Oncology Clinical Pathways
Endocrine Cancers – Thyroid Cancer

January 2026 – V1.2026

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Thyroid Cancer– Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans Exposed to Ionizing Radiation

- Cancer of the Thyroid

Gulf War and Post 9/11 Veterans

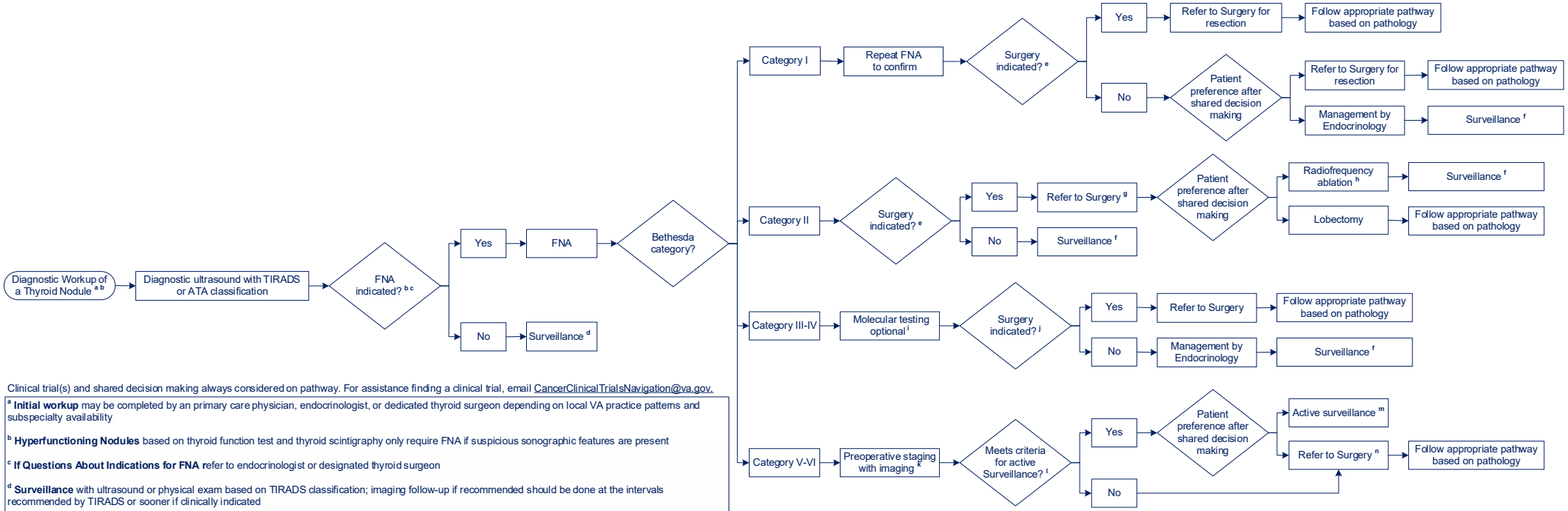
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if you served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Neck cancer of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov), eCFR :: 38 CFR 3.320a, eCFR :: 38 CFR 3.320b,

Thyroid Cancer – Diagnostic Workup of a Thyroid Nodule



Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Initial workup** may be completed by an primary care physician, endocrinologist, or dedicated thyroid surgeon depending on local VA practice patterns and subspecialty availability

[b] **Hyperfunctioning Nodules** based on thyroid function test and thyroid scintigraphy only require FNA if suspicious sonographic features are present

[c] **If Questions About Indications for FNA** refer to endocrinologist or designated thyroid surgeon

[d] **Surveillance** with ultrasound or physical exam based on TIRADS classification; imaging follow-up if recommended should be done at the intervals recommended by TIRADS or sooner if clinically indicated

[e] **Surgery Indications** include compressive symptoms, functional concerns, large nodule size, tracheal deviation and/or compression, goiter with symptoms or significant substernal extension

[f] **Surveillance** with ultrasound or physical exam based on TIRADS classification; imaging follow-up if recommended should be done at the intervals recommended by TIRADS or sooner if clinically indicated; de-escalation of ongoing ultrasound surveillance can be considered if no significant change in size or sonographic features at 5 years

[g] **Surgery** options are lobectomy or radiofrequency ablation based on size, location, and/or cystic vs. solid composition

