

Multidisciplinary Management of Aggressive Thyroid Cancer

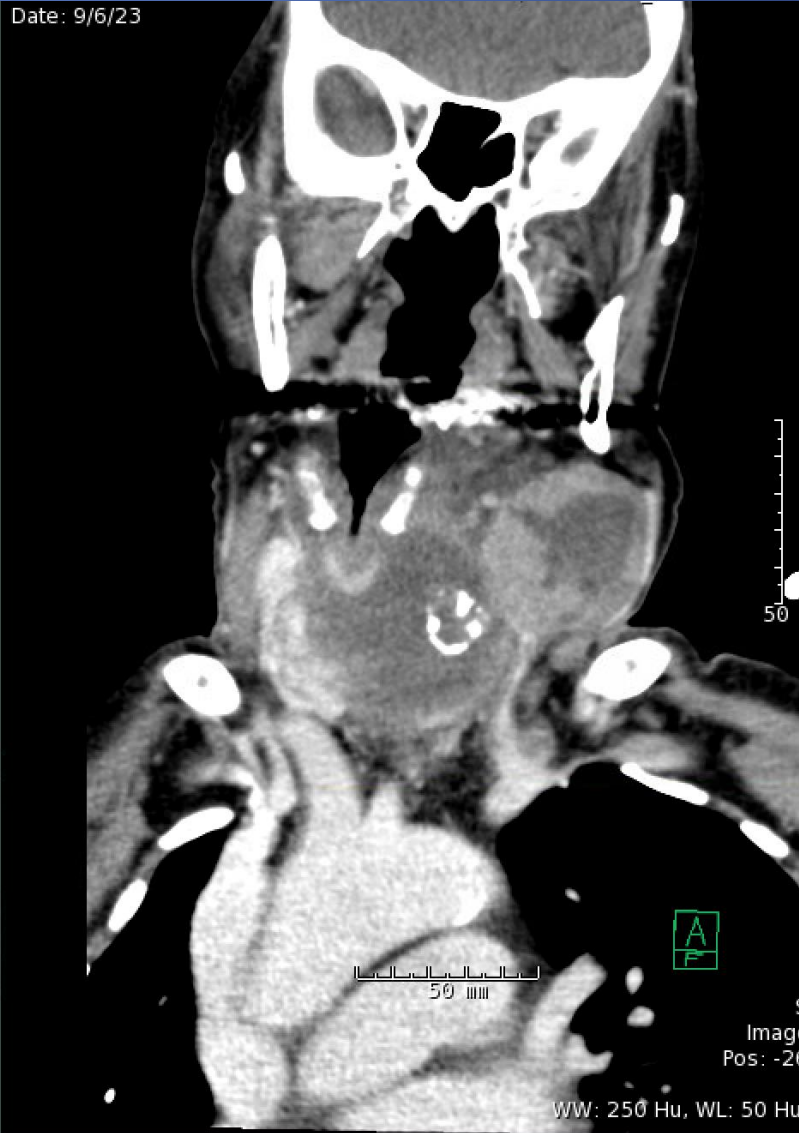
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Introduction



Background and Statistics

ATC

- 1 to 2% of all thyroid cancer diagnoses, responsible for 50% of all deaths caused by thyroid cancer
- SEER data from 1986 to 2015 showed an incidence of .9 cases per 1 million people
- In non-white and non-black races the incidence is 1.1 cases per 1 million.
- May originate de novo but also can arise as a conversion of differentiated cancer
 - The cells do not retain any of the biological features of the original follicular cells so they don't produce thyroglobulin or uptake iodine.

Background and Statistics

ATC

50% will present with distant disease (lung, bone, brain)

- Prior to the past 5-10 years, the median survival was 3 to 6 months, and a 20% one year survival rate
 - The most common cause of death is respiratory insufficiency (40%) due to pulmonary metastatic disease burden
 - 60% is due to major vessel involvement
 - 16% due to airway obstruction and 13% due to hemorrhage

Risk Factors

- Older age (mean 68-73)
- blood group type B
- Multinodular goiter (iodine deficiency)
- Low level of education/less access to care
- Environmental factors (?volcanic areas)

Clinical Presentation

History

- Rapid enlargement of a neck mass over weeks to days
- Dyspnea, dysphagia hoarseness and cough

