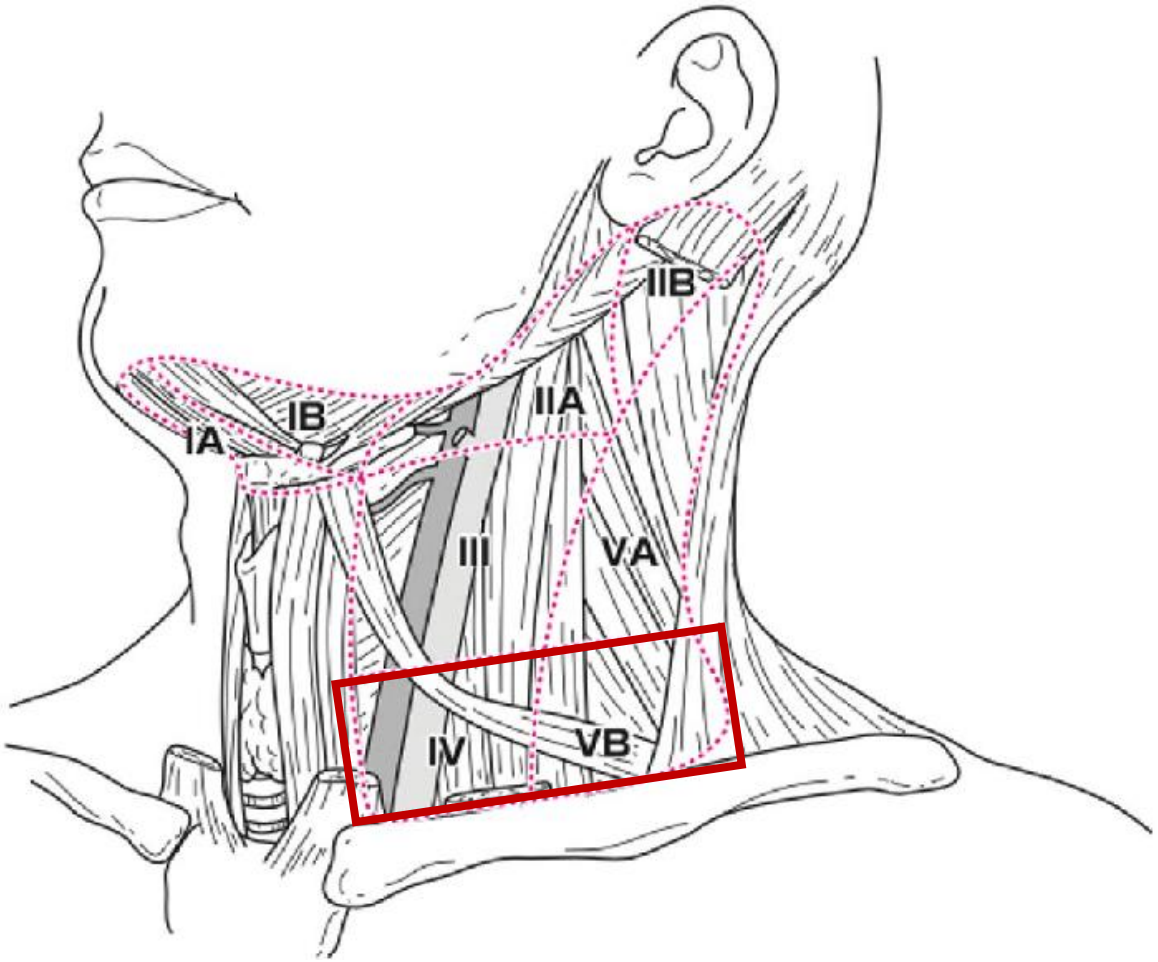
