

New Treatment Strategies for Advanced Thyroid Cancer (DTC and ATC)

**Sociedad Puertorriqueña de Endocrinología y Diabetología
(SPED)**

May 22, 2021

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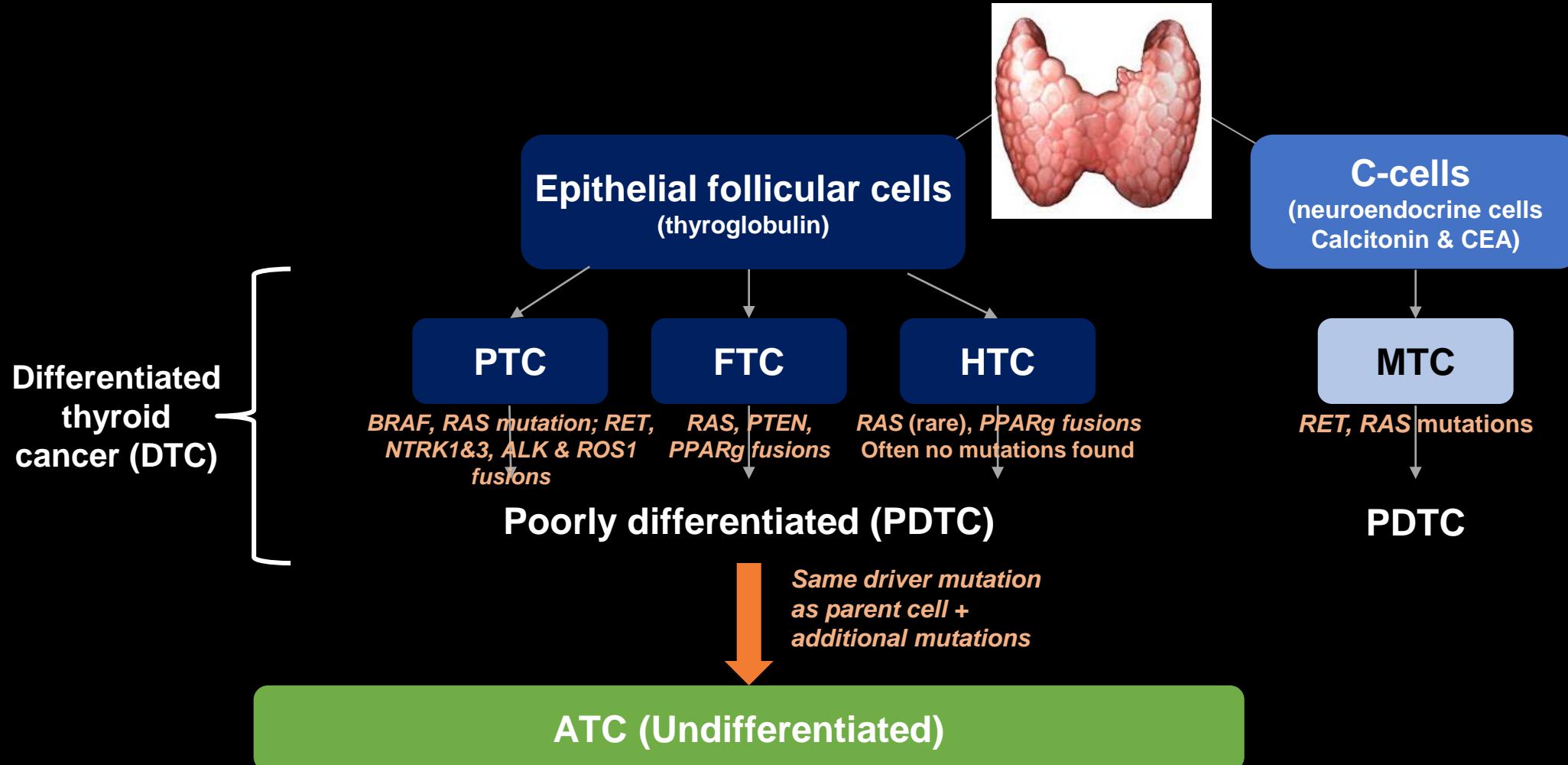
**The University of Texas MD Anderson Cancer Center
Houston, Texas, USA**