Exam

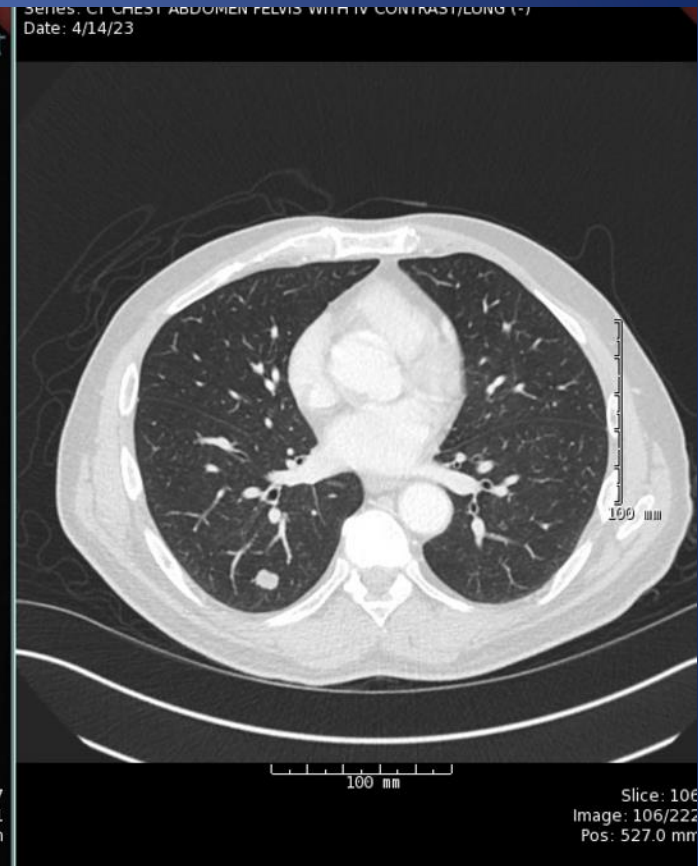
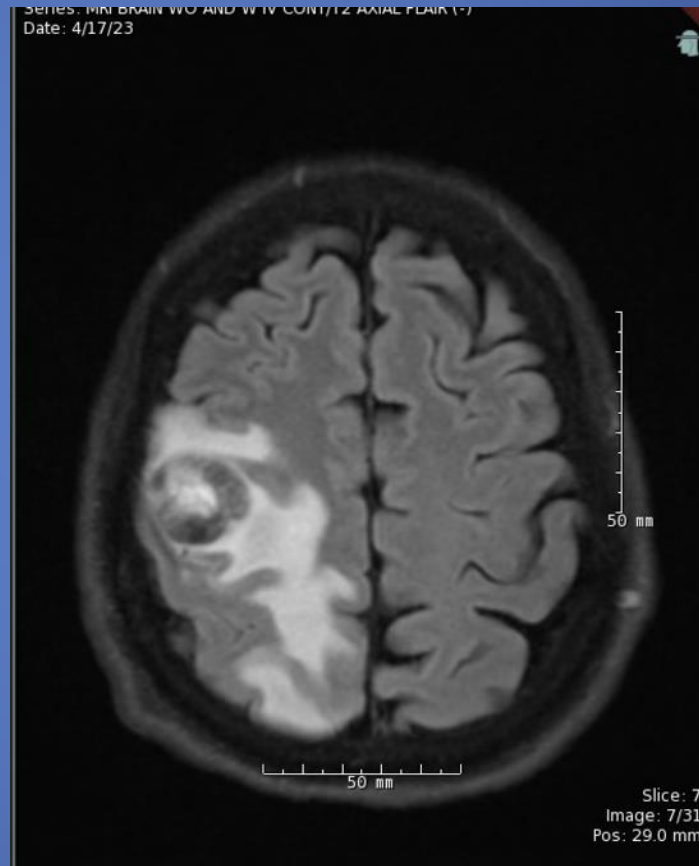
- Firm and fixed mass
- Erythematous neck skin
- Vocal cord paralysis, pooled secretions
- Superior vena cava syndrome with retrosternal extension



Staging

Staging: AJCC 8th Edition

- IVA only intrathyroidal (10%)
- IVB gross extrathyroidal extension and/or cervical metastatic disease (40%)
- IVC when there are distant mets (50%)



Key Steps in ATC Management

1. Rapidly/definitively establish diagnosis
2. Multidisciplinary involvement and coordination
3. Determine Extent of disease
4. Patient Counseling
 - Establish individualized goals of care

