Il carcinoma anaplastico della tiroide: stadiazione pre-trattamento

Massimo Torlontano

San Giovanni Rotondo

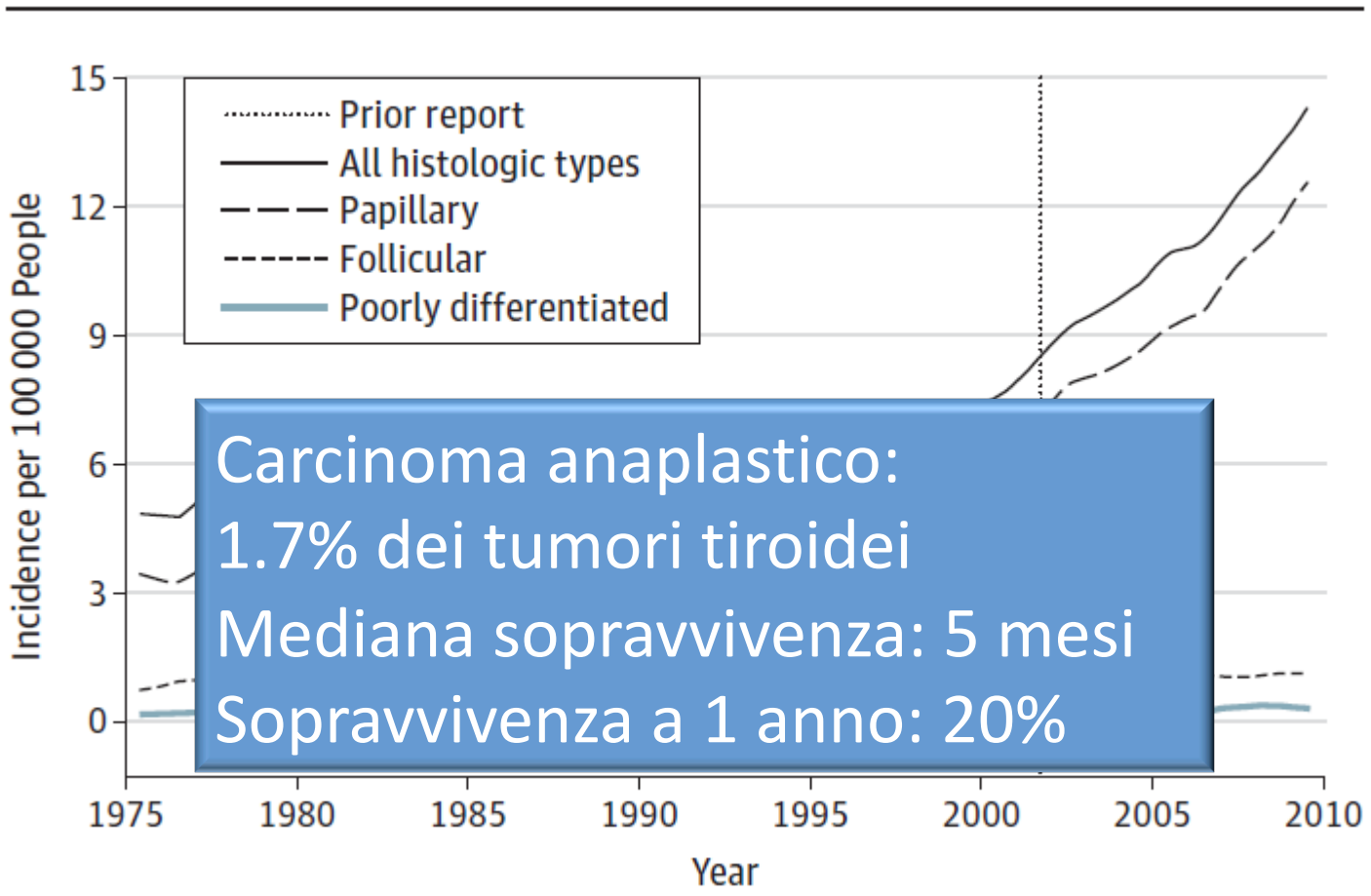
16° Congresso Nazionale AME

Joint Meeting with AACE Italian Chapter

Update in Endocrinologia Clinica

Roma, 9 - 12 novembre 2017

Incidenza crescente dei tumori tiroidei



Davies, 2006, 2014

Differentiated and anaplastic thyroid carcinoma TNM staging AJCC UICC 2017

Primary tumor (T)	
Papillary, follicular, poorly differentiated, Hurthle cell and anaplastic thyroid carcinoma	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤1 cm in greatest dimension limited to the thyroid
T1b	Tumor >1 cm but ≤2 cm in greatest dimension limited to the thyroid
T2	Tumor >2 cm but ≤4 cm in greatest dimension limited to the thyroid
T3	Tumor >4 cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a	Tumor >4 cm limited to the thyroid
T3b	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing the carotid artery or mediastinal vessels from a tumor of any size
NOTE: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No evidence of locoregional lymph node metastasis
N0a	One or more cytologically or histologically confirmed benign lymph nodes
N0b	No radiologic or clinical evidence of locoregional lymph node metastasis
N1	Metastasis to regional nodes
N1a	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes
Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis

Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis

Prognostic stage groups

Differentiated

When age at diagnosis is...	And T is...	And N is...	And M is...	Then the stage group is...
<55 years	Any T	Any N	M0	I
<55 years	Any T	Any N	M1	II
≥55 years	T1	N0/NX	M0	I
≥55 years	T1	N1	M0	II
≥55 years	T2	N0/NX	M0	I
≥55 years	T2	N1	M0	II
≥55 years	T3a/T3b	Any N	M0	II
≥55 years	T4a	Any N	M0	III
≥55 years	T4b	Any N	M0	IVA
≥55 years	Any T	Any N	M1	IVB

Anaplastic

When T is...	And N is...	And M is...	Then the stage group is...
T1-T3a	N0/NX	M0	IVA
T1-T3a	N1	M0	IVB
T3b	Any N	M0	IVB
T4	Any N	M0	IVB