[h] **Radiofrequency Ablation** after 2 benign biopsies

[i] **Molecular Testing** thyroid specific genomic classifier or mutational analysis (see Molecular Testing table)

[j] **Proceed with Surgery** if molecular testing indicates higher risk of thyroid malignancy

[k] **Imaging** with neck ultrasound with or without cross-sectional imaging depending on suspicion of advanced disease

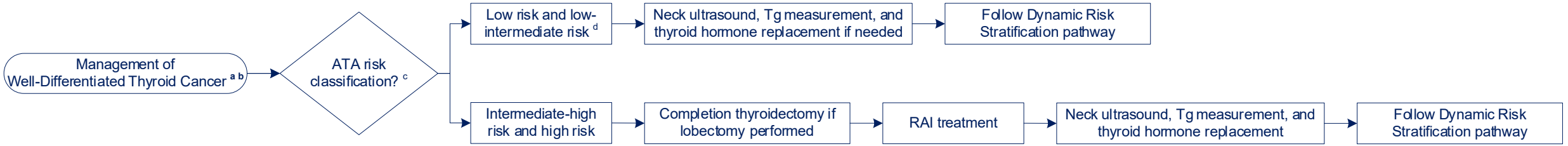
[l] **Active Surveillance** is appropriate when nodule ≤ 1 cm, no threat to critical structures (e.g. trachea, carotid, recurrent laryngeal nerve, esophagus), no concern for local invasion, lymph node, or distant metastasis; limited life expectancy, and/or overriding comorbidities

[m] **Active Surveillance** by thyroid specialist

[n] **Choice of surgery** is based on preoperative staging; total thyroidectomy is indicated for bilateral disease, cT3 and cT4, cN1 or cM1

ATA American Thyroid Association
FNA Fine Needle Aspiration
TIRADS Thyroid Imaging Reporting and Data Systems

Thyroid Cancer– Management of Well-Differentiated Thyroid Cancer



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[a] **Refer to Endocrinology** if not already followed by endocrinology

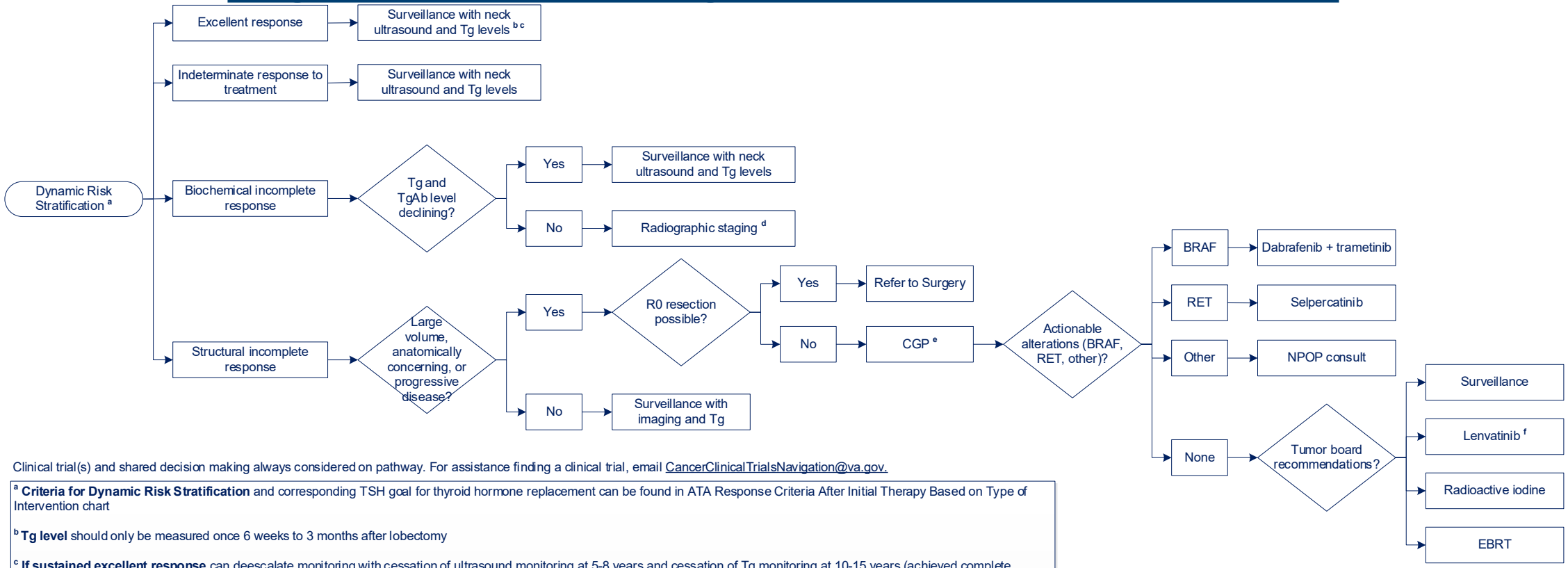
[b] **Well Differentiated** includes papillary, follicular, and oncocytic (previously known as hurthle cell) carcinomas