Key Steps in ATC Treatment

5. Evaluate Surgical options

6. Surgical decision-making

7. Non-surgical management decision making

8. Maintain ongoing hospice and end-of-life conversations

Rapidly/definitively establish diagnosis

- FNA/Core Biopsy

High Mutational Burden/unstable chromosome

IHC for BRAF; present in 40-70% ATC; surrogate for molecular testing while waiting for result

- Molecular testing of tissue

BRAF

TERT (in 65-70% ATC)

RAS (in 15-40% ATC)

Rapidly/definitively establish diagnosis; Determine Extent of disease

- Consider admission for workup
- Imaging
 - CT neck, chest, abdomen, pelvis
 - PET scan
 - MRI brain
 - Laryngoscopy/esophagoscopy
- Immediate airway evaluation
 - stridor

Multidisciplinary Involvement and Coordination; Patient Counseling

- Goals of Care

Full disclosure of benefits/risks

Patient preferences honored

Ethical Issues

- Feeding
- Tracheotomy

Hospice when patients decline treatment that intends to prolong life

Evaluate Surgical Options: Surgical Decision-Making

Immediate Airway Evaluation

- Is there stridor?

Is R0/R1 resection expected?

- Based on imaging; extent of local invasion

Is the patient fit for surgery?

- Comorbidities, psychosocial fitness; team consensus

Multiple studies confirm superior survival with R0/R1 surgery, with or without post-op treatment



Evaluate Surgical Options: Surgical Decision-Making

Palliative Surgery

- Impending airway compromise, pain, bulky disease
- Consider for patients with low-volume metastatic disease

Prophylactic tracheostomy not recommended;

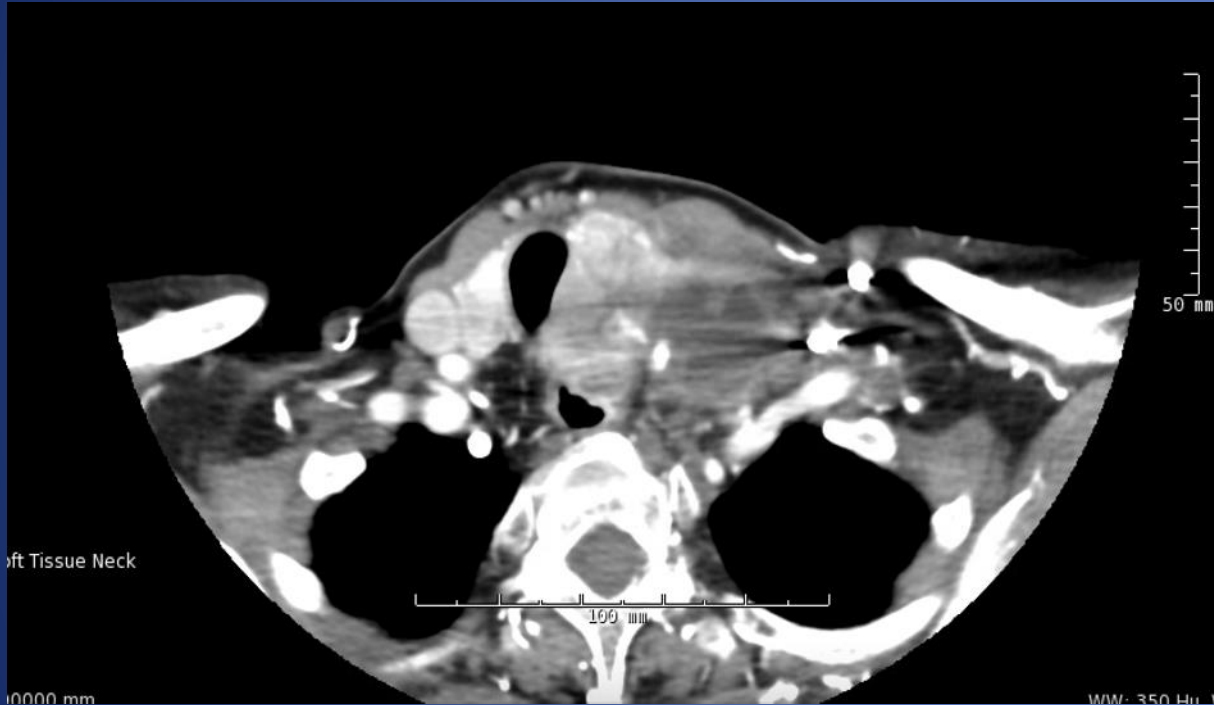
- Associated with decreased survival perhaps due to aggressive disease or by delaying radiation

Debulking surgery is not recommended

TABLE I.
Resectability Criteria and Surgical Patient Selection.