Any T	Any N	M1	IVC

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

IVA: tumore intra-tiroideo: indicazione chirurgica
IVB: sviluppo extra-tiroideo e/o metastasi linfonodali: no chirurgia
IVC: metastasi a distanza

THYROID
Volume 22, Number 11, 2012

DOI: 10.1089/thy.2012.0302

American Thyroid Association Guidelines for Management of Patients with Anaplastic Thyroid Cancer

Robert C. Smallridge,[1,*] Kenneth B. Ain,[2,3] Sylvia L. Asa,[4,5] Keith C. Bible,[6] James D. Brierley,[4,5] Kenneth D. Burman,[7] Electron Kebebew,[8] Nancy Y. Lee,[9] Yuri E. Nikiforov,[10] M. Sara Rosenthal,[11] Manisha H. Shah,[12] Ashok R. Shaha,[9] and R. Michael Tuttle[9]

for the American Thyroid Association Anaplastic Thyroid Cancer Guidelines Taskforce

Imaging

- Estensione della malattia
- Pianificazione terapia
- Valutazione risposta al trattamento

ATA Guidelines 2012

Valutazione morfologica (raccomandazioni ATA)

- ETG collo
- ^{18}F-FDG-PET
- TAC collo-mediastino-torace-(addome)
- RMN o TAC cerebrale
- (Rx segmenti scheletrici)
- (Scintigrafia ossea)

ATA Guidelines 2012

Vie aeree superiori

- Visita ORL + tracheoscopia !!!

Airway and vocal cord assessment. Vocal cord paralysis is quite common in patients with ATC, as compared with those with well-differentiated thyroid cancer. Because of the rapid increase in tumor size, the patient may present with obvious hoarseness of voice, raising the question of vocal cord mobility. The best way to evaluate vocal cord mobility is laryngeal evaluation, which can easily be performed in the office with mirror or fiber optic laryngoscopy. Most patients will present with one paralyzed vocal cord and an adequate airway. The endolaryngeal mucosa is generally normal. The fiber optic laryngoscopy will also help to evaluate whether there is direct involvement of the tumor, either in the larynx or the upper trachea. In patients with airway invasion on laryngoscopy, a bronchoscopy to evaluate the trachea is helpful to determine extent of disease and resectability.