[c] **ATA Risk Classification** based on the surgical pathology following thyroid surgery

[d] **RAI May Be Appropriate in Select Low-Intermediate Risk** patients based on shared decision making; if the original operation was a lobectomy, completion thyroidectomy will be needed prior to RAI

ATA American Thyroid Association
RAI Radioactive Iodine
Tg Thyroglobulin

Thyroid Cancer – Dynamic Risk Stratification



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[a] **Criteria for Dynamic Risk Stratification** and corresponding TSH goal for thyroid hormone replacement can be found in ATA Response Criteria After Initial Therapy Based on Type of Intervention chart

[b] **Tg level** should only be measured once 6 weeks to 3 months after lobectomy

[c] **If sustained excellent response** can deescalate monitoring with cessation of ultrasound monitoring at 5-8 years and cessation of Tg monitoring at 10-15 years (achieved complete remission)

[d] **Radiographic Staging** with imaging modalities including neck ultrasound, diagnostic radioactive iodine whole body scan, CT scan, and/or FDG-PET/CT

[e] **CGP** can identify mutations that can be germline in origin; germline testing should be performed if a mutation is found in one of the genes recommended by the ESMO guidelines at an allele frequency >30%

[f] **For Lenvatinib Intolerance** administer sorafenib

ATA American Thyroid Association
CGP Comprehensive Genomic Profiling
FDG Fludeoxyglucose-18
EBRT External Beam Radiotherapy
NPOP National Precision Oncology Program
Tg Thyroglobulin
TgAb Thyroglobulin Antibody

Thyroid Cancer – ATA Response Criteria After Initial Therapy Chart

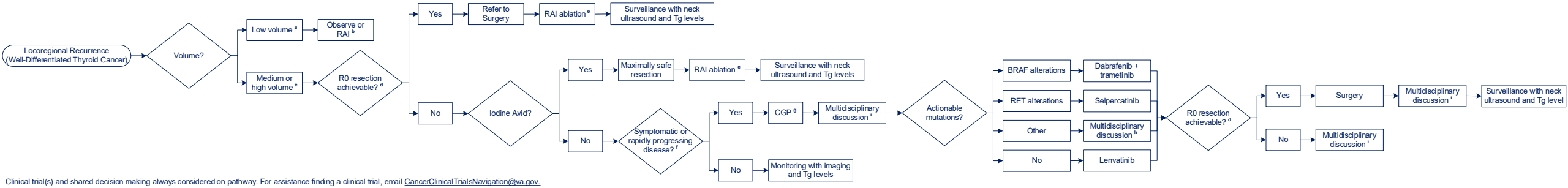
ATA Response Criteria After Initial Therapy Based on Type of Intervention				
Response to therapy	Post total thyroidectomy and/or neck dissection with RAI ablation or therapy	Post total thyroidectomy and/or neck dissection without RAI ablation	Post hemithyroidectomy	TSH goal
Excellent	Nonstimulated Tg <0.2 or stimulated Tg <1 and negative imaging	Nonstimulated Tg <2.5	Normal or low-risk nodules in the contralateral lobe nodules with benign biopsy AND no abnormal lymph notes on imaging	TSH within normal reference range
Indeterminate	Nonspecific findings on imaging studies or nonstimulated Tg 0.2-1 or stimulated Tg 1-10 or stable/declining TgAb levels	Nonspecific findings on imaging studies or nonstimulated Tg 2.5-5, or stable/declining TgAb levels	N/A [a]	TSH within normal reference range [b]
Biochemically incomplete	Nonstimulated Tg >1 or stimulated Tg >10 or increasing TgAb levels and negative imaging	Nonstimulated Tg >5 or increasing TgAb levels and negative imaging	N/A [a]	TSH below normal reference range [c]
Structurally incomplete	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	TSH below normal reference range [c]