Conflictos de intereses

Grant funding: Eisai, Exelixis, Genentech, Merck and Kura

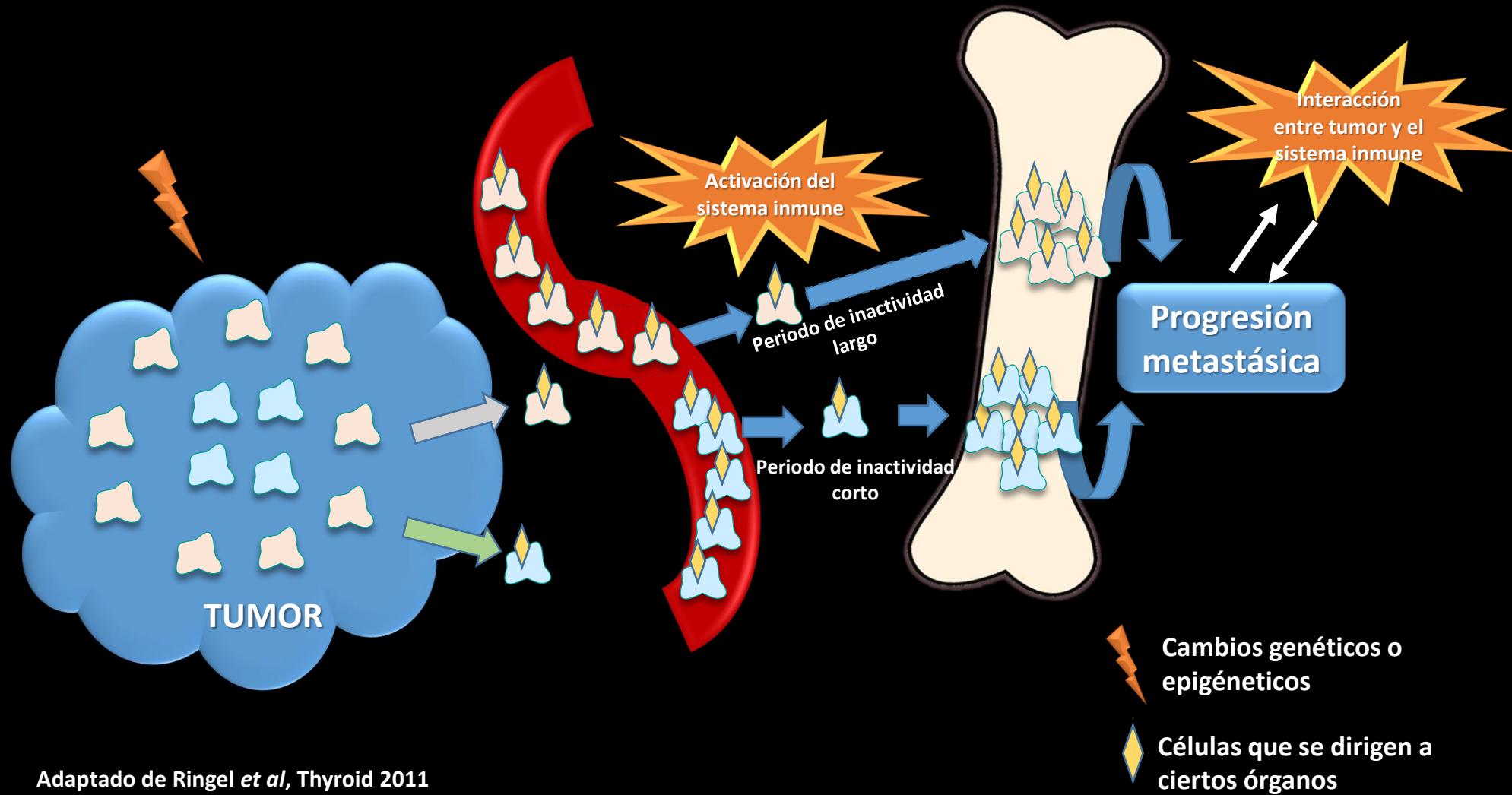
Advisory boards: Exelixis, Blueprint, Ignyta, Bayer and LOXO