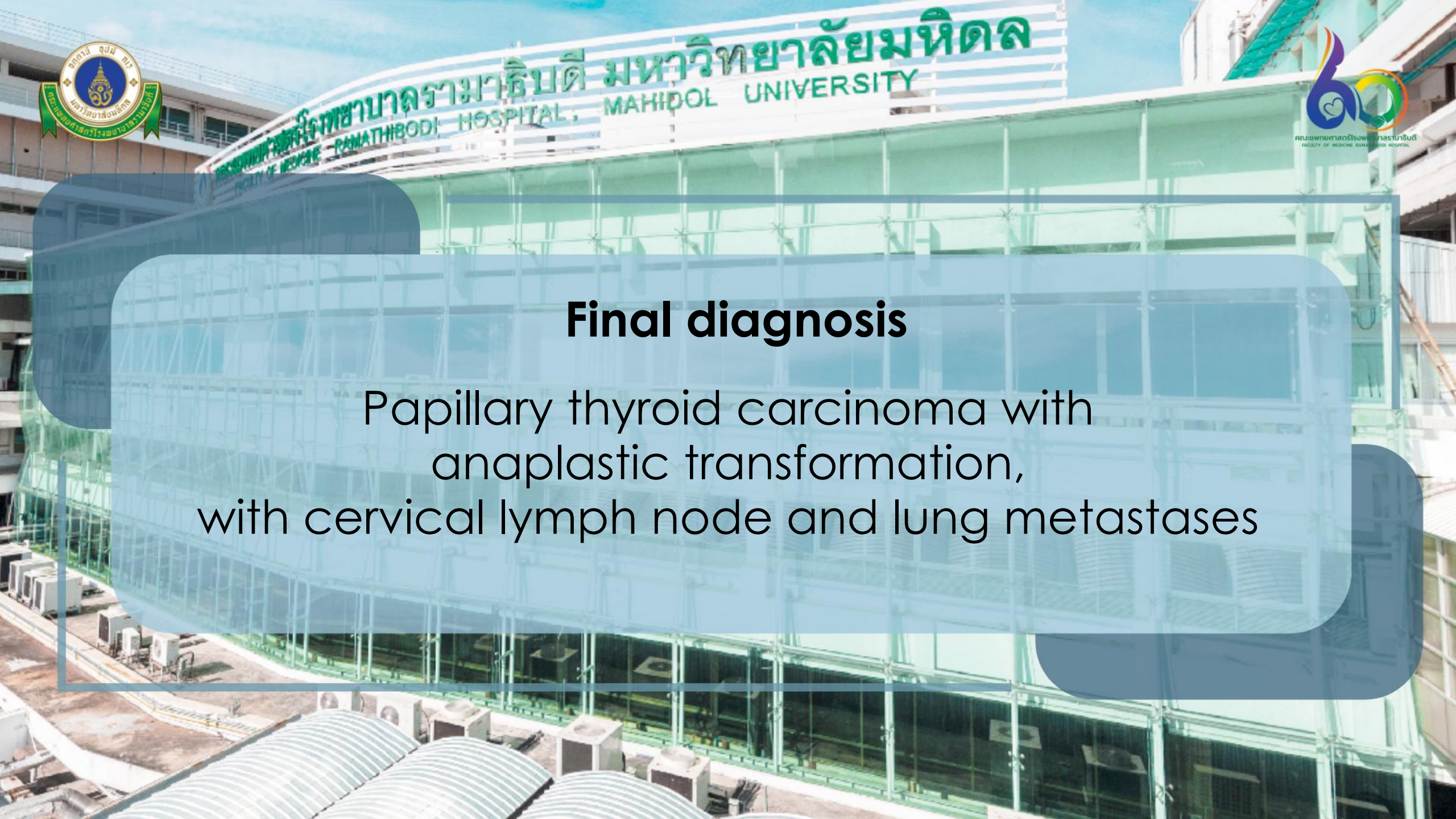
Chief Complaint

