any T and gross ETE invading only strap muscle, any N, M0

Data from Edge et al. (3, 5). Abbreviations: M0, no distant metastases; M1, distant metastases; N0, no evidence of regional lymph node metastasis; N1, metastases to cervical/upper mediastinal lymph nodes; NX, unknown status of regional lymph node metastasis; T, tumor size.

Table 2. Defining Low Risk Based on Recurrence

ATA Risk Stratification	
PTC (with all of the following):	
	No local or distant metastases
	All macroscopic tumor has been resected
	No tumor invasion of loco-regional tissues or structures
	The tumor does not have aggressive histology (eg, tall cell, hobnail variant, columnar cell carcinoma)
	If I-131 is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first post-treatment whole-body RAI scan
	No vascular invasion
	Clinical N0 or ≤five pathologic N1 micrometastases (<0.2 cm in largest dimension)
Intrathyroidal, encapsulated follicular variant of PTC	
Intrathyroidal, well-differentiated follicular thyroid cancer with capsular invasion and no or minimal (<four foci) vascular invasion	
Intrathyroidal, papillary microcarcinoma, unifocal, or multifocal, including BRAF V600E mutated (if known)	

Data from Haugen et al. (8). Abbreviations: I-131, iodine-131; N0, no evidence of regional lymph node metastasis; N1, metastases to cervical/upper mediastinal lymph nodes.

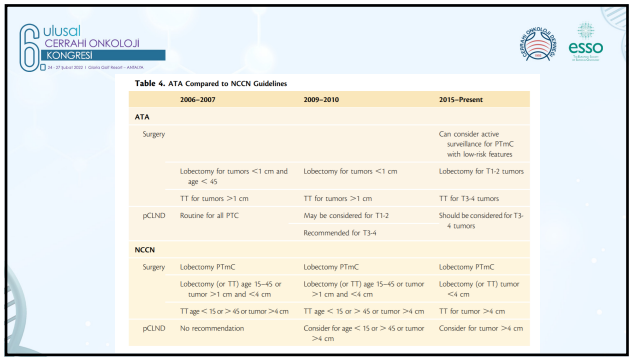
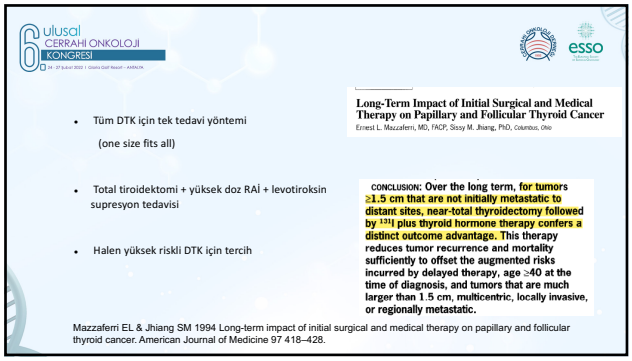


Table 4. ATA Compared to NCCN Guidelines

	2006–2007	2009–2010	2015–Present
ATA			
Surgery			Can consider active surveillance for PTmC with low-risk features
	Lobectomy for tumors <1 cm and age < 45	Lobectomy for tumors <1 cm	Lobectomy for T1-2 tumors
	TT for tumors >1 cm	TT for tumors >1 cm	TT for T3-4 tumors
pCLND	Routine for all PTC	May be considered for T1-2	Should be considered for T3-4 tumors
		Recommended for T3-4	
NCCN			
Surgery	Lobectomy PTmC	Lobectomy PTmC	Lobectomy PTmC
	Lobectomy (or TT) age 15–45 or tumor >1 cm and <4 cm	Lobectomy (or TT) age 15–45 or tumor >1 cm and <4 cm	Lobectomy (or TT) tumor <4 cm
	TT age < 15 or > 45 or tumor >4 cm	TT age < 15 or > 45 or tumor >4 cm	TT for tumor >4 cm
pCLND	No recommendation	Consider for age < 15 or > 45 or tumor >4 cm	Consider for tumor >4 cm