Origen del cáncer de tiroides

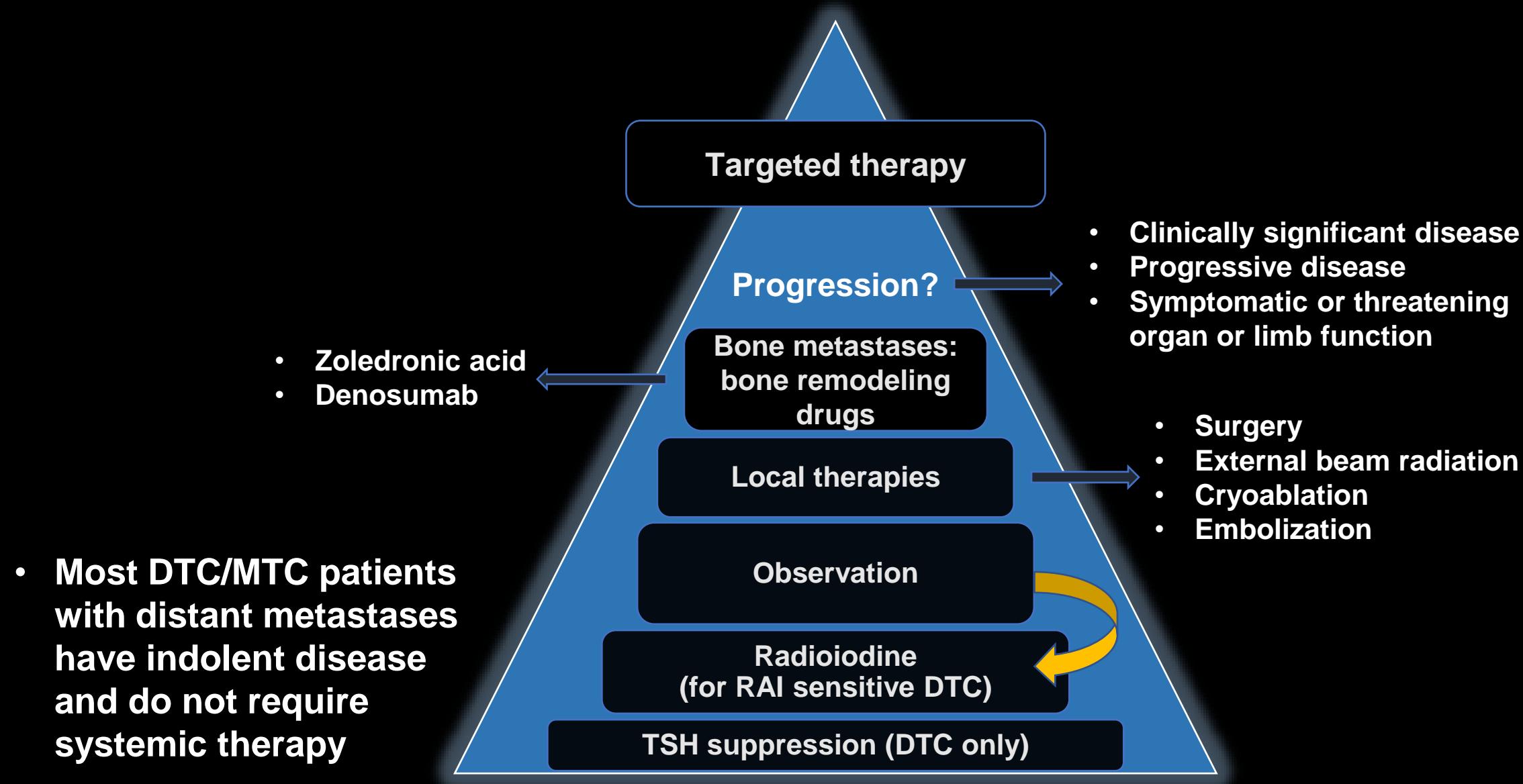


PTC=papillary thyroid cancer; FTC=follicular thyroid cancer; HTC=Hürthle cell thyroid cancer; PDTC=poorly differentiated thyroid cancer;
ATC=anaplastic thyroid cancer; MTC=medullary thyroid cancer

La mayoría de los canceres de tiroides (DTC/MTC) son indolentes aun cuando metastatizan