คลำได้ก้อนที่คอซ้าย 6 เดือน

ก่อนมาโรงพยาบาล





Final diagnosis

Papillary thyroid carcinoma with
anaplastic transformation,
with cervical lymph node and lung metastases

Panel of Routine Immunohistochemical Markers for the Evaluation of Suspected Anaplastic Thyroid Cancer and Expected Results Compared with Other Tumor Types

IHC marker	*DTC*	*PDTC*	*ATC*	*MTC*	*SCC*	*Lymphoma*
Pan-cytokeratins	+++	+++	+++/–	+++	+++	–
Thyroglobulin	+++	+/–	–	–	–	–
Thyroid-transcription factor 1	+++	+/–	–/+	+/–	–	–
$BRAF^{V600E}$	+/–	–/+	–/+	–	–	–
PAX8	+++	+++	+/–	+/–	–	+/–[a]
Ki-67[b]	<5%	5–30%	>30%	<20%	>30%	variable
Chromogranin	–	–	–	+++	–	–
Calcitonin	–	–	–	+++/–	–	–
Carcinoembryonic antigen	–	–	–	+++	–	–
p53	– (rare +)	–/+	+/–	–	+/–	+/–
CD45, other lymphoid markers	–	–	–	–	–	+++

+ indicates relative positive staining, – indicates negative staining, +/– indicates variable positivity.
[a]PAX8 antibodies can cross-react with PAX5, which is expressed in lymphoid cells.
[b]Percentage of nuclei positive for Ki-67.
DTC, differentiated thyroid cancer; IHC, immunohistochemistry; MTC, medullary thyroid cancer; PDTC, poorly differentiated thyroid cancer.

Thyroid. 2021;31(3):337-386.

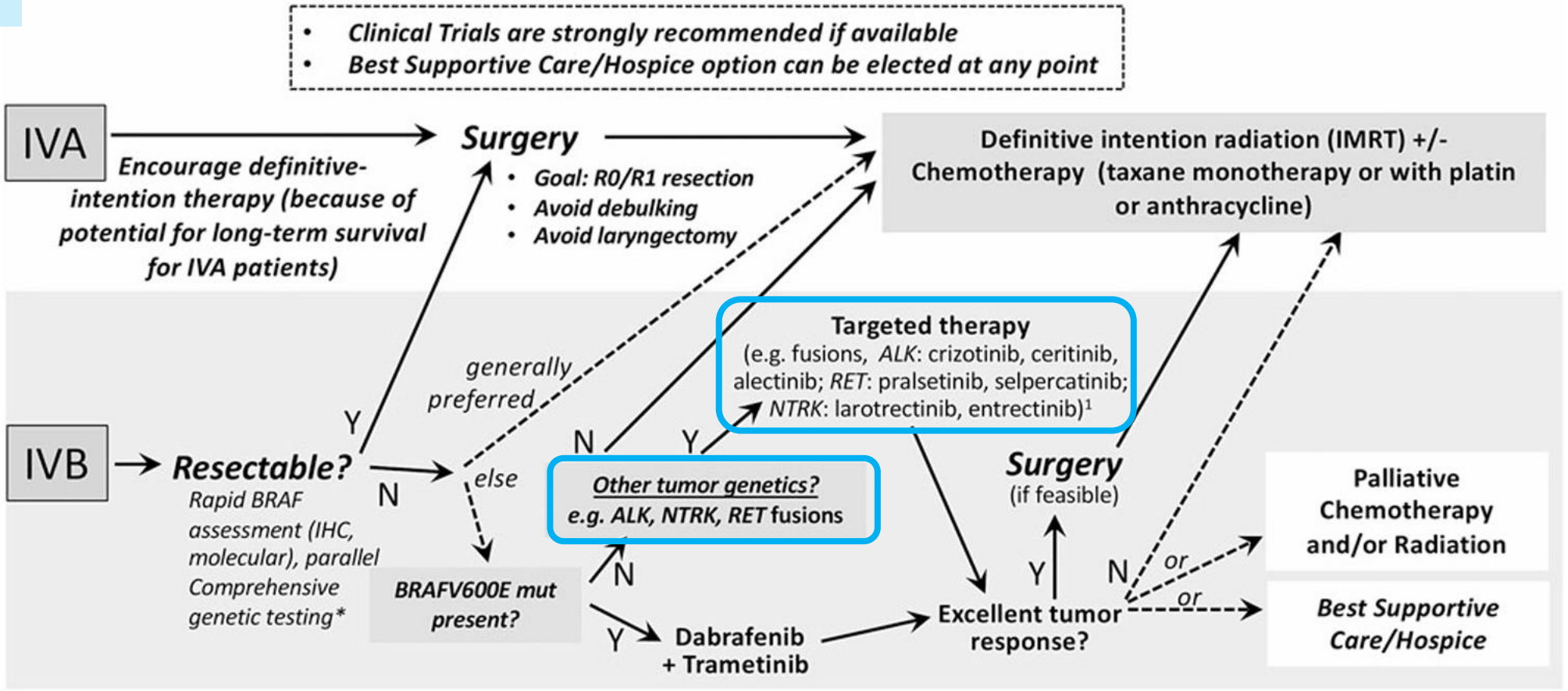
Anaplastic Thyroid Cancer (ATC)

