2021 ATA® Guidelines for Management of Patients with Anaplastic Thyroid Cancer

Systemic therapy for unresectable ATC stage IVB and stage IVC patients & Approach to Metastases

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Systemic therapy for unresectable ATC stage IVB and stage IVC patients

- ATC patients with **unresectable** or **advanced disease wishing aggressive therapy**, we recommend ***early initiation of cytotoxic chemotherapy*** as an initial and potentially bridging approach until mutational interrogation results and/or mutationally-specified therapies might be available, and if appropriate (R.19)

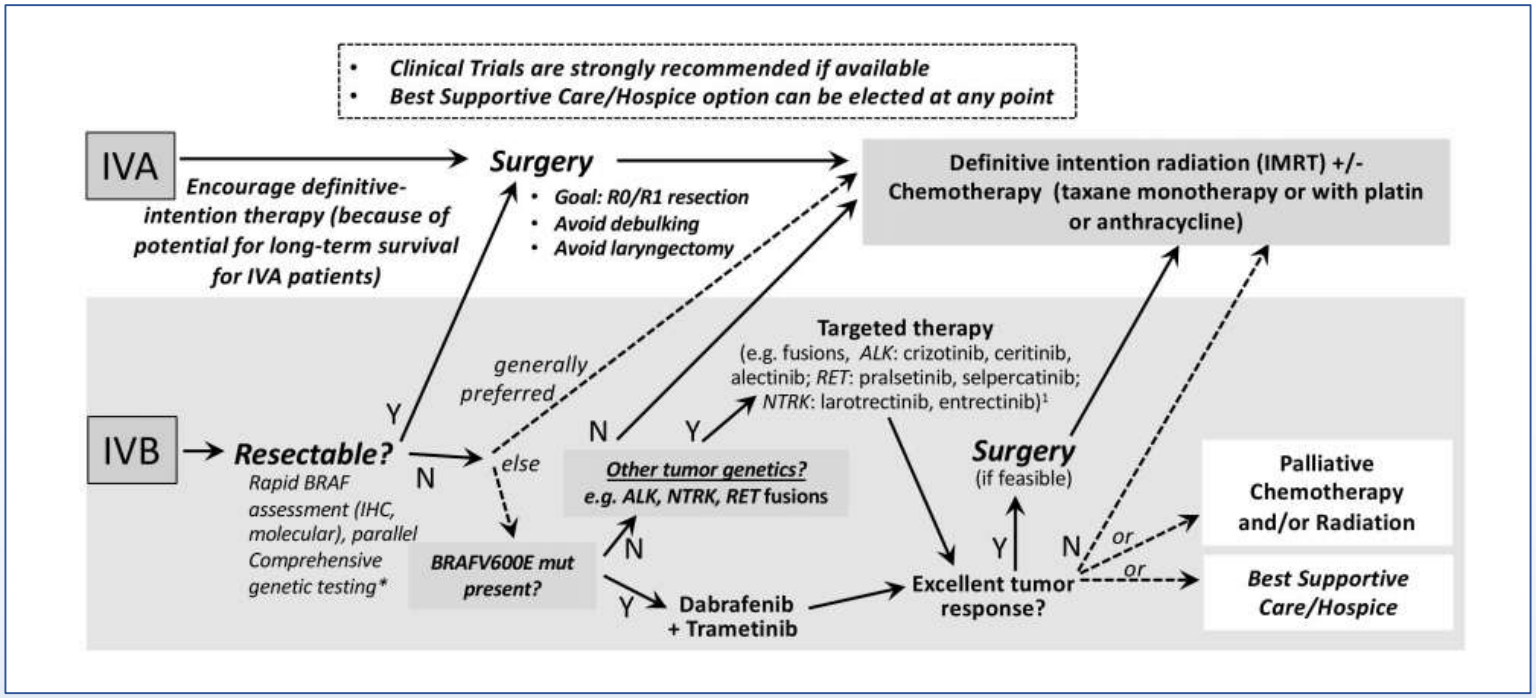

Figure 1- 2021 ATC Guidelines

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Systemic therapy for unresectable ATC stage IVB and stage IVC patients

- While awaiting molecular information or targeted drug approval, radiotherapy and/or the expeditious initial use of these cytotoxic chemotherapy drugs as "bridging" chemotherapy are prudent among patients wishing aggressive treatment

TABLE 6. EXAMPLES OF CONCURRENT (IN COMBINATION WITH RADIATION THERAPY) CHEMOTHERAPY REGIMENS IN PATIENTS WITH ANAPLASTIC THYROID CANCER

Regimen	*Agents/dosages*	*Frequency*
Paclitaxel/carboplatin	Paclitaxel 50 mg/m^2, carboplatin AUC2 IV	Weekly
Docetaxel/doxorubicin	Docetaxel 20 mg/m^2 IV, doxorubicin 20 mg/m^2 IV	Weekly
Paclitaxel	Paclitaxel 30–60 mg/m^2 IV	Weekly
Docetaxel	Docetaxel 20 mg/m^2 IV	Weekly

AUC, area under the curve.

