Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

THE MANAGEMENT OF METASTATIC DISEASE

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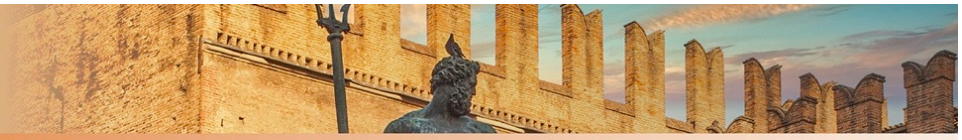


DICHIARAZIONE

Relatore: IRENE TURTURICI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Consulenza ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazione ad Advisory Board NIENTE DA DICHIARARE
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE

Differentiated thyroid cancer (DTC) accounts for 85% of all thyroid cancers and is generally an indolent tumor, cured with surgery alone or in combination with I-131 radioiodine (RAI) therapy.

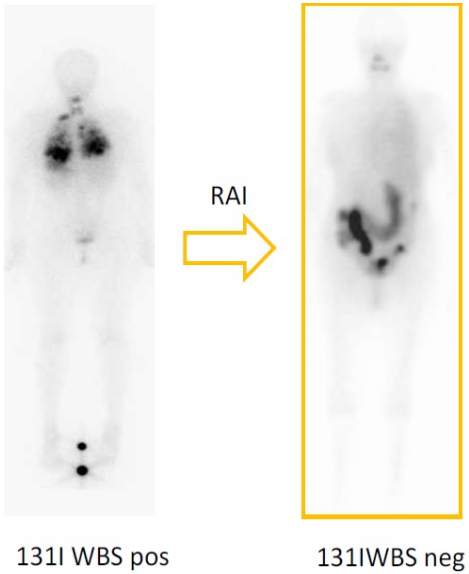
However, 10-15% of patients have advanced/metastatic disease, mainly in lung and bone.

Main prognostic factors after metastases
- age
- iodine-131 or 18F-FDG uptake
- histologic sub-type
- tumor burden at diagnosis
- site of metastases
- multiple organ metastases

Treatment Approch

The treatment strategy of metastatic DTC (mDTC), should be based on multiple factors
- Symptoms
- Tumour burden
- PS
- Lesion characteristics
- RAI avidity/refractoriness
- Disease progression (RECIST)

RAI-avid



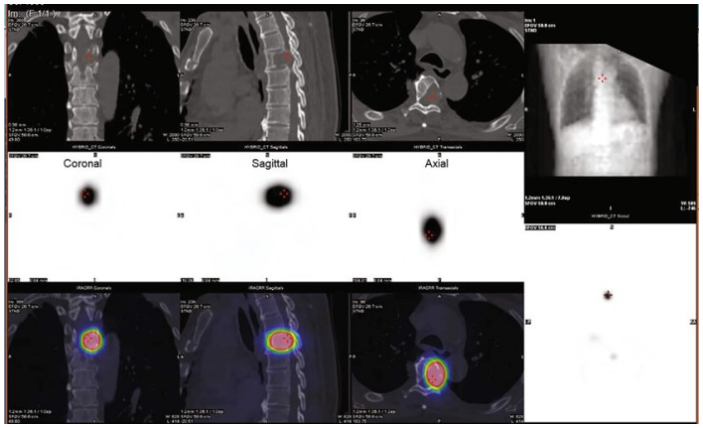
RAI therapy (150-200 mCi)