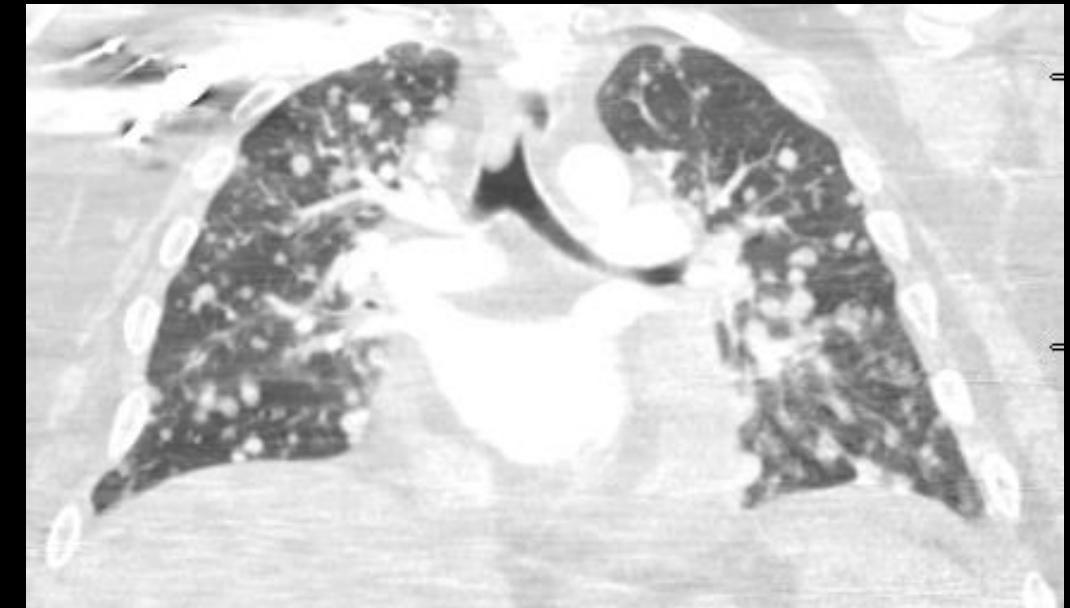


Cuando Empezar Terapias Dirigidas



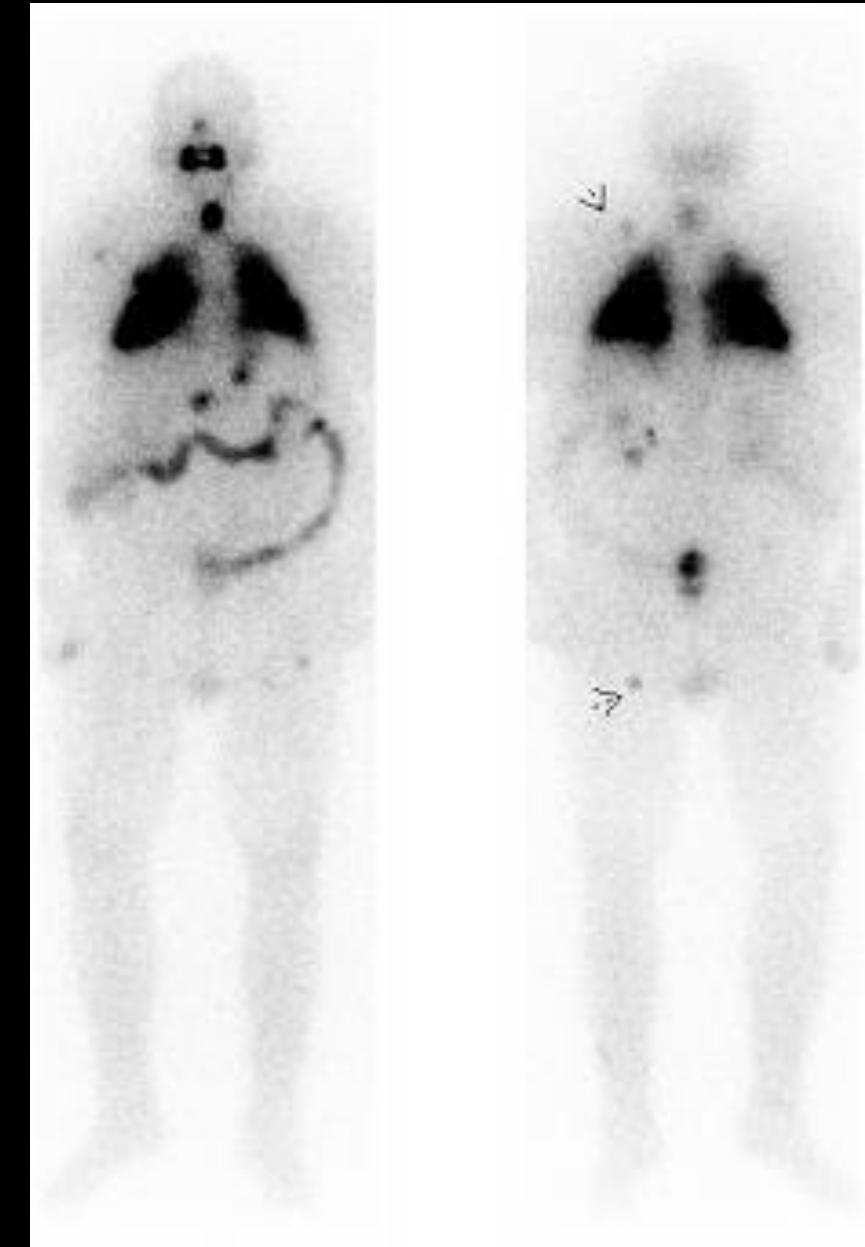
55 y.o. man with papillary thyroid cancer