[a] See Recommendation 48 for specific comments regardign Tg levels (ng/mL) in patients treated with hemithyroidectomy
[b] Data on optimal TSH target range are inconclusive
[c] Data on optimal TSH target range are inconclusive and/or conflicting. It there is progression of residual disease or development of new recurrence, targeting a TSH below normal reference range may be reasonable. However, comorbidities such as atrial fibrillation and osteoporosis shoucl be factored into the decision making process

RAI Radioactive Iodine
Tg Thyroglobulin
TgAb Thyroglobulin Antibody
TSH Thyrotropin

Ringel MD, Sosa JA, Baloch Z, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. Thyroid. 2025;35(8):841-985. doi:10.1177/10507256251363120

Thyroid Cancer – Locoregional Disease (Well-Differentiated Thyroid Cancer)



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[a] **Low Volume** in shortest dimension < 8mm in central neck or < 10mm in lateral neck

[b] **Lesions** detected by RAI whole body scan may be appropriate for RAI ablation, especially if there is limited or no previous RAI treatment

[c] **Medium or High Volume** in shortest dimension ≥ 8mm central neck or ≥ 10mm in lateral neck

[d] **Neck Surgery** should be reserved for locally symptomatic disease for palliative instead of curative purposes if distant metastasis is the primary concern and is present

[e] **RAI Ablation** if iodine or expected to be iodine avid

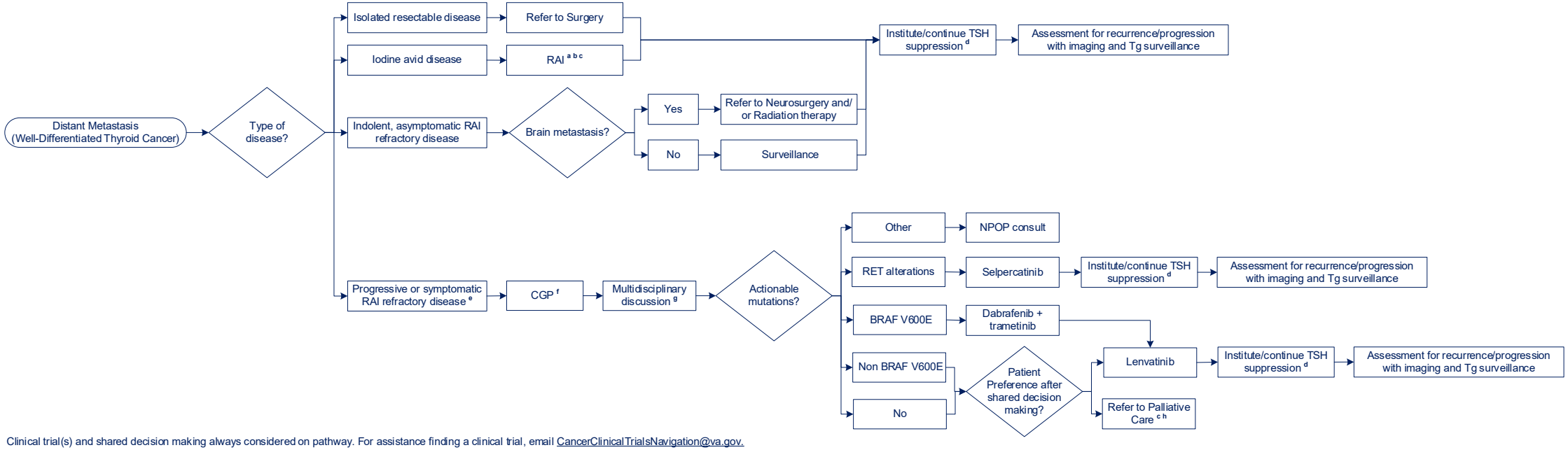
[f] **Symptomatic or Rapidly Progressing Disease** includes disease that is expected to threaten vital structures within 6 months

[g] **CGP** can identify mutations that can be germline in origin; follow-up germline testing is recommended for pathogenic variants with allele frequency 20% in the following genes: BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, MUTYH (biallelic), PALB2, PMS2, RAD51C, RAD51D, RET, SDHAF2, SDHA, SDHB, SDHC, SDHD, TMEM127, TSC2, VHL. Referral may be indicated for other genes based on age and tumor type. Please see CGS germline testing referral guidelines which can be accessed via the NPOP SharePoint site.