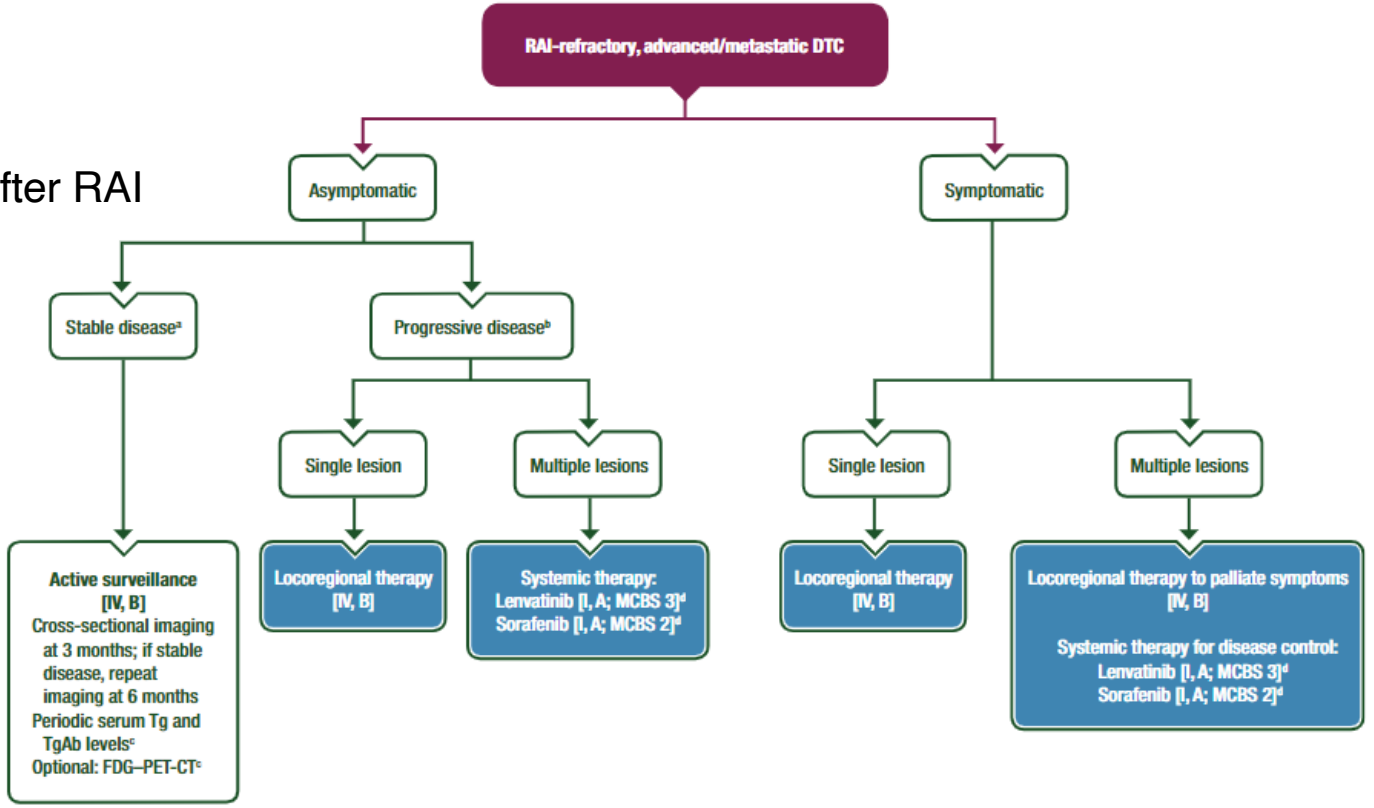
Lesions persistence after cumulative dose of 600 mCi → Multidisciplinary discuss for valuate to continue RAI therapy will be based on:
- tumour burden
- RAI-uptake intensity
- responses to previous RAI administrations

Thyroid cancer: ESMO Clinical Practice Guidelines fordiagnosis, treatment and follow-up. Filetti S. et al. Annals of Oncology 30: 1856-1883,2019 doi:10.1093/annonc/mdz400

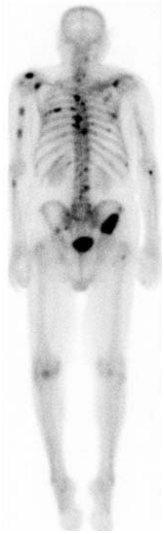
RAI-refractory

- elderly patients
- multiple and large metastases
- PET-FDG metastases uptake
- structural progression 6-12 months after RAI





Thyroid cancer: ESMO Clinical Practice Guidelines fordiagnosis, treatment and follow-up.
Filetti S. et al. Annals of Oncology 30: 1856-1883,2019 doi:10.1093/annonc/mdz400



Bone Metastases

Risk of skeletal-related events (ex. pathological fractures, spinal cord compression)

Treatment

- resorption inhibitors (bisphosphonates or denosumab), in pts with multiple bone metastases

- RAI therapy, in RAI- avid mts

- external beam radiotherapy (EBRT)

Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with uncomplicated bone metastases

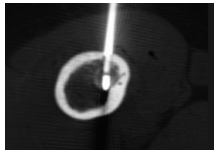
Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases

- surgery (indicated if life expectancy is longer than 3 months and there are no contraindications)

- cementoplasty and thermal ablation

- radiofrequency ablation or cryotherapy (limited evidence)



- other locoregional treatments

Lung Metastases

Usually multiple lesions, bilateral, of varying size and asymptomatic.