1. Disease is loco-regionally confined without distant metastasis.
 2. The extent of local invasion of nearby structures has been defined and does not involve extensive laryngeal, tracheal, esophageal, or vascular structures
 3. The deep neck musculature is not involved
 4. R0/R1 resectability is expected
 5. Patient is fit for surgery with acceptable risk
 6. Patient is competent to make decisions. Surrogate decisions makers should be involved as needed
 7. Patient's goals of care, code status, advanced directives, and healthcare proxies have been defined
 8. Postoperative recovery time allows for adjuvant therapies as needed (chemoradiation, immunotherapy).
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Non-surgical management decision making



Early use of radiotherapy in patients with IVA and IVB disease ATC is advised.

Systemic concomitant chemotherapy is considered

Targeted therapy, esp for BRAF-mutated

Multimodality therapy associated with improved survival

Non-surgical management decision making

- Patients with unresectable but nonmetastatic disease who have a good performance status and who wish an aggressive approach should be offered standard fractionation IMRT plus systemic therapy
- Alternatively in BRAF-mutated ATC, combined BRAF/MEK inhibitors

If there is a response after systemic or targeted therapy, surgery can be reconsidered.

Non-surgical management decision making

Systemic approaches to unresectable and/or metastatic disease

- Early use of systemic therapy and/or radiotherapy; bridging cytotoxic therapy while awaiting molecular testing

Targeted Approaches for BRAF-mutated

- BRAF/MEK (protein kinase) inhibitor combination
- Dabrafenib/trametinib
- Surgical resection following favorable response can lead to prolonged survival