Staging

All ATCs are stage 4

Lesions are still localized within thyroid

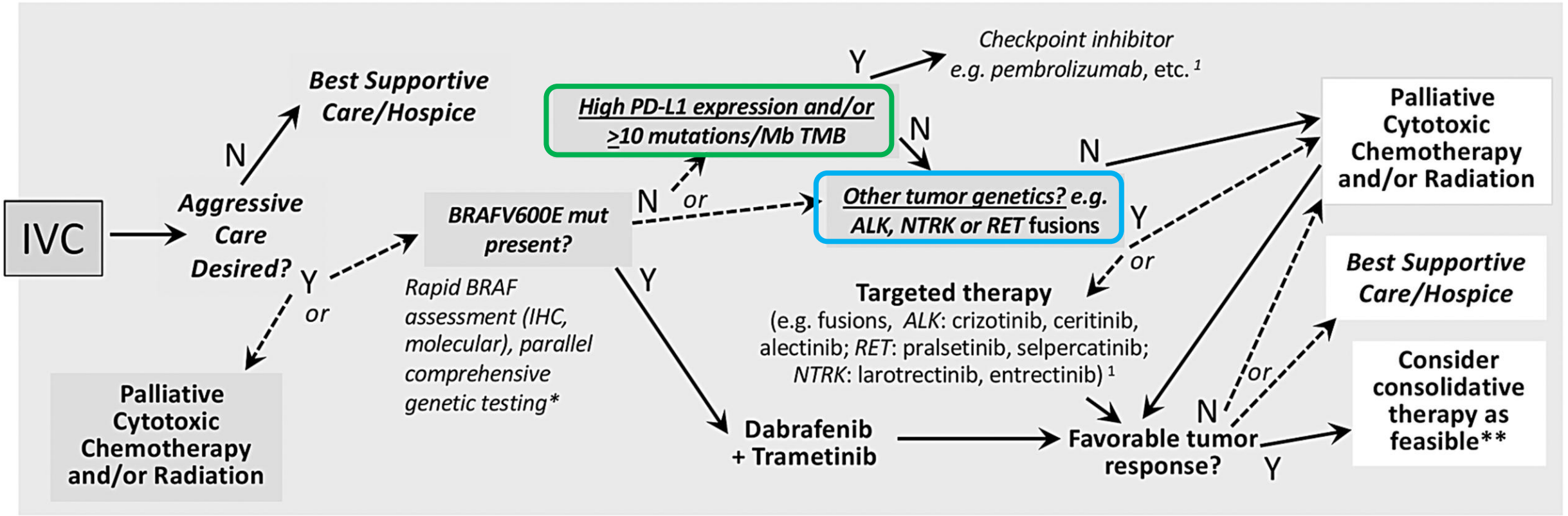
Tumor has grown outside thyroid capsule and/or involving locoregional lymph nodes