(Strong recommendation)

ATA Guidelines 2012

Stadiazione e priorità di terapia

Staging and order of therapies. In the context of a rapidly growing neck mass that may compromise the airway and cause

In oltre 80% dei casi ampiamente invasivo:

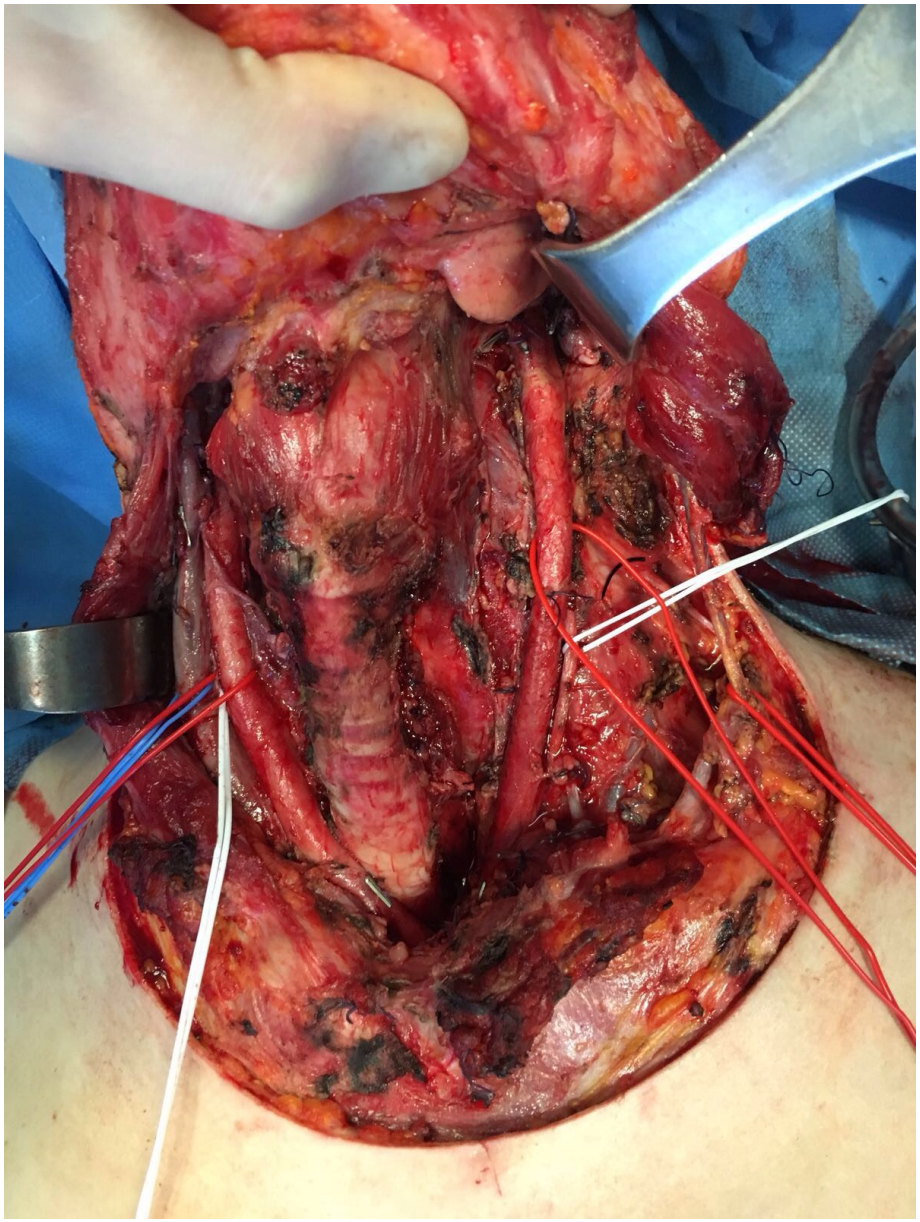
- ✓ Trachea 69%
- ✓ Esofago 55%
- ✓ A. carotide 39%