- Patient presented with vocal cord paralysis and shortness of breath. CT showed large infiltrative left sided thyroid mass and bilateral adenopathy and lung metastases
 - Biopsy of thyroid and lung: papillary thyroid cancer (PTC)
 - Diabetic, obese, hypertensive, coronary artery disease
- Total thyroidectomy and bilateral neck dissection and excision of skin lesion on his face
 - Path: 4.9 cm left sided PTC with lymphovascular invasion, perineural invasion, and extension to strap muscles; 12/120 involved nodes, largest node was 2.5 cm.
 - Skin lesion confirmed to be a dermal metastasis
- Post-operative clinical information:
 - Patient requires 4 liters of oxygen by nasal canula
 - Thyroglobulin (Tg) 907 with Tg antibodies 27



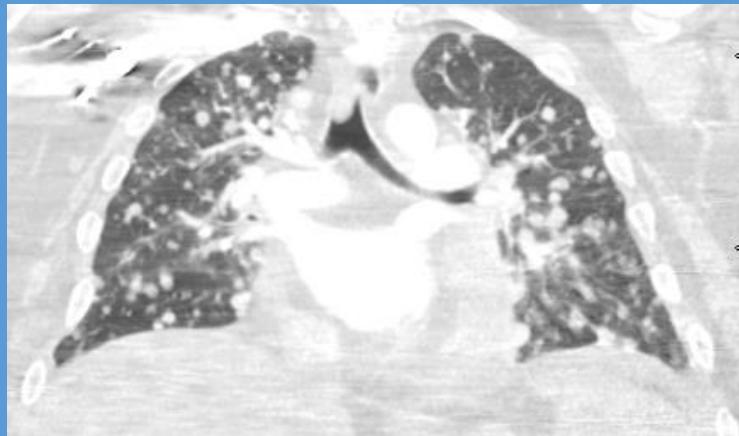
55 y.o. man with papillary thyroid cancer

- Patient given 200 mCi of I-131 with good uptake in lungs and mediastinal adenopathy. New bone mets identified (arrows; faint uptake)
- Biomarker/sequencing of lung tissue:
 - BRAF by immunohistochemistry is negative
 - Thyroidectomy specimen sent for fusions: *NCOA4-RET* fusion found