- Tüm DTK için tek tedavi yöntemi
  (one size fits all)
- Total tiroidektomi + yüksek doz RAİ + levotiroksin supresyon tedavisi
- Halen yüksek riskli DTK için tercih

Long-Term Impact of Initial Surgical and Medical Therapy on Papillary and Follicular Thyroid Cancer

Ernest L. Mazzaferri, MD, FACP, Sissy M. Jhiang, PhD, Columbus, Ohio

CONCLUSION: **Over the long term, for tumors ≥1.5 cm that are not initially metastatic to distant sites, near-total thyroidectomy followed by ^{131}I plus thyroid hormone therapy confers a distinct outcome advantage. This therapy reduces tumor recurrence and mortality sufficiently to offset the augmented risks incurred by delayed therapy, age ≥40 at the time of diagnosis, and tumors that are much larger than 1.5 cm, multicentric, locally invasive, or regionally metastatic.**

Mazzaferri EL & Jhiang SM 1994 Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. American Journal of Medicine 97 418–428.

- Tanı alan kanserlerin büyük çoğunluğu düşük mortalite ve nüks riskine sahip
- Agresif tedavilerin yaralı olduğuna dair kanıt yok

Pupillary Thyroid Carcinoma (PTC) in Children and Adults: Comparison of Initial Presentation and Long-Term Postoperative Outcome in 4432 Patients Consecutively Treated at the Mayo Clinic During Eight Decades (1936–2015)

Conclusions Children, despite presenting with more extensive PTC when compared to adults, have postoperative recurrences at similar frequency, typically coexist with DM and die of PTC less often. Since 1976, both children and adults with MACIS <6 PTC have a <1% chance at 30 years of CSM; adults with higher MACIS scores (6 or more) have a 30-year CSM rate of 30%.

- Güncel yaklaşım hasta bazında kişiselleştirilmiş yaklaşımla daha sınırlı cerrahi ve takip

Follow-up of differentiated thyroid cancer – what should (and what should not) be done

and the current trend is towards the use of more individualized approaches. Management options now include active surveillance for select very low-risk tumours[10] and incomprehensive surgery[1] (that is, total thyroidectomy with no prophylactic lymph node dissection or lobectomy) for intermediate-risk tumours. In patients with a significant risk of persistent disease after total thyroidectomy, management options include selective use of radioiodine remnant ablation[10,11]. Patients with DTC are also prescribed levothyroxine, but the aims and drawbacks of levothyroxine treatment (notably the risks of long-term TSH suppression, which is now restricted to patients with persistent disease) are being redefined[12].

- Tiroid kanserine bağlı mortalite düşüktür (<%2 / 5 yıl)
- DTK büyük çoğunluğu (%90-95) Evre 1 veya 2 dir (kansere bağlı ölüm riski < %1)
- NCCN 8. baskı yaş sınırı 45 ten 55 e çıktı
- Santral ve lateral lenf nodu metastazları evre 2 ye indi (uzak metastaz varlığı/yokluğuna göre daha fazla hasta evre 1 veya 2 de)

Updated American Joint Committee on Cancer/ Tumor-Node-Metastasis Staging System for Differentiated and Anaplastic Thyroid Cancer (Eighth Edition): What Changed and Why?

8th edition (age of patient <55 years)			
I	Any T	Any N	M0
II	Any T	Any N	M1
8th edition (age of patient ≥55 years)			
I	T1 or T2	N0 or Nx	M0
II	T1 or T2	N1	M0
	T3a or T3b	Any N	M0
III	T4a	Any N	M0
IVa	T4b	Any N	M0
IVb	Any T	Any N	M1

Persistan veya rekürren DTK riski, kansere bağlı ölüm riskinden çok daha fazla
ATA risk sınıflama sistemi persistan ve/veya rekürren hastalık olasılığını 3 e ayırır

Düşük (<%5) (%57)
Orta (%5–20) (%38)
Yüksek (>%20)

Table 2 | **American Thyroid Association risk of thyroid cancer recurrence**[11]