Treatment

- Metastasectomy is not the standard approach, but it may be considered for oligometastasis in pts with good performance status

- STR or Radiofrequency ablation, for solitary lesions or those causing a specific symptom

Published in final edited form as:
Eur J Cardiothorac Surg. 2009 July ; 36(1): 155–158. doi:10.1016/j.ejcts.2008.12.055.

Thoracic metastasectomy for thyroid malignancies☆,☆☆

John Roland Porterfield, Stephen D. Cassivi*, Dennis A. Wigle, K. Robert Shen, Francis C. Nichols, Clive S. Grant, Mark S. Allen, and Claude Deschamps

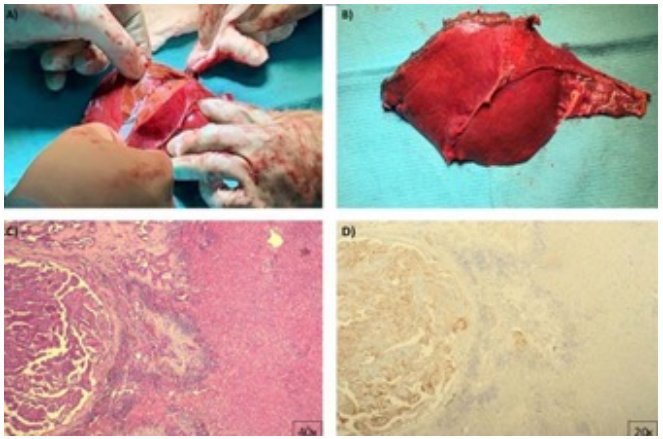
48pts
- papillary 31 (65%)
- follicular 8 (17%)
- medullary 5 (10%)
- Hürthle cell 4 (8%)

Thoracotomy in 28 pts (58%)
Sternotomy in 12 pts (25%)
Thoracoscopy in 8 pts (17%)

R0 in 33 pts (69%)
R1-R2 in 15 pts (31%)
Complication post-op in 8 pts

Median FUP 10 years
OS to 5 years = 60%

Liver Metastases



0.5% from DTC. Usually multiple lesions, candidates for local ablation in case of solitary lesions.
Individuals who are ineligible for surgery are not the best candidates for percutaneous ablation.

Treatment

- Surgery, to prevent recurrent cholangitis and reduce tumor burden

- Radiofrequency ablation → size (<30mm)
  location (3mm from all vessels)
  visibility to US

- Hepatic intra-arterial embolisation with drug-eluting beads (if surgery and RFA are contraindicated)

JSCR Journal of Surgical Case Reports

Journal of Surgical Case Reports, 2020;9, 1–4

doi: 10.1093/jscr/rjaa370
Case Report

Liver resection for metastatic thyroid carcinoma. Case report and literature review

Jesús Emiliano Sánchez-Garavito[1], Jorge Sanchez-Garcia[1], Daniel Olsen[2], Rami M. Shorti[3], Fidel Lopez-Verdugo[1] and Manuel I. Rodriguez-Davalos[1,*]

Study	Number of patients	Liver resection	RAI	TKI	Pathology diagnosis	Survival
Dinneen *et al.*	100 (1% with liver metastasis)	12% underwent surgery (not specified)	Yes (31%)	No	PTC	Overall survival rates at 5, 10 and 15 years were 37%, 24% and 20%, respectively
Hirsch *et al.*	138 (3.6% with liver metastasis)	One liver resection	Yes (96.4%)	No	PTC follicular variant (66.7%), FTC (13.8%), poorly differentiated thyroid cancer (10.9%) and intermediate-risk tumors (8.7%)	One patient with liver metastases was disease-free at last follow-up 40.6% have died during the study years, disease-specific mortality rate was 23.2%
Zunino *et al.*	36 (8% with liver metastasis)	Surgery not specified	Yes	Yes	72.2% with PTC, 27.7% with FTC	Survival in patients with liver metastases ranged from 4.75 to 28 months in patients who were not treated and those who received TKI, respectively
Madani *et al.*	492 (8% with liver metastasis)	Surgical metastasectomy	Yes	Yes (3%).	57% with PTC, 39% with FTC, four with Hürthle-cell, 43% with FTC (liver specific)	Mean overall survival after diagnosis 60 months
Farina *et al.*	103 (1% with liver metastasis)	No	Yes	Yes	PTC	6-month survival in patient with liver metastases

Brain Metastases

Rare (frequency of 0.15-1.3%) and with poor prognosis (median survival time of 4-33 months).