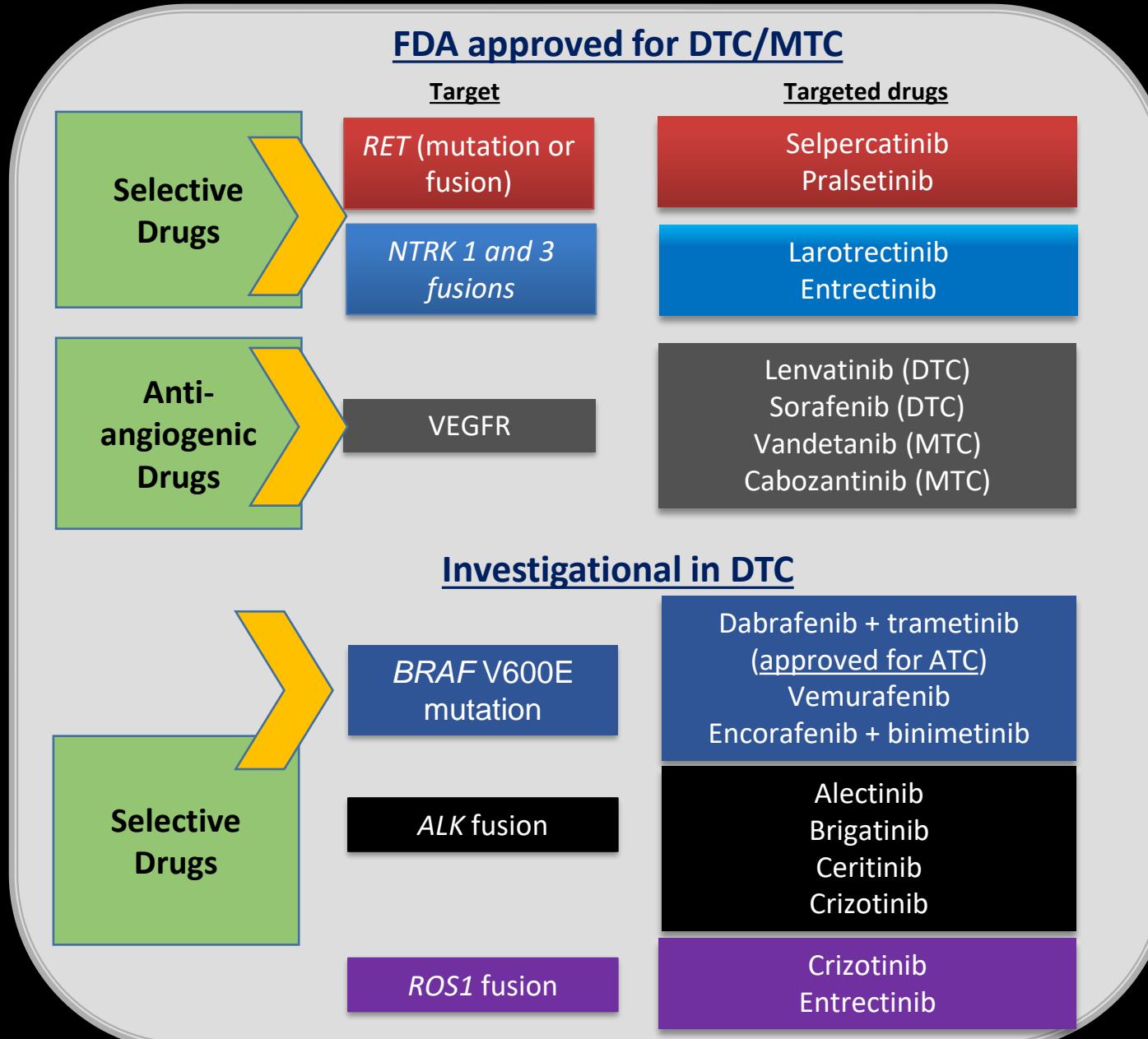


55 y.o. man with papillary thyroid cancer

- After 3 months of observation, more skin metastases appeared, and patient's oxygen requirement did not improve after RAI
→ meets criteria for systemic therapy