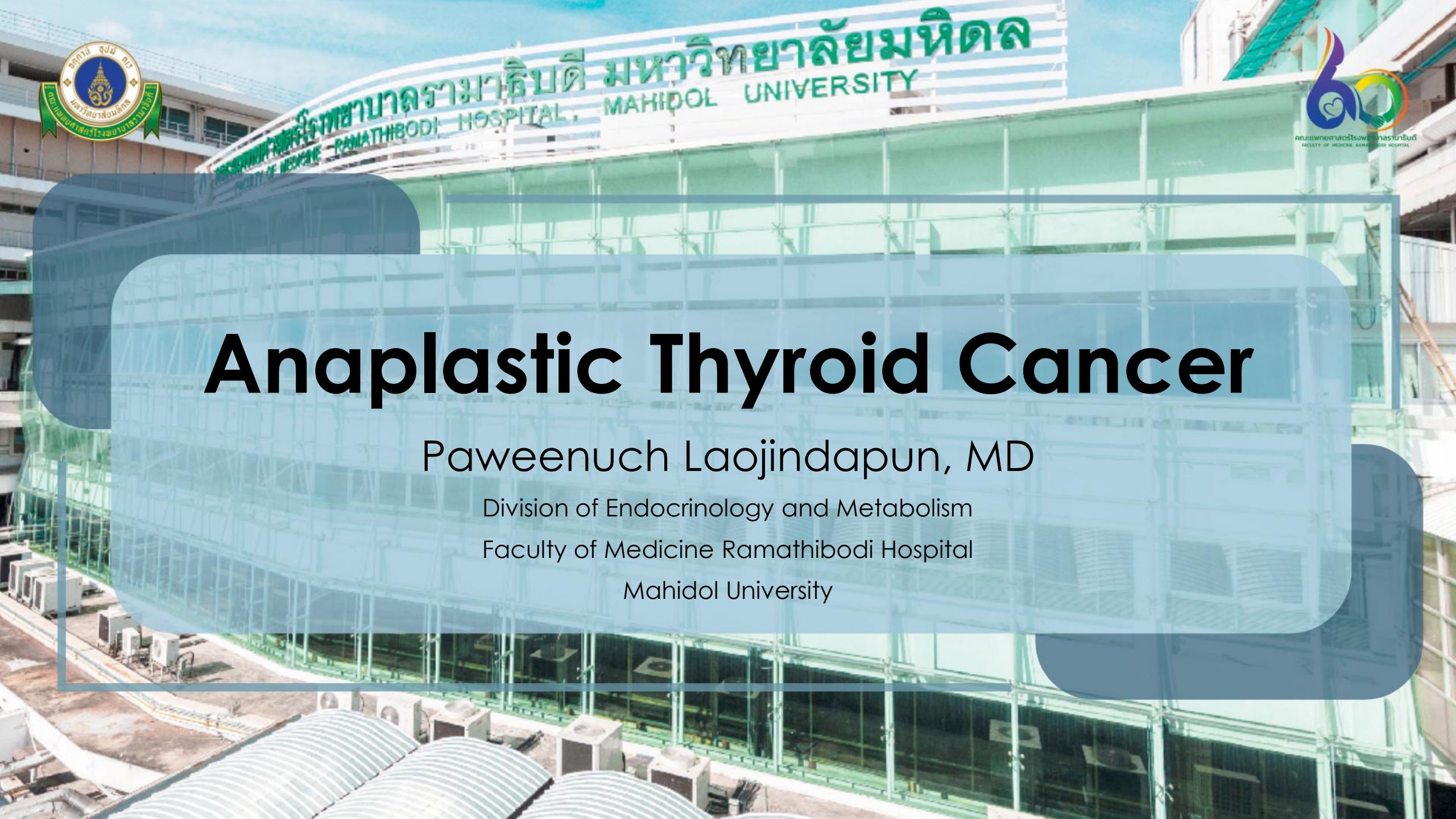
Thyroid. 2021;31(3):337-386.

Anaplastic Thyroid Cancer (ATC)

- *Clinical Trials are strongly recommended if available*
- *Best Supportive Care/Hospice option can be elected at any point*



Thyroid. 2021;31(3):337-386.