Risk of recurrence class	Definition	Risk estimate (%)
Papillary thyroid cancer		
Low	• Absence of distant metastases[a] • Intrathyroidal tumour, ≤4 cm in size; absence of gross extra thyroid extension[a] • Absence of clinically evident lymph node metastases[a] • ≤5 microscopic (<2 mm in size) lymph node metastases[a] • Absence of aggressive histology[a] • Absence of vascular invasion[a] • Complete macroscopic tumour resection[a] • No uptake outside thyroid bed on post-therapeutic whole-body scan if radioiodine ablation is performed[b]	≤5
Follicular thyroid cancer		
Low	• Well differentiated[a] • Capsular invasion only or less than four foci of vascular invasion[a]	–

- Genel yaklaşım 1 cm den büyük kanserlerde cerrahi ağır basmakta
- PtmC aktif takip güvenli bir alternatif olabilir ?
- ATA 1 cm altında malignite açısından şüpheli usg bulguları olsa da İİAB önermez
  - Hipoekojenite
  - Mikrakalsifikasyon varlığı
  - Boy>genişlik
  - Rim kalsifikasyondan tümör taşması
  - Düzensiz sınır
  - ETE ve lenf nodu metastazı hariç

Table 4. ATA Compared to NCCN Guidelines

	2006–2007	2009–2010	2015–Present
ATA			
Surgery			Can consider active surveillance for PTmC with low-risk features
	Lobectomy for tumors <1 cm and age < 45	Lobectomy for tumors <1 cm	Lobectomy for T1-2 tumors
	TT for tumors >1 cm	TT for tumors >1 cm	TT for T3-4 tumors
pCLND	Routine for all PTC	May be considered for T1-2	Should be considered for T3-4 tumors
		Recommended for T3-4	
NCCN			
Surgery	Lobectomy PTmC	Lobectomy PTmC	Lobectomy PTmC
	Lobectomy (or TT) age 15–45 or tumor >1 cm and <4 cm	Lobectomy (or TT) age 15–45 or tumor >1 cm and <4 cm	Lobectomy (or TT) tumor <4 cm
	TT age < 15 or > 45 or tumor >4 cm	TT age < 15 or > 45 or tumor >4 cm	TT for tumor >4 cm
pCLND	No recommendation	Consider for age < 15 or > 45 or tumor >4 cm	Consider for tumor >4 cm

- 2007, Bilimoria ve ark.
- Total tiroidektomi lobektomiye göre daha iyi 10 yıllık sağkalım sağlıyor
- 52173 hasta
- PTC nedeniyle opere 1985 - 1998.
- Lobektomi / Total tiroidektomi
- Ölüm riskinde %21 artış
  - (Hastaların %23.9 u PtmC)
- Demografik klinik ve patolojik özelliklere göre

Extent of Surgery Affects Survival for Papillary Thyroid Cancer

Annals of Surgery • Volume 246, Number 3, September 2007

Conclusions: The results of this study demonstrate that total thyroidectomy results in lower recurrence rates and improved survival for PTC ≥1.0 cm compared with lobectomy. This is the first study to demonstrate that total thyroidectomy for PTC ≥1.0 cm improves outcomes.

- 2014, Adam ve ark
- 61775 hasta 1998 – 2006 NCDB
- PTK 1.0 – 4.0 cm 82 ay takip
- TT/ Lobektomi genel sağkalım farkı yok
- NCDB 2003 ten sonra komorbiditeler ve 2004 ten sonra ETE ve multifokalite verilerini kaydetmeye başlamıştır
- Charlson Komorbidite indeksi >2 genel sağkalımla ilişkili
- Bilimorianın çalışmasında dikkate alınmıyor
-

Extent of Surgery for Papillary Thyroid Cancer Is Not Associated with Survival: An Analysis of 61,775 Patients

Mohamed Abdelgadir Adam, MD, John Pura, MPH, Lin Gu, MS, Michaela A. Dinan, PhD, Douglas S. Tyler, MD, Shelby D. Reed, PhD, Sanziana A. Roman, MD, and Julie A. Sosa, MD, MA

Ann Surg. 2014 October ; 260(4): 601–607. doi:10.1097/SLA.0000000000000925.