Il termine *«inoperabile» varia a seconda dell'operatore*

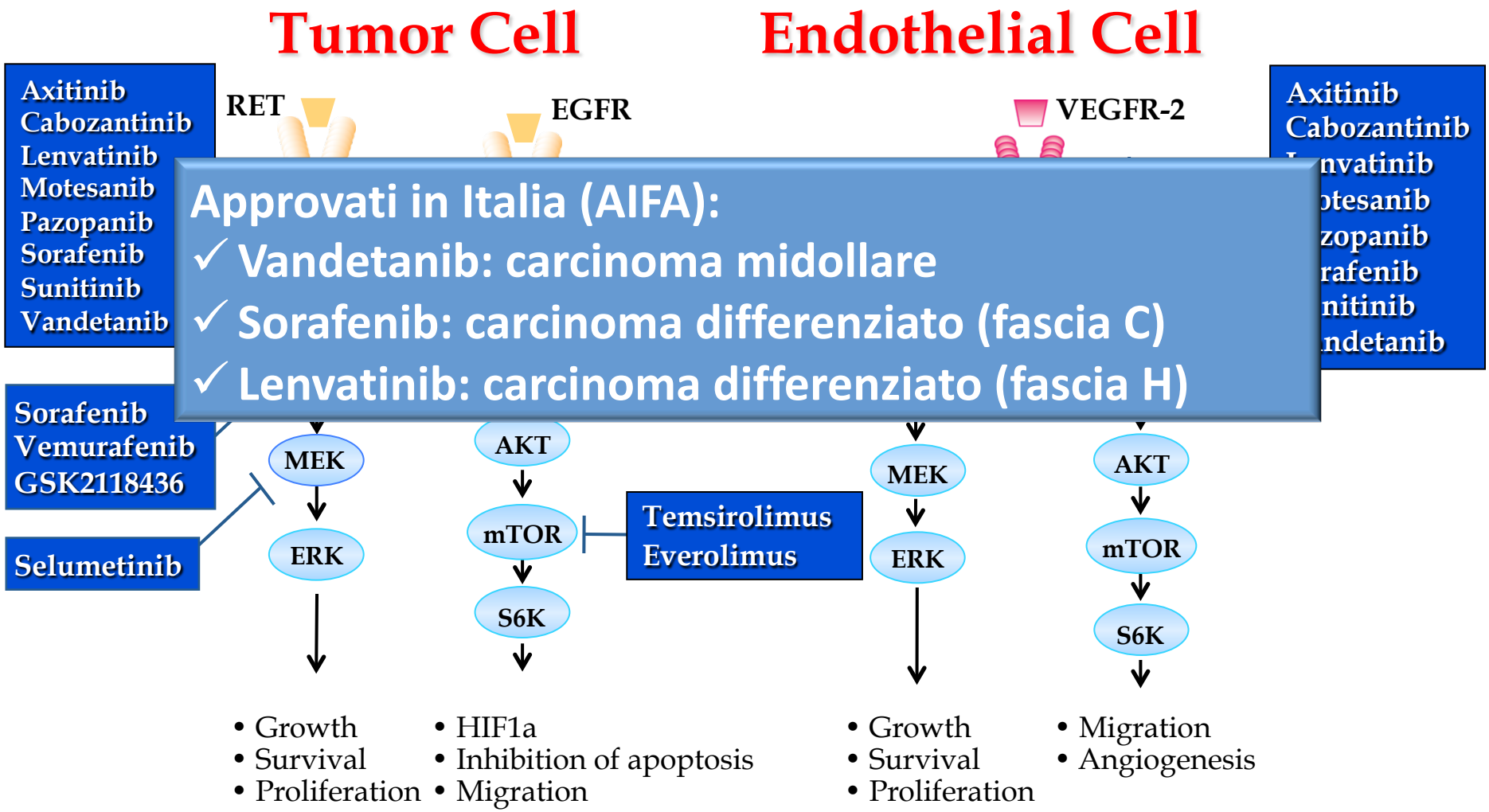
of spine metastases or pulmonary hemorrhage) should prevent primary surgical management of neck disease if achievable.