Treatment

- Surgical resection (associated with better outcomes)
- Stereotactic radiosurgery
- Radiotherapy

European Thyroid JOURNAL | J Yoo *et al.* | 11:5 | e220087

RESEARCH

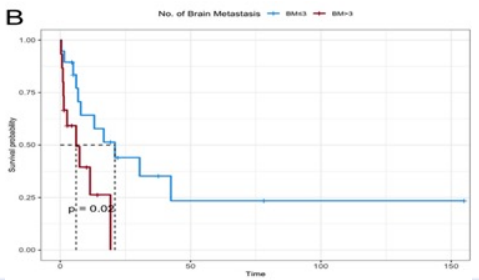
Prognostic factors to predict the efficacy of surgical interventions against brain metastasis secondary to thyroid cancer

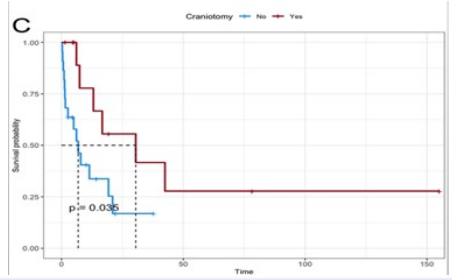
Jihwan Yoo[1,2,*], Hee Jun Kim[3,*], Seok Mo Kim[4] and Hun Ho Park[1]

34pts

Median OS 11.4 months

Craniotomies indicated a survival benefit only when the number of brain metastases was ≤3.



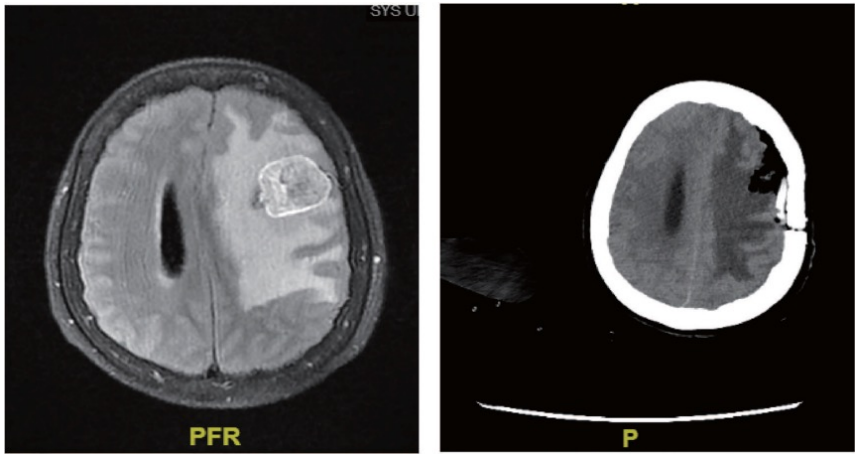


frontiers in Endocrinology

ORIGINAL RESEARCH
published: 16 September 2021
doi: 10.3389/fendo.2021.730025

Brain Metastases From Differentiated Thyroid Carcinoma: A Retrospective Study of 22 Patients

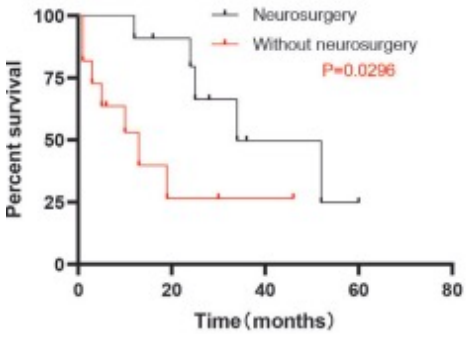
*Tong Wu, Zan Jiao, Yixuan Li, Jin Peng, Fan Yao, Weichao Chen and Ankui Yang**