Conclusions—Current guidelines suggest total thyroidectomy for PTC tumors >1 cm. However, we did not observe a survival advantage associated with total thyroidectomy compared to lobectomy. These findings call into question whether tumor size should be an absolute indication for total thyroidectomy.

- Hemitiroidektomi sonrası PO TSH hastaların 2/3 ünde normal sınırda
- Levotiroksin replasmanına gerek kalmayabilir

Ann Surg Oncol (2011) 18:2548–2554
DOI 10.1245/s10434-011-1627-1

ORIGINAL ARTICLE – ENDOCRINE TUMORS

Detection and Management of Hypothyroidism Following Thyroid Lobectomy: Evaluation of a Clinical Algorithm

Amanda Jolner, MD[1], Ohi L. Griffith, PhD[1,2], Blair Walker, MD, FRCPC[3], Leanne Wood, MD[1], Hannah Piper, MD, FRCSC[1], Grasme Wilkins, MD, FRCPC[4], Christopher Babiuk, MD, FRCSC[5], Steven J. M. Jones, PhD[1,2], and Sam M. Wiseman, MD, FRCSC[1]

Conclusions. The incidence of hypothyroidism following TL is low, and a significant proportion of individuals who become biochemically hypothyroid will demonstrate only a transient elevation in their TSH levels. As well, individuals with LI, or GC formation, within their resected thyroid lobe may be at increased risk for post-TL hypothyroidism.

-
- Düşük risk DTK TSH supresyonu şart değil

Does Postoperative Thyrotropin Suppression Therapy Truly Decrease Recurrence in Papillary Thyroid Carcinoma? A Randomized Controlled Trial

Iwao Sugitani, Yoshihide Fujimoto

The Journal of Clinical Endocrinology & Metabolism, Volume 95, Issue 10, 1 October 2010, Pages 4576–4583, https://doi.org/10.1210/jc.2010-0161
Published: 01 October 2010 **Article history**

Results: Eligible participants were recruited from 1996–2005, with 218 patients assigned to group A and 215 patients to group B. Analysis was performed on an intention-to-treat basis. DFS did not differ significantly between groups. The 95% confidence interval of the hazard ratio for recurrence was 0.85–1.27 according to Cox proportional hazard modeling, within the margin of 2.12 required to declare 10% noninferiority.

Conclusions: DFS for patients without TSH suppression was not inferior by more than 10% to DFS for patients with TSH suppression. Thyroid-conserving surgery without TSH suppression should be considered for patients with low-risk PTC to avoid potential adverse effects of TSH suppression.

- BRAFV600E mutasyonu multifokalite, minimal ekstratiroidal uzanım ve lenf nodu metastazı ile ilişkili
  - Xing 2007, Tallini et al.2015) nonetheless, the presence of BRAFV600E mutation
- Düşük riskli hastalarda hemitiroidektomi için kontrendikasyon değil
  - (Haugen et al. 2016).

THYROID
Volume 26, Number 1, 2016
© American Thyroid Association
DOI: 10.1089/thy.2015.0020

SPECIAL ARTICLE

2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer

Bryan R. Haugen,[1,*] Erik K. Alexander,[2] Keith C. Bible,[3] Gerard M. Doherty,[4] Susan J. Mandel,[5] Yuri E. Nikiforov,[6] Furio Pacini,[7] Gregory W. Randolph,[8] Anna M. Sawka,[9] Martin Schlumberger,[10] Kathryn G. Schuff,[11] Steven I. Sherman,[12] Julie Ann Sosa,[13] David L. Steward,[14,*] R. Michael Tuttle,[15] and Leonard Wartofsky[16]

- DTK da aktif takip

Early Diagnosis of Low-Risk Papillary Thyroid Cancer Results Rather in Overtreatment Than a Better Survival

Jolanta Krajewska[1*], Aleksandra Kukulska[1,2], Małgorzata Oczko-Wojciechowska[3], Agnieszka Kotecka-Blichara[1], Katarzyna Drosik-Rutowicz[1,2], Małgorzata Haras-Gil[1], Barbara Jarzab[1] and Daria Handkiewicz-Junak[1]

CONCLUSIONS

To sum up, overdiagnosis of indolent low-risk PTCs is a global phenomenon leading to overtreatment in many cases without any beneficial effect on survival and patients' well-being. Numerous clinical trials are needed to provide the data, fulfilling evidence-based medicine criteria necessary to change our routine clinical management in PTMC patients. We may expect substantial changes in the near future. The question is whether we, both patients and physicians, are ready for it?