Table 6. 2021 ATC Guidelines

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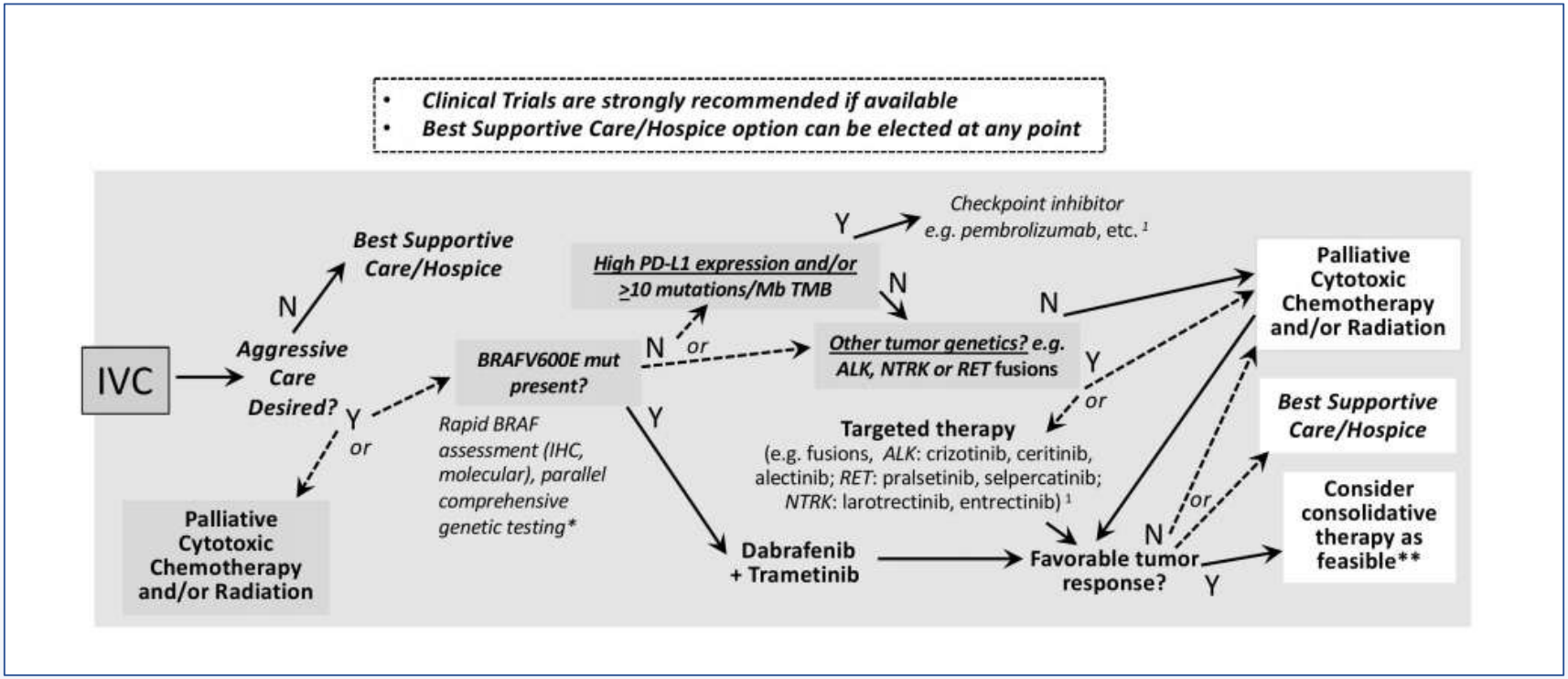

*Cytotoxic chemotherapy may be started as a ‘‘bridge’’ while awaiting genomic information or while awaiting targeted therapy (e.g., dabrafenib and trametinib).

**Consolidate Rx refers to focal therapy intended to control residual macrometastatic disease among those electing aggressive therapy.