Non-surgical management decision making

BRAF Non-mutated

Concomitant chemoradiotherapy to maintain airway and lessen disease burden

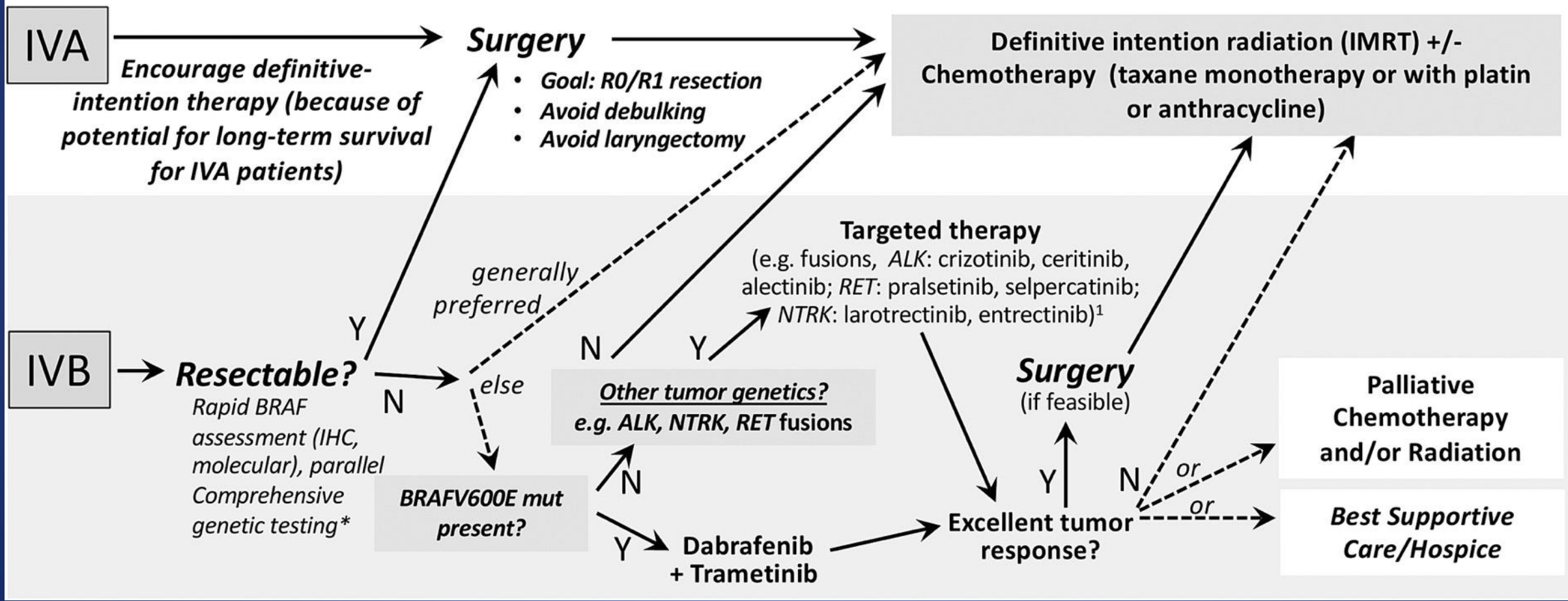
Targeted

- NTRK/RET fusion
Selpercatinib; Larotrectinib; entrectinib
- High PDL-I
Immunotherapy

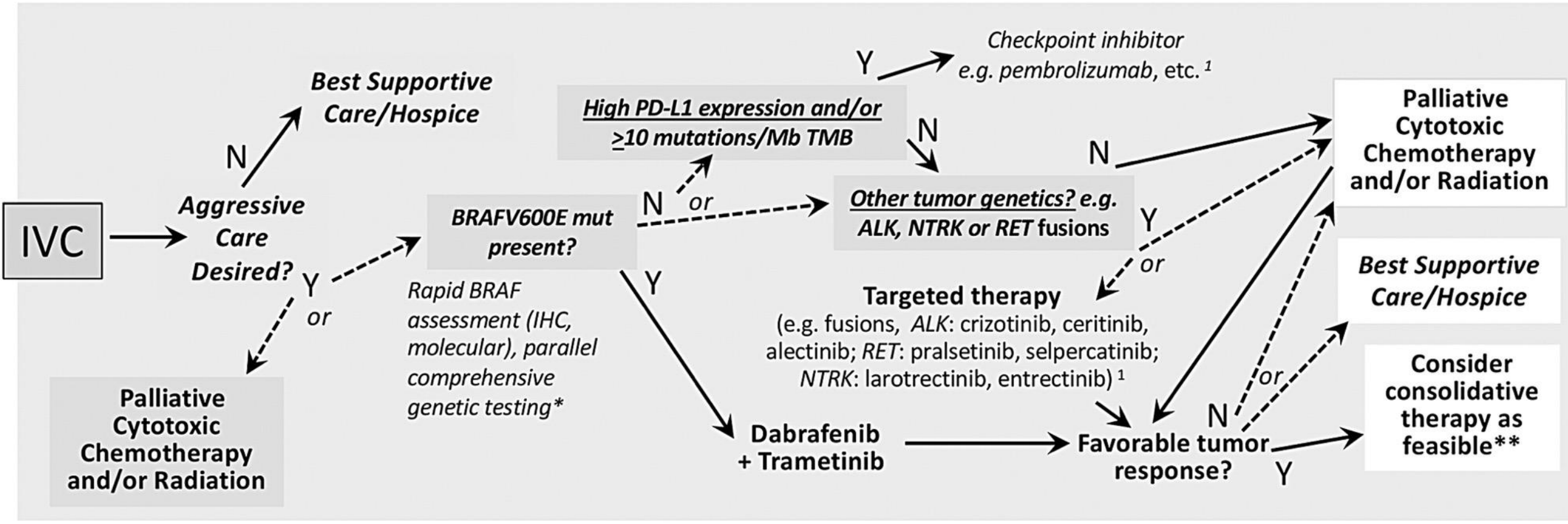
Radiation therapy for bone and brain metastatic disease

Treatment Schema and New Paradigms

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



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Survival and Health Disparities

Newer treatments associated with significantly improved survival at one year: 80% with ten months of DT vs 20-40%

- NCDB 1998-2012 ATC (Glaser 2016)

Private health-care insurance associated with improved chance of undergoing surgery and receiving radiation

- NCDB 2004-2020 ATC (Ginzburg 2023)

Patients from minority backgrounds less likely to undergo chemotherapy

Significant increase HR of death (1.13) for minority race

Less likely to be treated at high volume hospitals

Multifactorial challenge and access to care