Anaplastic Thyroid Cancer

Paweenuch Laojindapun, MD

Division of Endocrinology and Metabolism

Faculty of Medicine Ramathibodi Hospital

Mahidol University

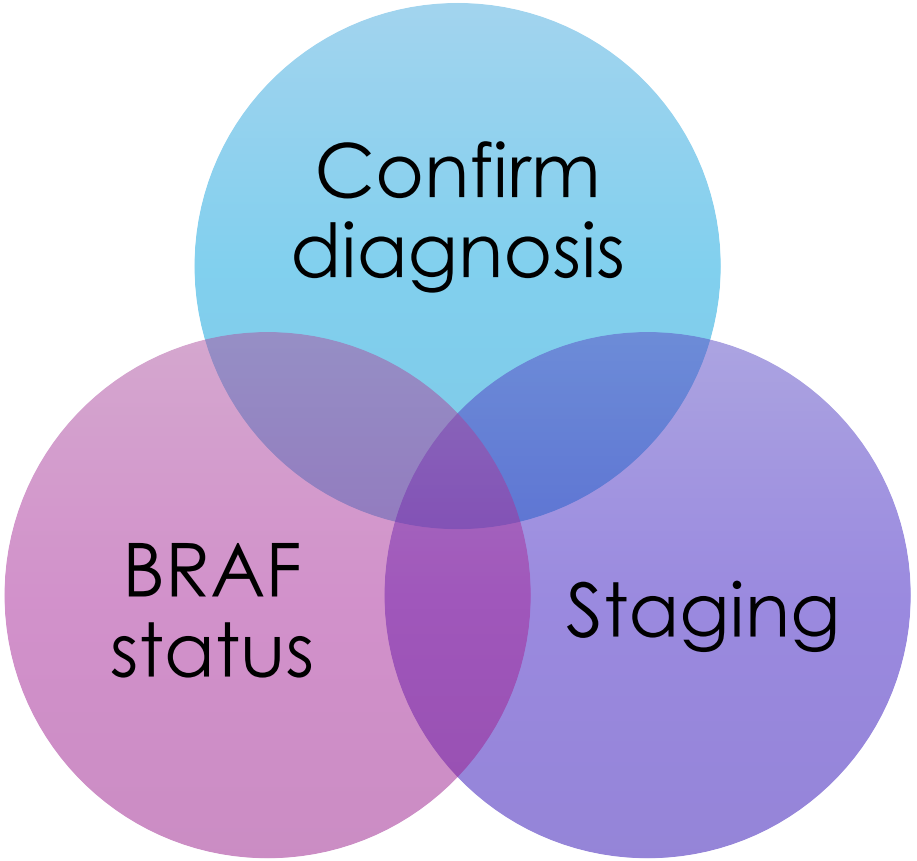
Anaplastic Thyroid Cancer (ATC)

- **ATC development:** can develop *de novo* or from anaplastic transformation of other thyroid tumors.
- **DTC association:** present in 7-89% of ATC cases
  - PTC (especially tall cell subtype) is the most common
  - Other: conventional or oncocytic subtype of FTC

DTC, differentiated thyroid cancer; FTC, follicular thyroid cancer; PTC, papillary thyroid cancer

Nat Rev Endocrinol. 2017;13(11):644-660.

Key Initial Steps in ATC Management



- All performed simultaneously and expeditiously
- Discussion of goals of care and advanced directives

JAMA Oncol. 2024 ;10(9):1264-1271.

Key Initial Steps in ATC Management

Confirm diagnosis

- Ultrasonography-guided biopsy of the primary tumor or metastatic neck nodes

Assess disease extent

- Contrast-enhanced CT or MRI of the neck
- Cross-sectional imaging of the chest, abdomen, and pelvis
- MRI of the brain, with and without contrast
- MRI of the spine when vertebral metastases are clinically suggestive of disease or are identified on cross-sectional imaging
- ^{18}F-FDG PET/CT
- Flexible laryngoscopy