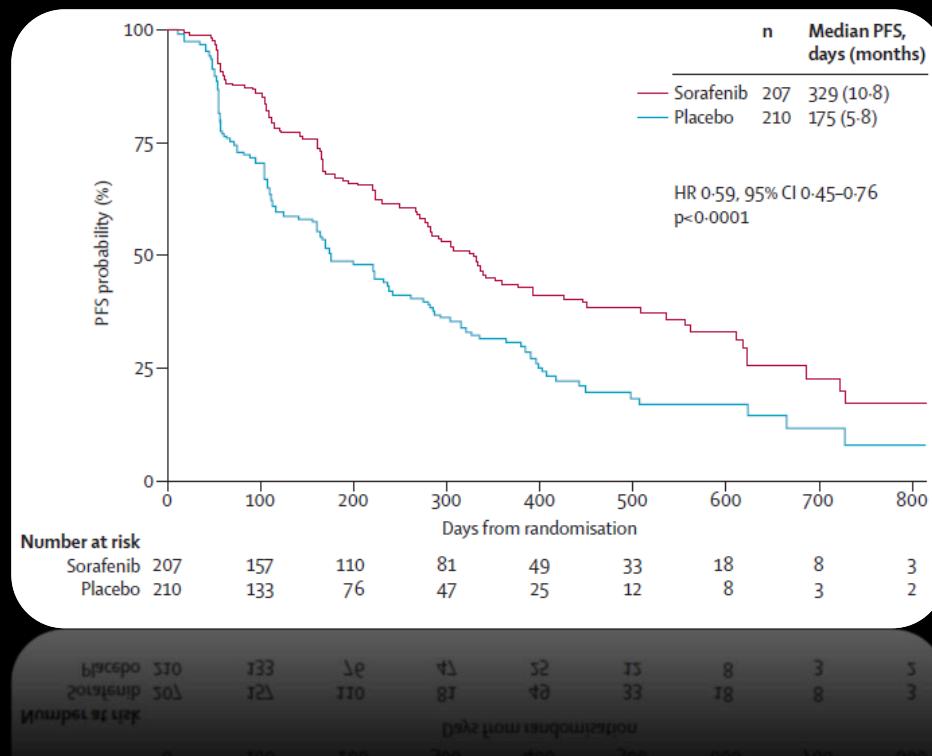
Terapias Dirigidas Para Cáncer de Tiroides



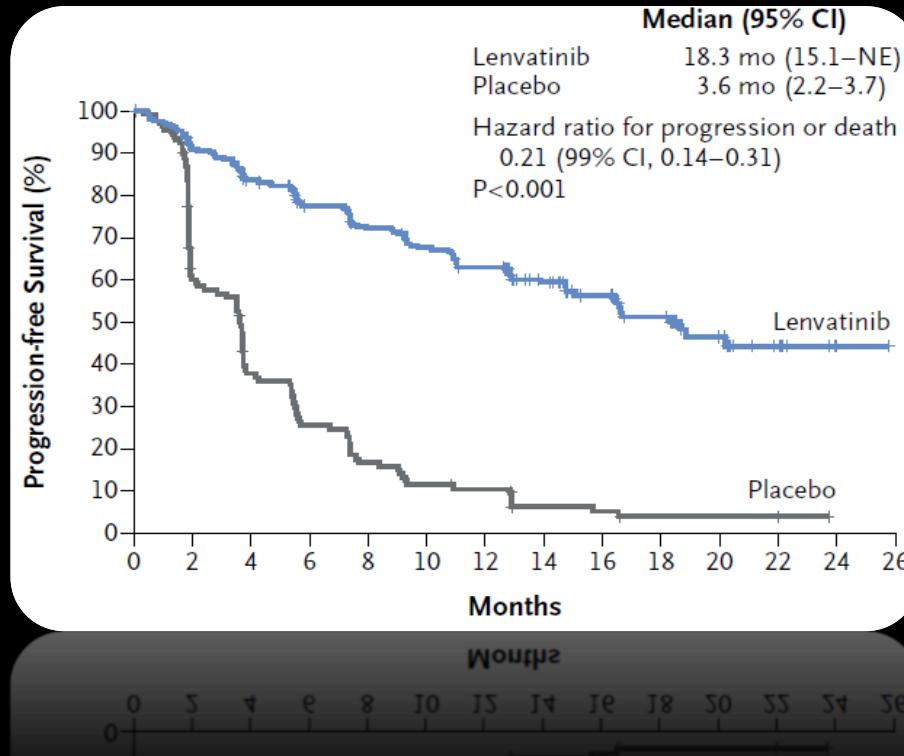
Terapias antiangiogénicas

Los inhibidores multiquinasa (anti-angiogénicos) mejoran supervivencia libre de progresión en cáncer tiroides diferenciado