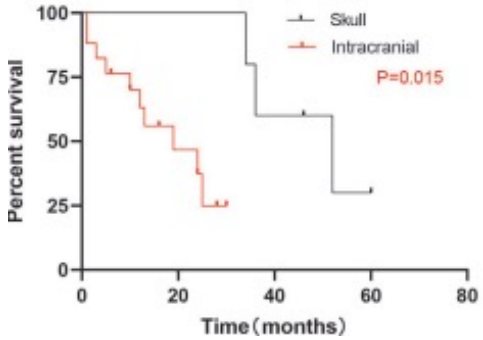


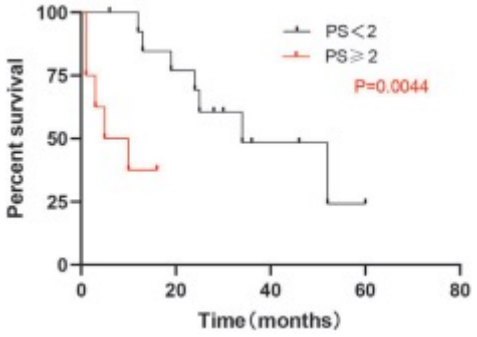
22pts → Brain metastasectomy 11 pts
SRS 4 pts

Median OS 17.5 months

Performance statue (PS), tumor site and neurosurgery impacted survival.







Systemic therapy

Treatment timing

- Treatment should be initiated when patients are still in good general condition to take full advantage of its efficacy.
- Should be continued until the disease progresses, unacceptable toxicities occur or the patient asks to stop treatment.
- In the presence of single-site progression, locoregional treatment can be done for local control, without discontinuing systemic therapy.