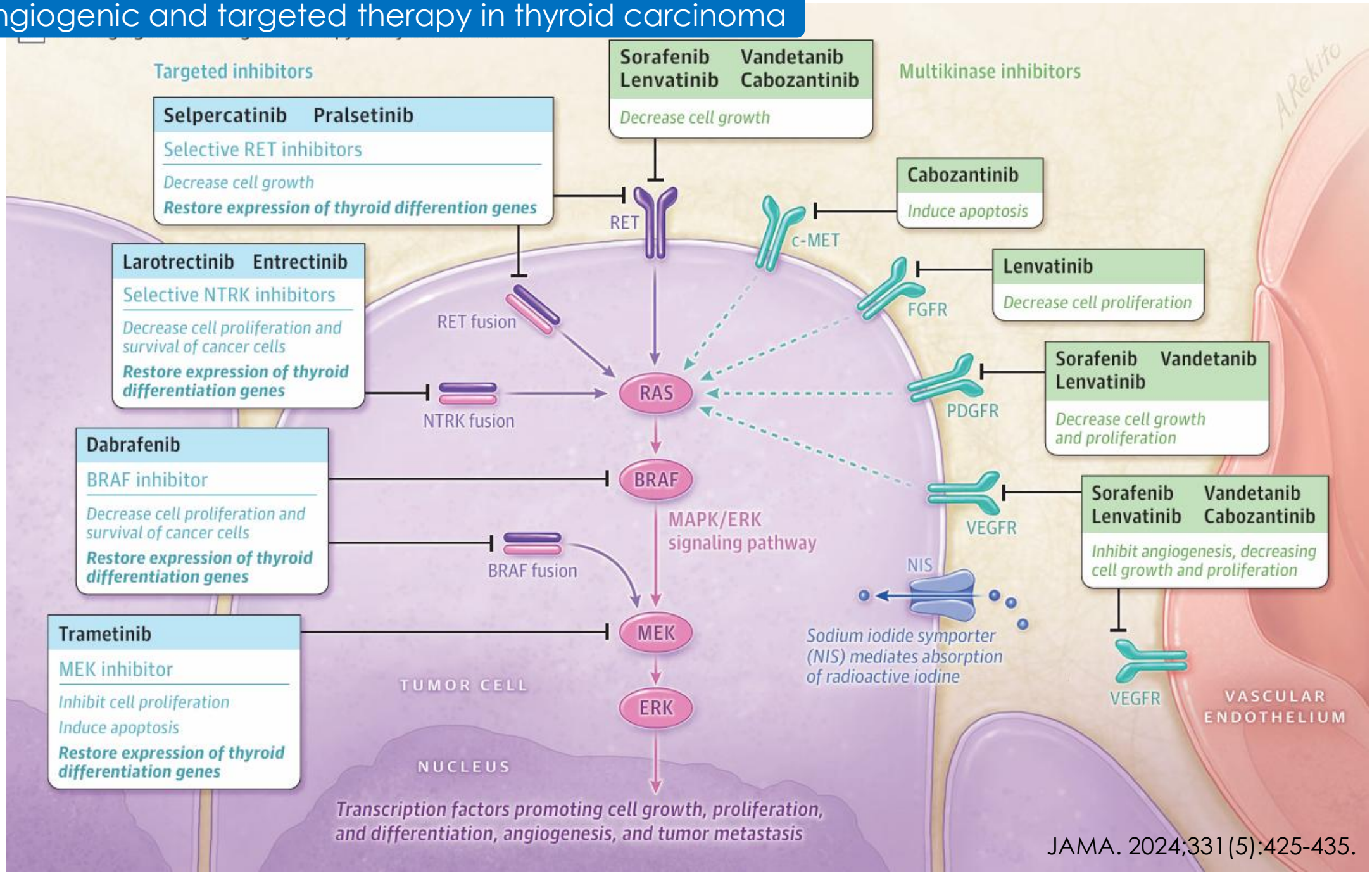
Evaluate tumor

- Expedited assessment of *BRAF* status by IHC or PCR
- Whole-exome DNA and RNA testing by NGS of tumor tissue

- Core-needle biopsy (CNB) increases diagnostic yield
- BRAF IHC should be **avoided on FNA smears** due to the high false-positive rate; instead, they should be performed on FNA cell block preparations or CNB samples.

JAMA Oncol. 2024 ;10(9):1264-1271.