TABLE 1 | Summary of the results of studies on active surveillance presented in this review.

Study data	Size of thyroid nodules included	Number of patients subjected to AS	Disease progression criteria	Mean follow-up	Percentage of patients with tumor progression	Percentage of patients with LN metastases
Retrospective studies						
Ito (Japan) (63)	PTMC	162	Nodule increase ≥2 mm	47 months (18–113)	10.2%	1.2%
Ito (Japan) (27)	PTMC	340	Nodule increase by ≥3 mm; development of LN metastases	74 months (18–187)	6.4%* 15.9%**	1.4%* 3.4%**
Ito (Japan) (28)	PTMC	1,235	Nodule increase up to 12 mm or more; development of LN metastases	60 months (18–228)	4.6%	1.5%
Prospective studies						
Sugitani (Japan) (29)	PTMC	230 (300 nodules)	Nodule increase ≥3 mm; invasion of local structures; development of LN or distant metastases	5 years (1–17)	7%	1%
Tuttle (USA) (64)	PTC ≤ 15 mm	291	Nodule increase ≥3 mm; extrathyroidal extension; invasion of local structures; development of nodal or distant metastases	25 months (6–166)	3.8%	0%
Sakai (Japan) (65)	PTC T1bN0M0	61	Nodule increase ≥3 mm; development of nodal or distant metastases	7.4 years (0.5–25)	7%	3%
Molinaro (Italy) (66)	Bethesda V (suspicious for PTC) or VI (PTC) nodules ≤13 mm	93	Nodule increase by ≥3 mm; development of LN metastases	19 months (6–54)	2%	1%

*PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; LN, lymph nodes; AS, active surveillance; *5-year follow-up; **10-year follow-up.*

- Aktif takip kararında üç ana bölüm değerlendirilmeli
- Tümör/boyun USG özellikleri
- Hastaya ait özellikler
- Tıbbi ekip özellikleri

THYROID
Volume 20, Number 1, 2010
© American Thyroid Association
DOI: 10.1089/thy.2010.0178

THYROID CANCER AND NODULES

A Clinical Framework to Facilitate Risk Stratification When Considering an Active Surveillance Alternative to Immediate Biopsy and Surgery in Papillary Microcarcinoma

Juan P. Brito,[1] Yasuhiro Ito,[2] Akira Miyauchi,[2] and R. Michael Tuttle[3]

TABLE 1. A RISK-STRATIFIED APPROACH TO DECISION MAKING IN PROBABLE OR PROVEN PAPILLARY MICROCARCINOMA

Candidates for observation	*Tumor/neck US characteristics*	*Patient characteristics*	*Medical team characteristics*
Ideal	• Solitary thyroid nodule • Well-defined margins • Surrounded by ≥2 mm normal thyroid parenchyma • No evidence of extrathyroidal extension • Previous US documenting stability • cN0 • cM0	• Older patients (>60 years) • Willing to accept an active surveillance approach • Understands that a surgical intervention may be necessary in the future • Expected to be compliant with follow-up plans • Supportive significant others (including other members of their healthcare team) • Life-threatening comorbidities	• Experienced multidisciplinary management team • High-quality neck ultrasonography • Prospective data collection • Tracking/reminder program to ensure proper follow-up
Appropriate	• Multifocal papillary microcarcinomas • Subcapsular locations not adjacent to RLN without evidence of extrathyroidal extension • Ill-defined margins • Background ultrasonographic findings that will make follow-up difficult (thyroiditis, nonspecific lymphadenopathy, multiple other benign-appearing thyroid nodules) • FDG-avid papillary microcarcinomas	• Middle-aged patients (18–59 years) • Strong family history of papillary thyroid cancer • Child bearing potential	• Experienced endocrinologist or thyroid surgeon • Neck ultrasonography routinely available
Inappropriate	• Evidence of aggressive cytology on FNA (rare) • Subcapsular locations adjacent to RLN • Evidence of extrathyroidal extension • Clinical evidence of invasion of RLN or trachea (rare) • N1 disease at initial evaluation or identified during follow-up • M1 disease (rare) • Documented increase in size of ≥3 mm in a confirmed papillary thyroid cancer tumor	• Young patients (<18 years) • Unlikely to be compliant with follow-up plans • Not willing to accept an observation approach	• Reliable neck ultrasonography not available • Little experience with thyroid cancer management