[h] **Multidisciplinary Discussion** to determine if patient is appropriate for maximally safe resection, redifferentiation therapy followed by RAI ablation, systemic therapy, and/or locally directed therapies including EBRT and/or thermal ablation

CGP Comprehensive Genomic Profiling
CGS Comprehensive Genetics Service
EBRT External Beam Radiotherapy
RAI Radioactive Iodine
Tg Thyroglobulin

Thyroid Cancer – Distant Metastasis (Well-Differentiated Thyroid Cancer)



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[a] **RAI** may follow surgery

[b] **RAI** every 6-12 months as long as clinical responses are observed and lesions continue to concentrate iodine, guided by cumulative RAI dose

[c] **Symptomatic bone metastasis** denosumab or bisphosphonates may be used

[d] **For TSH goal** refer to ATA Response Criteria Chart

[e] **RAI Refractory Disease** that is rapidly progressive, symptomatic, threatening vital structures, or failing or not amenable to locally directed therapy (EBRT, thermal ablation, etc.)

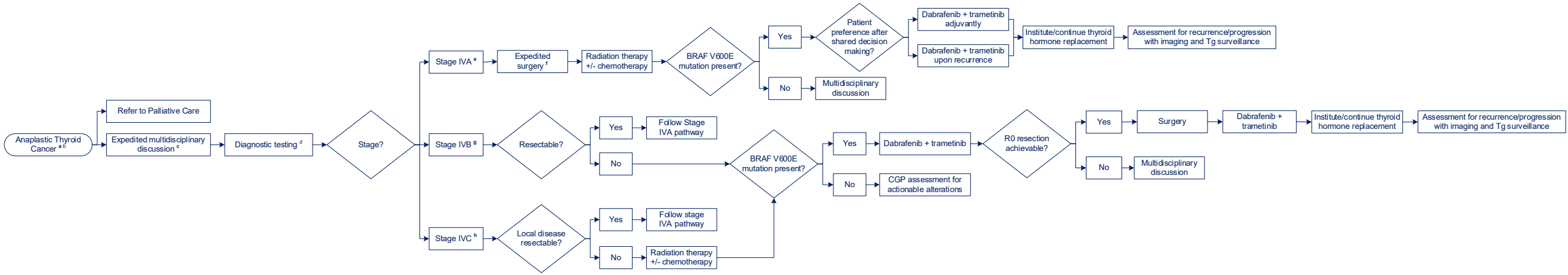
[f] **CGP** can identify mutations that can be germline in origin; follow-up germline testing is recommended for pathogenic variants with allele frequency >20% in the following genes: BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, MUTYH (biallelic), PALB2, PMS2, RAD51C, RAD51D, RET, SDHAF2, SDHA, SDHB, SDHC, SDHD, TMEM127, TSC2, VHL. Referral may be indicated for other genes based on age and tumor type. Please see CGS germline testing referral guidelines which can be accessed via the NPOP SharePoint site.

[g] **Multidisciplinary Discussion** to determine if patient is appropriate for maximally safe resection, redifferentiation therapy followed by RAI ablation, systemic therapy, and/or locally directed therapies including EBRT and/or thermal ablation

[h] **Palliative therapy** includes EBRT, thermal ablation, palliative surgery, ethanol ablation

CGP Comprehensive Genomic Profiling
CGS Comprehensive Genetics Service
EBRT External Beam Radiotherapy
RAI Radioactive Iodine
Tg Thyroglobulin

Thyroid Cancer – Anaplastic Thyroid Cancer



Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Diagnosis** confirmed through urgent biopsy of neck mass or metastatic site; BRAF V600E plus CGP should be completed if feasible but should not delay care

[b] **Prompt Airway Evaluation** is essential for identifying airway compromise and ensuring a secure airway by a local multidisciplinary team, which includes ENT, anesthesia, ICU, surgery, and oncology specialists