First Line

Lenvatinib: inibitor of VEGFR, FGFR, RET, c-KIT and PDGFR

Sorafenib: inibitor of VEGFR, PDGFR, FGFR, RET, c-KIT and BRAF

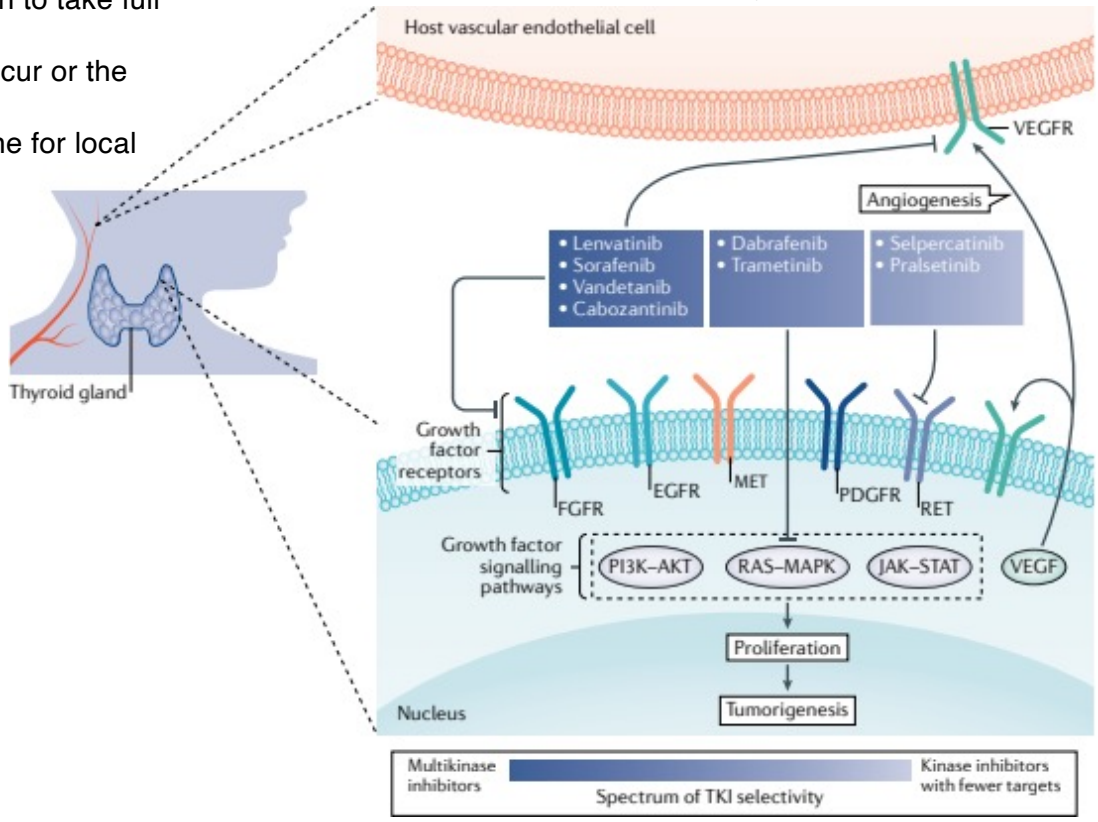
Second Line

Cabozantinib: inibitor of MET, RET, AXL, VEGFR2, FLT3 and c-KIT

Larotrectinib
Entrectinib
} NTRK fusion

Selpercatinib
Pralsetinib
} RET mutation/fusion

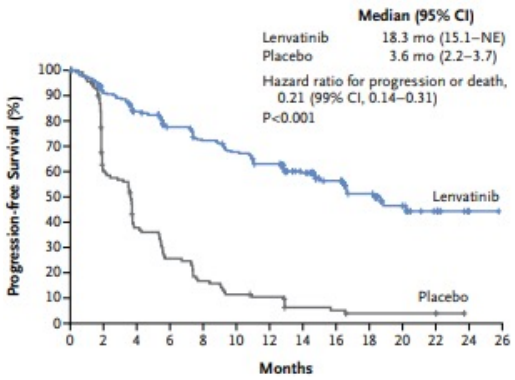
Multikinase inhibitors in thyroid cancer: timing of targeted therapy
Gildi et al. Nat Rev Endocrinol. 2021 Apr;17(4):225-234.
doi: 10.1038/s41574-020-00465-y. Epub 2021 Feb 18.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenvatinib versus Placebo in Radioiodine-Refractory Thyroid Cancer



SELECT trial phase III
(double-blind study)

392pts → Lenvatinib (n = 261)
Placebo (n = 131)

Results
- Better PFS with lenvatinib (18.3 mo vs 3.6)
- Responses to lenvatinib in 64.8% pts vs 1.5%

The Oncologist, 2022, **27**, 565–572
https://doi.org/10.1093/oncolo/oyac065
Advance access publication 28 April 2022
Review Article

OXFORD

Lenvatinib for the Treatment of Radioiodine-Refractory Differentiated Thyroid Cancer: Treatment Optimization for Maximum Clinical Benefit

Lori J. Wirth[1,*], Cosimo Durante[2], Duncan J. Topliss[3], Eric Winquist[4], Eyal Robenshtok[5], Hiroyuki Iwasaki[6], Markus Luster[7], Rossella Elisei[8], Sophie Leboulleux[9], Makoto Tahara[10]

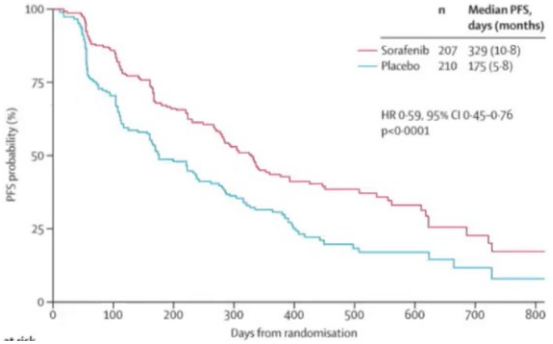
Low disease burden → early onset of Lenvatinib

Dose of lenvatinib 24 mg/day better outcomes respect to 18 mg/day.

Timely identification of adverse events, (ex. diarrhea, hypertension, proteinuria and decreased appetite), to avoid longer dose interruptions, and maximize efficacy.

Published in final edited form as:
Lancet. 2014 July 26; 384(9940): 319–328. doi:10.1016/S0140-6736(14)60421-9.