Strength of Recommendation: Strong
Quality of Evidence: Low

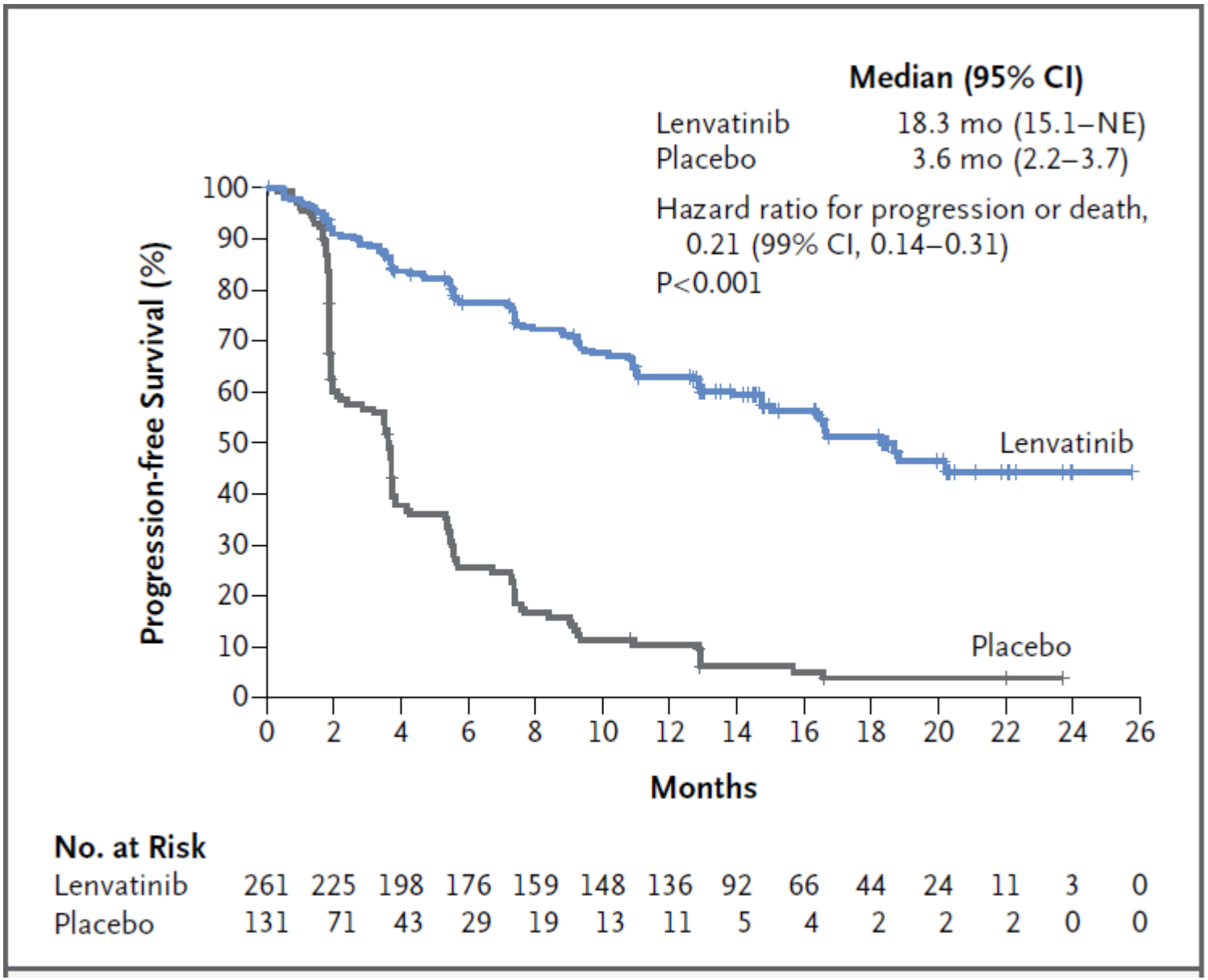
ATA Guidelines 2012



Inibitori delle tirosin-chinasi



Keefe SM, Clin Cancer Res, 2010

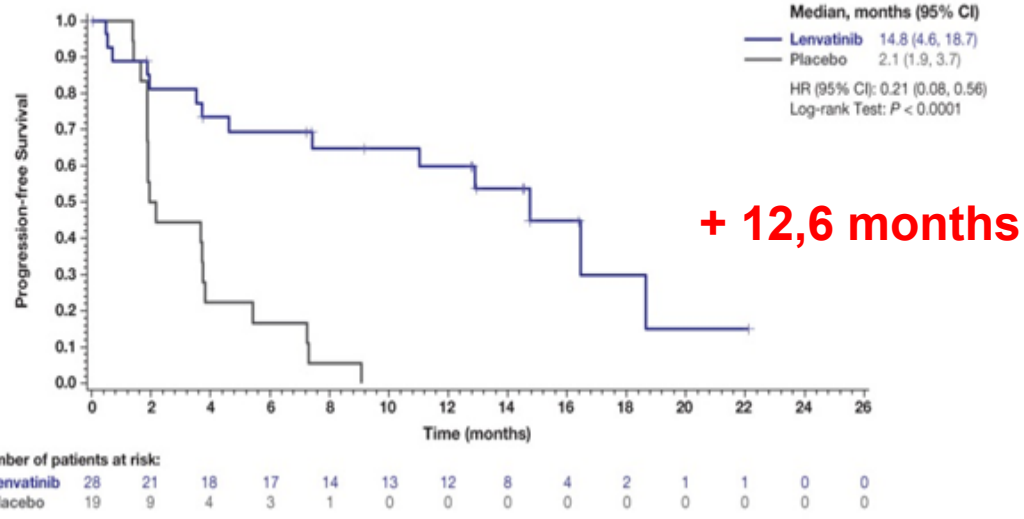


Schlumberger et al, NEJM 2015

Adverse events (AE) (all grades)	**Hypertension (69%)** **Diarrhea (59%)** **Fatigue/astenia (59%)** **Anorexia (50%)** **Weight loss (46%)** **Nausea (41%)** **Stomatitis** **Hand/foot syndr.** **Proteinuria**
Rare events	**Thromboembolism** **Hepatic, renal failure** **Gastrointestinal fistula** **Hemorrhagic stroke** **General deterioration**
Withdrawal due to AE	14% vs 2%