[c] **Team** to consist of designated thyroid surgeon, endocrinologist, medical oncologist, radiation oncologist, and palliative care; comprehensive care throughout the treatment should include palliative care

[d] **Diagnostic Testing** includes CT with contrast of Neck and Chest and PET CT

[e] **Stage IVA** is confined to thyroid (T1-T3a, N0, M0)

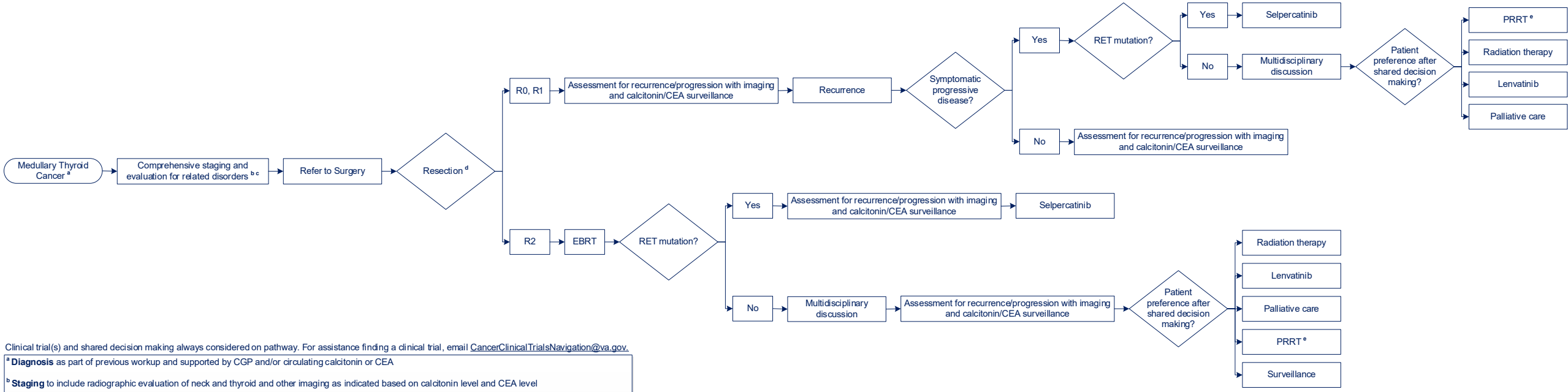
[f] **Surgical goal** is R0 resection; Surgical specimen should be sent for CGP

[g] **Stage IVB** is gross extrathyroidal extension or locally invasive or node positive (T3b, T4, any N, M0)

[h] **Stage IVC** metastatic disease (any T, any N, M1)

CGP Comprehensive Genomic Profiling
Tg Thyroglobulin

Thyroid Cancer – Medullary Thyroid Cancer



Clinical trial(s) and shared decision making always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Diagnosis** as part of previous workup and supported by CGP and/or circulating calcitonin or CEA

[b] **Staging** to include radiographic evaluation of neck and thyroid and other imaging as indicated based on calcitonin level and CEA level

[c] **Screen** for related disorders including pheochromocytoma and hyperparathyroidism with plasma fractionated metanephrines, parathyroid hormone panel, serum chemistry and germline testing including RET

[d] **Total thyroidectomy** and bilateral central neck dissection +/- lateral neck dissection based on ultrasound findings and/or calcitonin or CEA levels

[e] **177Lu-dotatate** if avidity shown on a dotatate scan

CEA Carcinoembryonic Antigen
CGP Comprehensive Genomic Profiling
EBRT External Beam Radiation Therapy
PRRT Peptide Receptor Radionuclide Therapy