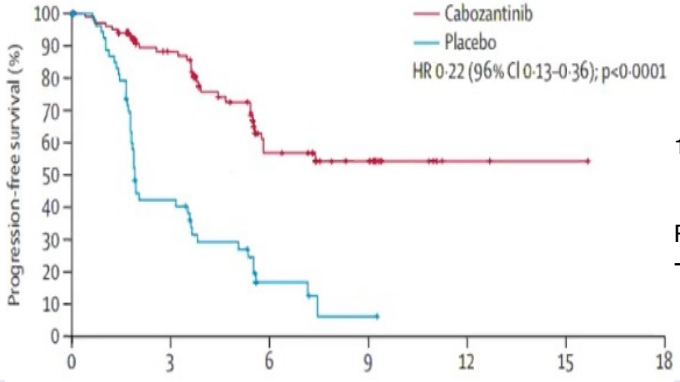
Sorafenib in locally advanced or metastatic, radioactive iodine-refractory, differentiated thyroid cancer: a randomized, double-blind, phase 3 trial



417pts → Sorafenib (n = 207)
Placebo (n = 210)

Results
- Better PFS with Sorafenib (10.8 mo vs 5.8)
- Parzial response to Sorafenib (12% vs 0.5%)
- Stable disease (42% vs 33%)

Cabozantinib for radioiodine-refractory differentiated thyroid cancer (COSMIC-311): a randomised, double-blind, placebo-controlled, phase 3 trial



187pts → Cabozantinib (n = 125)
Placebo (n = 62)

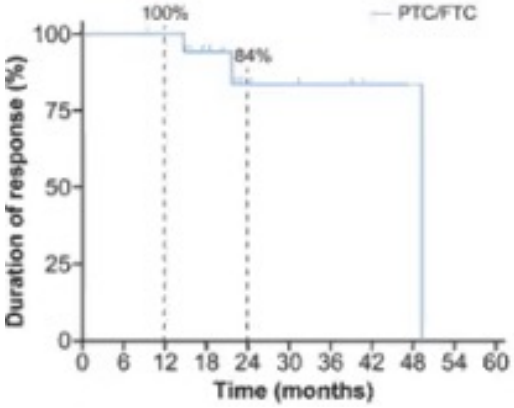
Results
- Better PFS with Cabozantinib

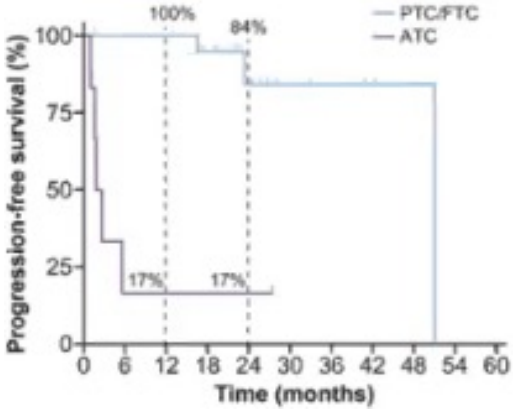
Clinical Study | S G Waguespack and others | Larotrectinib for TRK fusion thyroid carcinoma | 186:6 | 631–643

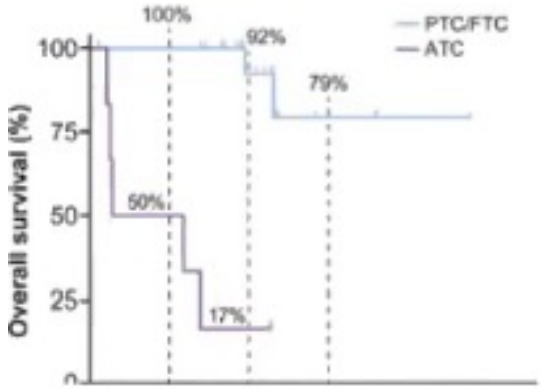
Efficacy and safety of larotrectinib in patients with TRK fusion-positive thyroid carcinoma

28pts → papillary 20 (69%)
→ follicular 2 (7%)
→ anaplastic 7 (24%)

Results
- complete response 2 (7%)
- parzial response 18 (64%)
- stable disease 4 (14%)
- progressive disease 3(11%)
- objective response rate → 86% for PTC/FTC
  → 29% for ATC







Take home message

Muldisciplinary assessment is mandatory to define the timing of therapy.

Local therapies need to be considered in the management of mDTC alone or in combination with systemic agents.

The choice of local treatment should consider the extent of disease, the expected results and toxicity and the prognosis of patients.

Contact

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