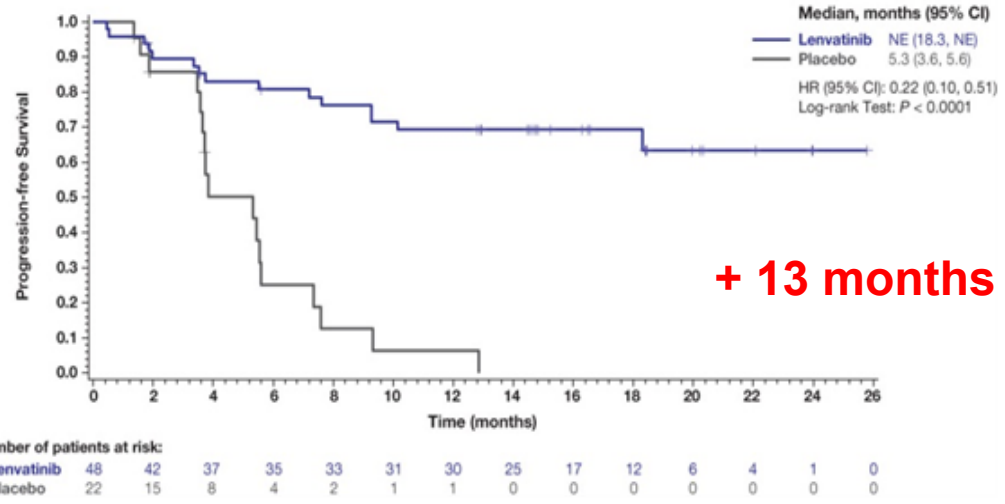
Schlumberger et al, NEJM 2015

Poorly differentiated thyroid cancer patients



+ 12,6 months

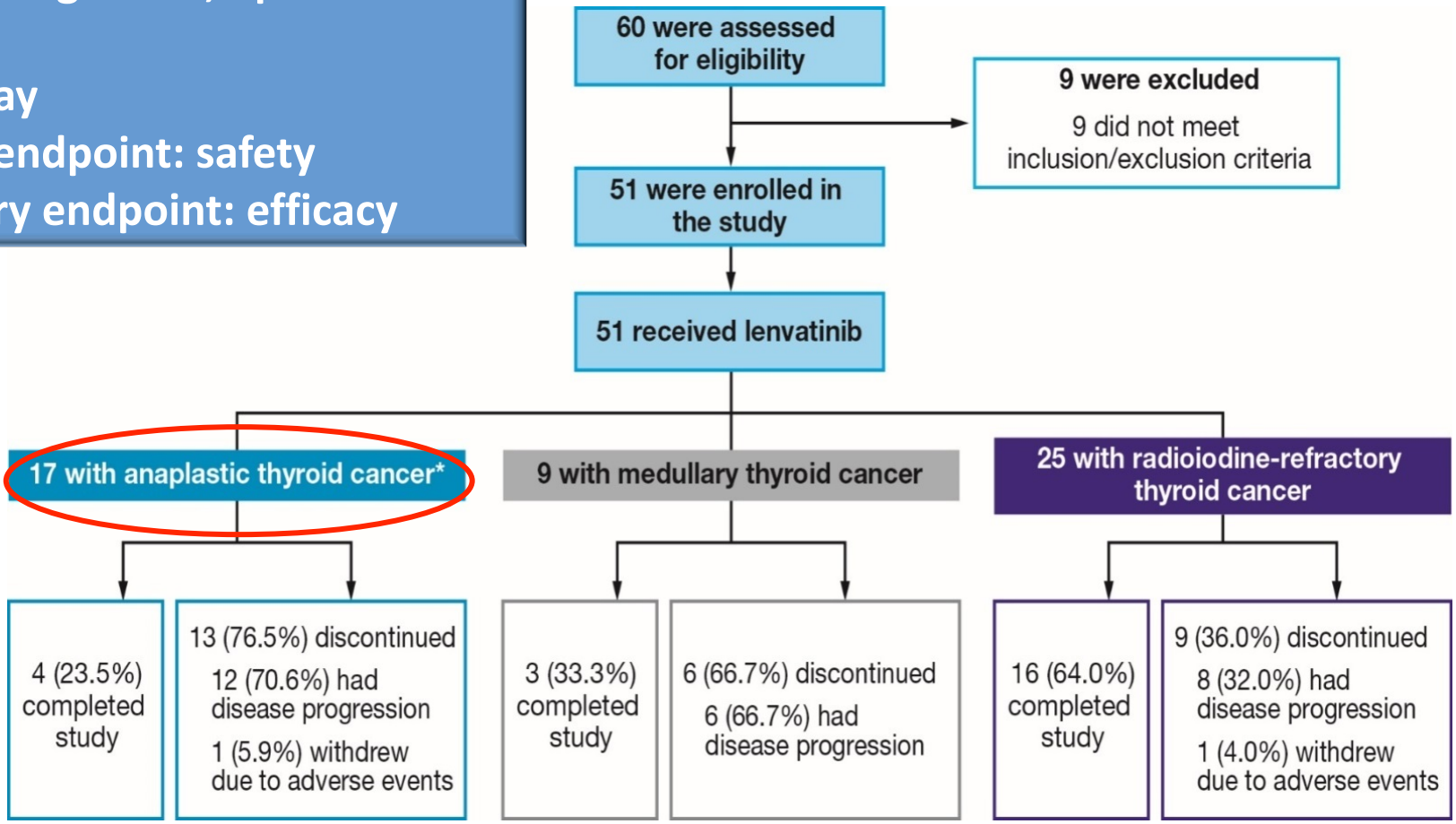
Hürthle cell carcinoma patients



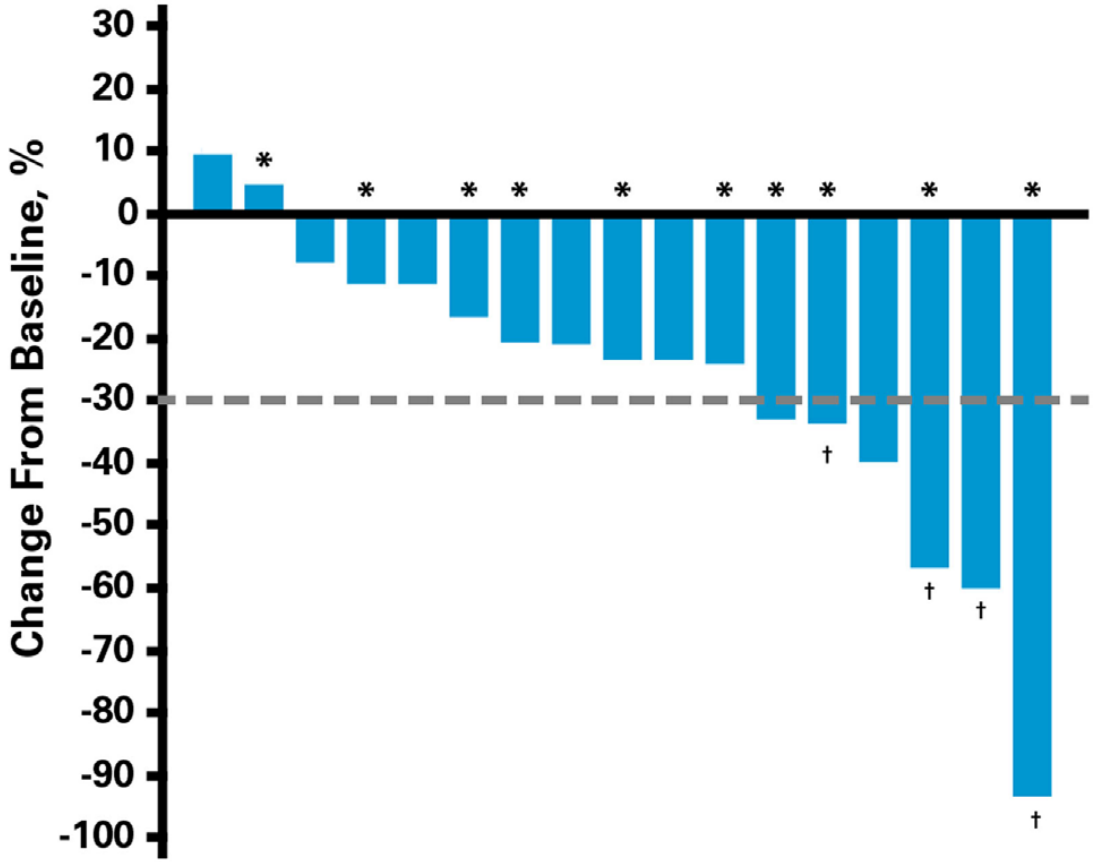
+ 13 months

Schlumberger et al, NEJM 2015

Phase 2, single arm, open label study
24 mg/day
Primary endpoint: safety
Secondary endpoint: efficacy



Tahara et al, Frontiers in Oncology 2017



*Anaplastic thyroid cancer confirmed by independent pathologic review.
†Patients with partial response as best overall response.

Tahara et al, Frontiers in Oncology 2017

Outcome	*n* = 17
Progression-free survival	
Median [95% confidence interval (CI)], months	7.4 (1.7–12.9)
Overall survival	
Median (95% CI), months	10.6 (3.8–19.8)
Be	
Not evaluable	0
Objective response rate, *n* (%)[b]	4 (24)
Disease control rate, *n* (%)[b]	16 (94)
Clinical benefit rate, *n* (%)[c]	12 (71)

N.B.
Il farmaco è stato recentemente approvato in Giappone anche per il trattamento del carcinoma anaplastico della tiroide!!

Tahara et al, Frontiers in Oncology 2017