US, ultrasound; RLN, recurrent laryngeal nerve; FDG, fluorodeoxyglucose; FNA, fine-needle aspiration.

Table 4. ATA

	2015–Present
ATA	
Surgery	Can consider active surveillance for PTmC with low-risk features
	Lobectomy for T1-2 tumors
	TT for T3-4 tumors
pCLND	Should be considered for T3-4 tumors
NCCN	
Surgery	Lobectomy PTmC
	Lobectomy (or TT) tumor <4 cm
	TT for tumor >4 cm
pCLND	Consider for tumor >4 cm

- Terapötik LND preoperatif kanıt varlığında endike
  - Düşük risk grubundan çıkar
- Profilaktik LND düşük riskli hastalarda nüks riskini azaltmıyor, morbiditede hafif artış (hipokalsemi)
  - Önerilmez
- BRAF + kararı değiştirmez

ORIGINAL ARTICLE

Prophylactic Central Compartment Lymph Node Dissection in Papillary Thyroid Carcinoma: Clinical Implications Derived From the First Prospective Randomized Controlled Single Institution Study

D. Viola,* G. Materazzi,* L. Valerio, E. Molinaro, L. Agate, P. Faviana, V. Secca, T. Sensi, C. Romei, P. Piaggi, L. Torregrossa, S. Sellari-Franceschini, F. Basolo, P. Vitti, R. Elisei, and P. Miccoli

J Clin Endocrinol Metab, April 2015, 100(4):1316–1324

Conclusions: cN0 patients with PTC treated either with TTx or TTx + pCCND showed a similar outcome. One advantage of TTx + pCCND was a reduced necessity to repeat ^{131}I treatments, but the disadvantage was a higher prevalence of permanent hypoparathyroidism. Almost 50% of patients with PTC had micrometastatic lymph nodes in the central compartment, but none of the presurgical features analyzed, including *BRAF* mutation, was able to predict their presence; moreover, to be aware of their presence does not seem to have any effect on the outcome. (*J Clin Endocrinol Metab* 100: 1316–1324, 2015)

Studies of the $BRAF^{V600E}$ mutation have suggested an association between presence of the mutation and the risk of nodal disease (369–371), although results across all patients with papillary thyroid carcinoma are mixed (372–375). However, the presence of a $BRAF^{V600E}$ mutation has a limited PPV for recurrence and therefore, $BRAF^{V600E}$ mutation status in the primary tumor should not impact the decision for prophylactic central neck dissection (376).

U.S. National Library of Medicine
ClinicalTrials.gov

Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Site ▾ PRS Login

Home > Search Results > Study Record Detail

Save this study

ESTIMation of the ABiLity of Prophylactic Central Compartment Neck Dissection to Modify Outcomes in Low-risk Differentiated Thyroid Cancer (ESTIMABL3)

Study Design Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	1000 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	ESTIMation of the ABiLity of Prophylactic Central Compartment Neck Dissection to Modify Outcomes in Low-risk Differentiated Thyroid Cancer
Actual Study Start Date:	August 29, 2018
Estimated Primary Completion Date:	June 2026
Estimated Study Completion Date:	June 2026

- Teşekkürler