Thyroid Cancer – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Indeterminate Thyroid Nodule Bethesda Category III-IV	Molecular Testing	Genomic sequencing classifier	Thyroseq Afirma ThyGeNEXT/ThyraMIR	No No No	FNA, FFPE FNA FNA
Advanced or Metastatic Thyroid Carcinoma*	Somatic NGS	CGP using both DNA and RNA based methodology	Tempus Foundation Medicine	Yes Yes	Tumor Tissue**, Blood
Thyroid Carcinoma, Any Stage, Suspicion for Germline Mutation***	Germline NGS	Refer to Genetics			
Medullary Thyroid Carcinoma, Any Stage	Germline NGS****	VA Common Hereditary Cancer Panel via Streamlined genetic testing	Fulgent	Yes	Blood, Saliva
*Advanced thyroid carcinoma includes non-resectable tumors, rapidly progressing tumors, anaplastic thyroid carcinoma, and medullary thyroid carcinoma					
**Tissue preferred, but liquid acceptable if tissue insufficient; blood only allowed if metastatic					
***Referral to genetics for evaluation is recommended for patients with thyroid cancer and one or more of the following: - A personal history of syndromic features (macrocephaly, multinodular goiter, multiple polyps, skin papules, autism spectrum disorder) - Multiple primary cancers (particularly if one or more is diagnosed <50) - Family history suggestive of hereditary predisposition (multiple relatives with the same or related cancers, early onset cancer, or multinodular goiter)					
****Germline NGS panel should include at minimum: RET. All are included on VA Common Hereditary Cancer Panel. Preferred for oncology provider to order VA Common Hereditary Cancer Panel via Streamlined genetic testing. Refer to NPOP SharePoint for further details.					

Thyroid Cancer – References

Thyroid Cancer Clinical Pathways References

Diagnostic Work Up of a Thyroid Nodule

1. Haugen BR, Alexander EK, Bible KC, et al. 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. *Thyroid*. 2016;26(1):1-133. doi:10.1089/thy.2015.0020
2. Kuzbari Z, Bandlamudi C, Loveday C, et al. Germline-focused analysis of tumour-detected variants in 49,264 cancer patients: ESMO Precision Medicine Working Group recommendations. Ann Oncol. 2023;34(3):215-227. doi:10.1016/j.annonc.2022.12.003

Management of Well-Differentiated Thyroid Cancer

1. Ringel MD, Sosa JA, Baloch Z, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. *Thyroid*. 2025;35(8):841-985. doi:10.1177/10507256251363120

Dynamic Risk Stratification

1. Kuzbari Z, Bandlamudi C, Loveday C, et al. Germline-focused analysis of tumour-detected variants in 49,264 cancer patients: ESMO Precision Medicine Working Group recommendations. Ann Oncol. 2023;34(3):215-227. doi:10.1016/j.annonc.2022.12.003

ATA Response Criteria After Initial Therpay Based on Type of Intervention

1. Ringel MD, Sosa JA, Baloch Z, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. *Thyroid*. 2025;35(8):841-985. doi:10.1177/10507256251363120

Locoregional Recurrence (Well-Differentiated Thyroid Cancer)

1. Kuzbari Z, Bandlamudi C, Loveday C, et al. Germline-focused analysis of tumour-detected variants in 49,264 cancer patients: ESMO Precision Medicine Working Group recommendations. Ann Oncol. 2023;34(3):215-227. doi:10.1016/j.annonc.2022.12.003

Distant Metastasis (Well-Differentiated Thyroid Cancer)

1. Finkel I, Korzets Y, Moore A, et al. BRAF inhibitor or BRAF/MEK inhibitor treatment for patients with metastatic BRAF V600E mutated differentiated thyroid cancer. *Arch Endocrinol Metab*. 2025;69(6):e250127. Published 2025 Oct 31. doi:10.20945/2359-4292-2025-0127

Thyroid Cancer – References

Thyroid Cancer Clinical Pathways References (continued)

Anaplastic Thyroid Cancer

1. Cabanillas ME, Akhave N, Banuchi V, et al. Reimagining the Therapeutic Approach for Anaplastic Thyroid Cancer: The Roadmap to a Cure. *Thyroid*. 2025;35(5):462-470. doi:10.1089/thy.2025.0044
2. Subbiah V, Kreitman RJ, Wainberg ZA, et al. Dabrafenib and Trametinib Treatment in Patients With Locally Advanced or Metastatic BRAF V600-Mutant Anaplastic Thyroid Cancer. *J Clin Oncol*. 2018;36(1):7-13. doi:10.1200/JCO.2017.73.6785

Medullary Thyroid Cancer

1. Wirth LJ, Sherman E, Robinson B, et al. Efficacy of Selpercatinib in *RET*-Altered Thyroid Cancers. *N Engl J Med*. 2020;383(9):825-835. doi:10.1056/NEJMoa2005651