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
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)

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Figure 1 - 2021 ATC Guidelines
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. 2021 ATC Guidelines

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Agents/dosages</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel/carboplatin</td>
<td>Paclitaxel 50 mg/m², carboplatin AUC2 IV</td>
<td>Weekly</td>
</tr>
<tr>
<td>Docetaxel/doxorubicin</td>
<td>Docetaxel 20 mg/m² IV, doxorubicin 20 mg/m² IV</td>
<td>Weekly</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Paclitaxel 30–60 mg/m² IV</td>
<td>Weekly</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Docetaxel 20 mg/m² IV</td>
<td>Weekly</td>
</tr>
</tbody>
</table>

AUC, area under the curve.
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.
**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 Brain**
(Initial Staging-Pre-systemic therapy)

**Follow up Brain MRI if symptoms**

**Brain Metastases Detected**

- **Neurologic brain compressive symptoms or signs**
  - Dexamethasone (4-16 mg/day)

- **Neurosurgery radiation oncology Referral**

- **Surgery vs Stereotactic radio surgery vs whole brain radiation**

**Counseling**
Increased risk if operating motor vehicles or if placed into situation wherein they may jeopardize themselves or others

*MRI sensitivity higher than CT and FDG PET Scan

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

- **Other metastatic sites**
  - Pleura/chest wall → Radiotherapy Palliation
  - Mediastinal nodes-bronchial compression → Palliative Radiotherapy
  - Endobronchial lesions → Endobronchial therapy (laser or radiotherapy)

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

Oligoproggressive 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