Antiangiogenic and targeted therapy in thyroid carcinoma



JAMA. 2024;331(5):425-435.

The impact of BRAF targeting agents in advanced ATC

- **40% of ATCs harbor a *BRAF* V600E pathogenic variant,**

  for which BRAF /MEK inhibitor (dabrafenib/trametinib) are available.

- Responses to dabrafenib plus trametinib (DT) in BRAF V600E-variant ATC are remarkable and rapid.

- **DT with pembrolizumab (DTP)** is favored over DT alone.
  - BRAF inhibition upregulates PD-L1 expression on tumor cells and increases T-cell infiltration in the tumor microenvironment, suggesting a potential for synergistic effect of this combination.
  - DTP substantially extends overall survival compared to DT alone.

JAMA Oncol. 2024 ;10(9):1264-1271.

JAMA Oncology | Special Communication

Initial Management of *BRAF* V600E-Variant Anaplastic Thyroid Cancer

The FAST Multidisciplinary Group Consensus Statement

Recommendations		
1. Patients with a tenuous airway and unknown *BRAF* status should be admitted to the hospital and treated with steroids and racemic epinephrine until *BRAF* status is known. If these measures are successful in temporarily stabilizing the airway, tracheostomy may be avoidable in patients with a *BRAF* V600E variation if BRAF-directed therapy is initiated in a timely manner.	Moderate	Strong
2. For patients with stage IVB *BRAF*v-ATC and unresectable or advanced disease (TNMC, ≥1), front-line neoadjuvant use of DT is recommended, followed by surgical resection of the primary tumor.	Moderate	Strong
3. For patients with stage IVB *BRAF*v-ATC, we favor the combination of DTP rather than DT alone. When not feasible up-front, adding pembrolizumab at progression on DT is also acceptable.	Low	Conditional
4. For patients with stage IVB *BRAF*v-ATC, after 2 to 3 mo of neoadjuvant therapy with DT±P, we recommend restaging with contrast-enhanced CT of the neck and whole-body ^{18}F-FDG-PET/CT imaging to assess response of the primary tumor and to determine the feasibility and morbidity of surgery using considering the TNMC score.	Moderate	Strong
5. For patients with stage IVB *BRAF*v-ATC, after neoDT±P and surgery, postoperative chemoradiation is recommended.	Moderate	Strong
6. For patients with stage IVB *BRAF*v-ATC treated with neoDT±P, after surgery and chemoradiation are completed:		
(a) DT should be resumed indefinitely for maintenance therapy until disease progression or substantial toxic effects occur.	Low	Conditional
(b) Addition of pembrolizumab to maintenance DT, for at least 1 year, should be strongly considered to reduce the risk of recurrence.		
7. In patients with stage IVB *BRAF*v-ATC treated with up-front surgery with or without chemoradiation, we recommend adjuvant pembrolizumab for at least 1 year, preferably on a clinical trial.	Low	Conditional
8. For all patients with stage IVC *BRAF*v-ATC, rapid initiation of DT is recommended.	Moderate	Strong
9. For patients with stage IVC *BRAF*v-ATC, we favor the combination of DT with pembrolizumab for at least 1 year, rather than DT alone. When not achievable up-front, adding pembrolizumab at progression to DT is also acceptable.	Moderate	Strong
10. For patients with stage IVC *BRAF*v-ATC, after 2 to 3 mo of DTP, we recommend restaging with contrast-enhanced CT of the neck and whole-body ^{18}F-FDG-PET/CT to assess feasibility of surgery using the TNMC score. If the primary tumor is considered resectable, we recommend surgery followed by resumption of DTP.	Moderate	Strong

JAMA Oncol. 2024;10(9):1264-1271.

Take Home Message: PTC/ATC

- **PTC is rarely rapidly progressive.**

  If encountering aggressive PTC, review clinical and pathological findings to consider alternative diagnoses.

- **Immunohistochemistry is essential** for definitive diagnosis.
- **When interpreting total body scan results**,

  always correlate findings with thyroglobulin levels.

- **For suspecting ATC**, promptly initiate staging and management.