Dashed arrows depict circumstances where competing therapeutic options may be of consideration

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Figure 2- 2021ATC Guidelines

BRAF V600E Mutated ATC

- In ***BRAF*** **V600E mutated IVC and unresectable IVB ATC patients who decline radiation therapy**, initiation of BRAF/MEK inhibitors (dabrafenib plus trametinib) is recommended over other systemic therapies if available (R.20)

- In ***BRAF*** **V600E mutated unresectable stage IVB ATC wherein radiation therapy is feasible**, *chemoradiotherapy or neoadjuvant dabrafenib/trametinib represent alternatives to initial therapy* (R.21)

BRAF Non-Mutated ATC

- *In* ***BRAF non-mutated patients****, radiation therapy with concurrent chemotherapy* should be considered in an effort to *maintain the airway* in patients with low burden of metastatic disease (R. 22)

- In ***NTRK*** **or** ***RET*** **fusion ATC patients with stage IVC disease**, we recommend initiation of a TRK inhibitor (either larotrectinib or entrectinib) or RET inhibitor (selpercatinib or pralsetinib), preferably in a clinical trial, if available (R23)

- In **IVC ATC patients with high PD-L1 expression**, checkpoint (PD-L1, PD1) inhibitors can be considered as first line therapy in the absence of other targetable alterations or as later line therapy, preferably in the context of a clinical trial. (R. 24)

ATC

- Patients with ***BRAF* wild type** (*BRAF* "negative" or unknown mutation status) **IVB unresectable or metastatic ATC wishing an aggressive approach** and not receiving chemoradiation should be encouraged to participate in clinical trials given the rarity of ATC, the paucity of data in support of improved survival or quality of life from any systemic therapeutics, and the need to develop evidence-based safe and effective therapeutic approaches in advanced ATC. (GPS 7)

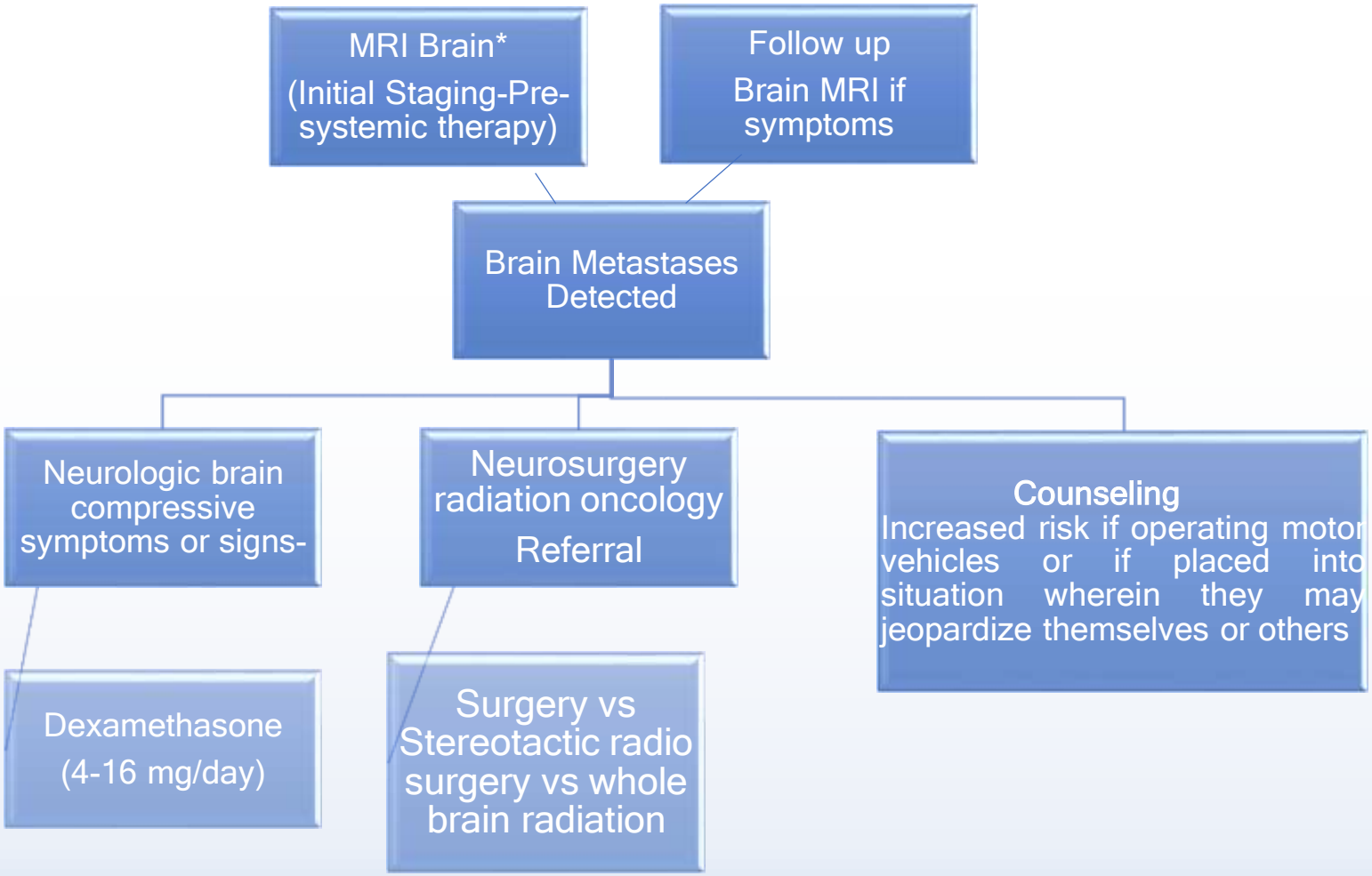
- **Metastatic ATC** patients lacking other therapeutic options including clinical trials- recommend **cytotoxic chemotherapy** (taxane and/or an anthracycline or taxane with or without cis- or carbo-platin) (R.25)

