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

Radiotherapy and Systemic Chemotherapy in Loco-regionally confined stages IVA and IVB
Approach towards Radiotherapy and Systemic Chemotherapy in Loco-regionally confined stages IVA and IVB

- Goal: To limit the threat from residual macro- or microscopic ATC in the neck for terminal airway and/or esophageal compromise
- Radiotherapy is provided after surgery or if unresectable
- Based on patient centered goals
  - Palliative
  - Potentially curative
- Different approaches
  - Locoregional: most commonly radiotherapy +/- chemotherapy
  - Systemic: conventional chemotherapy; also targeted therapies to specific somatic mutations, eg BRAFV600E
Radiotherapy after complete/near-complete (R0 or R1) resection

- Following R0 or R1 resection, we recommend that good performance status patients with no evidence of metastatic disease who wish an aggressive approach should be offered standard fractionation **Intensity-modulated radiation therapy (IMRT)** with concurrent systemic therapy (R.14)

- Radiation therapy should begin no later than 6 weeks after surgery (GPS 8)

- Patient goals of care, medical and psychosocial fitness for therapy, **potential toxicities**, financial considerations, and robustness of social support must be prominently considered in the decision to proceed with aggressive **multimodal therapy** (GPS 9)

- Cytotoxic chemotherapy can be initiated within one week of surgery, providing sufficient healing, in anticipation of subsequent chemoradiation (GPS 10)
Radiotherapy for Poor Performance Status

- In patients of **poor performance status**, palliative or preventative (no residual disease present) locoregional radiotherapy over high dose radiotherapy is suggested (GPS 11)
Radiotherapy and/or chemotherapy in patients with unresectable or gross residual locoregionally-confined disease

- We recommend that patients who have undergone R2 resection or have unresectable but non-metastatic disease with good performance status and who wish an aggressive approach be offered standard fractionation IMRT with systemic therapy. Alternatively, in BRAF V600E mutated ATC, combined BRAF/MEK inhibitors can be considered in this context (R.15)
  - BRAF V600E mutation status to guide therapy is a change from previous guidelines

- In patients with unresectable disease during initial evaluation in whom radiotherapy and/or systemic (chemotherapy or combined BRAF/MEK inhibitors) therapy renders the tumor potentially resectable, we recommend re-consideration of surgical resection (R.16)
Radiotherapy treatment volume and techniques

• Among patients who are to receive radiotherapy for unresectable thyroid cancer or in the postoperative setting, **intensity modulated radiotherapy (IMRT)** is recommended (R.17)
  • IMRT provides optimal balance of benefit versus potential toxicity
  • Acute toxicity: skin erythema, moist desquamation, mucositis of the esophagus, trachea, and larynx, and xerostomia
  • Late toxicity: skin telangiectasias, skin pigmentation, soft tissue fibrosis, and mild lymphedema, esophageal stenosis
Role of chemotherapy combined with radiotherapy as neo/adjuvant therapy in locoregionally-confined (Stages IVA or IVB) ATC

- The use of **cytotoxic chemotherapy** involving a taxane (paclitaxel or docetaxel), administered with or without anthracyclines (doxorubicin) or platin (cisplatin or carboplatin), is recommended in patients treated with **definitive-intention radiation** (R.18)
Management of stage IVA and IVB disease

Initial therapy

- **IVB**
  - **Resectable?**
    - Rapid BRAF assessment (IHC, molecular), parallel Comprehensive genetic testing
    - **Y**
      - BRAFV600E mut present?
        - **Y**
          - Dabrafenib + Trametinib
        - **N**
          - Other tumor genetics? (e.g. ALK, NTRK, RET fusions)
            - **Y**
              - Excellent tumor response?
                - **Y**
                  - Surgery (if feasible)
                - **N**
                  - Definitive intention radiation (IMRT) +/- Chemotherapy (taxane monotherapy or with platin or anthracycline)
            - **N**
              - Targeted therapy (e.g. fusions, ALK: crizotinib, ceritinib, alectinib; RET: pralsetinib, selpercatinib; NTRK: larotrectinib, entrectinib)
              - Radiation

  - **N**
    - Best Supportive Care/Hospice

**Surgery**
- **Goal:** R0/R1 resection
- Avoid debulking
- Avoid laryngectomy

**Definitive intention radiation (IMRT)**

**Follow-up**

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