ATC

- Therapeutic decision making in the setting of progressive disease after initial therapy regardless of somatic mutational status or therapy is very complex and not easily defined by an algorithmic approach. In this setting, ***care guided by an expert in ATC therapeutics is best pursued*** (GPS 8)

- As prognosis is dire in metastatic and progressive ATC, ***best supportive care (hospice) should also be discussed as an option***. (GPS9)

Brain Metastases in ATC



*MRI sensitivity higher than CT and FDG PET Scan

Adapted from Approach to Brain Metastases R26-28 & GPS 10

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Bone Metastases in ATC

Palliative radiotherapy

- Criteria:
- a) Symptomatic or threatening bone metastasis without structural compromise
- b)No threatened spinal cord compression

Orthopedic fixation

- Criteria:
- a) Structural compromise in a weight-bearing region
- b) Or threatening spinal cord compression
- **Fixation needs to occur prior to palliative radiotherapy

Antiresorptive Therapy

•Bisphosphonate infusions

•Dose reduction if reduced renal function

• OR

•Subcutaneous RANK Ligand inhibitor

•**With either option calcium and vitamin D supplementation are essential

Adapted from Approach to Bone Metastases R29-31

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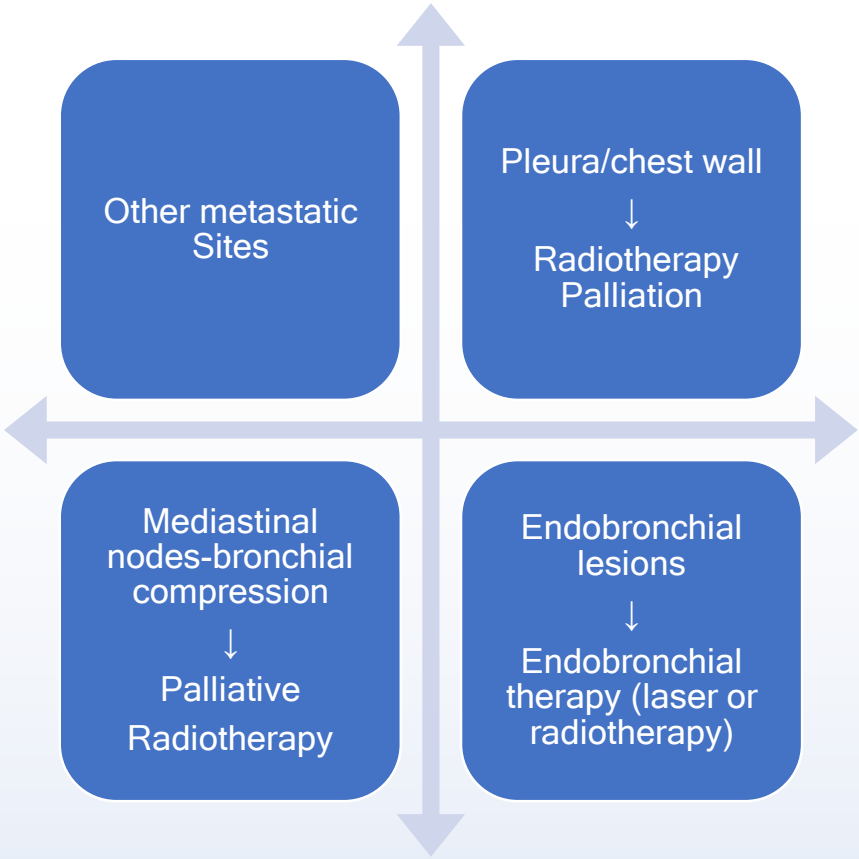
Approach to Other Metastatic Sites



Concept: Thoughtfully individualize therapy in the context of threat posed by lesion

Oligoprogressive Metastatic ATC

- **Patients on systemic therapy who develop oligo-progressive disease, local tumor-directed therapy may be considered to postpone the need to change otherwise beneficial systemic therapy (GPS 11)**

Stereotactic Body Radiotherapy (SBRT)

Radiofrequency ablation (RFA)

Surgery*

Immunotherapy**

Oligoprogressive metastases= 5 or less metastatic lesions
*surgery not typical for metastatic ATC, can be considered on a case-by-case basis
**addition of pembrolizumab has been described anecdotally