Sorafenib



Lenvatinib

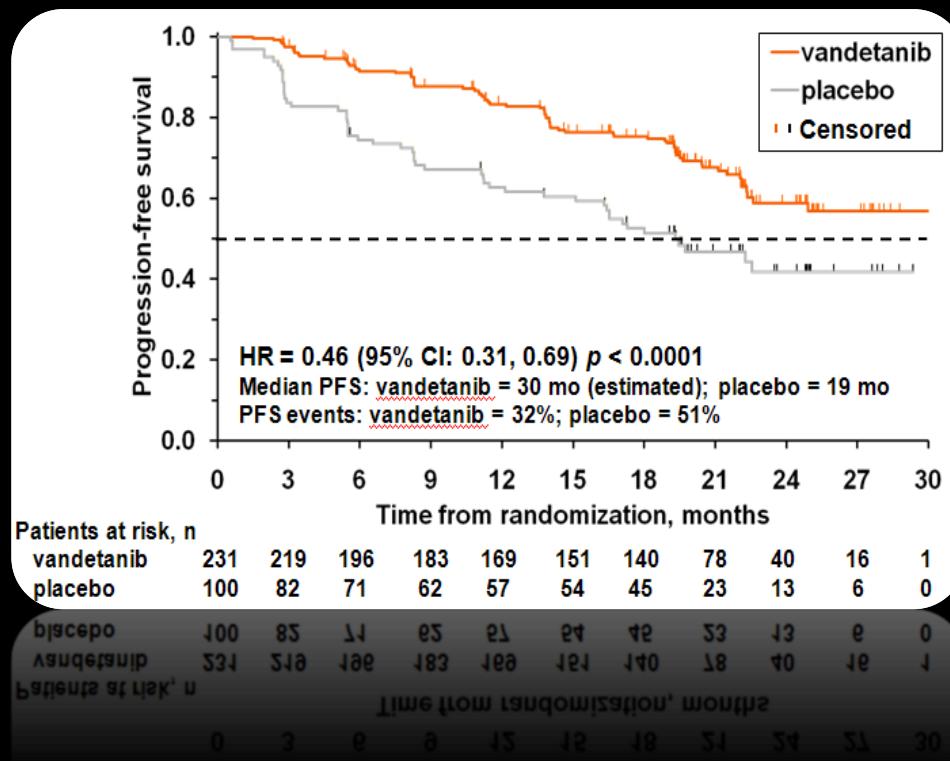


Brose, et al., Lancet Oncol 2014

Schlumberger, et al., N Engl J Med 2015

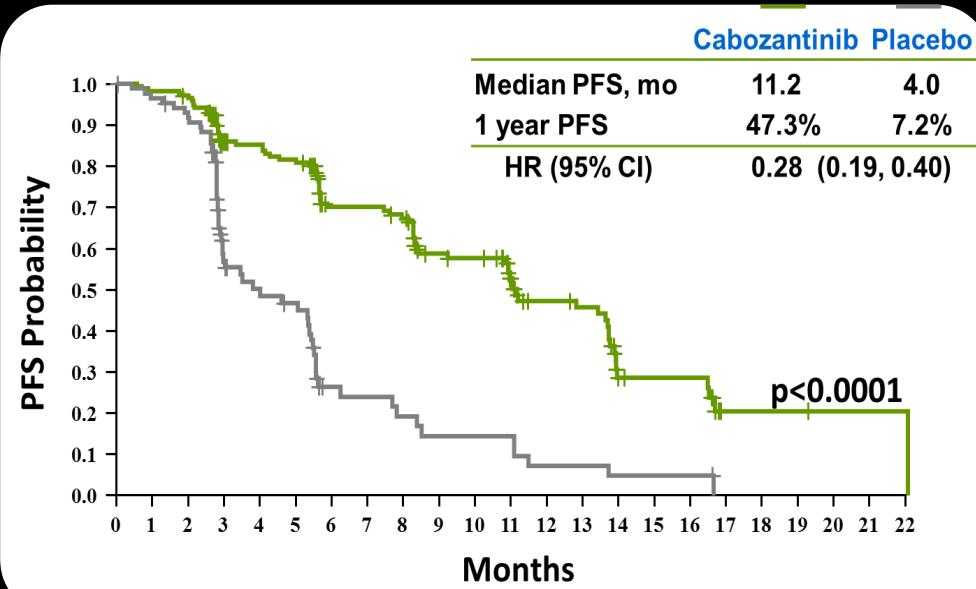
Los inhibidores multiquinasa mejoran supervivencia libre de progresión en cáncer medular

Vandetanib



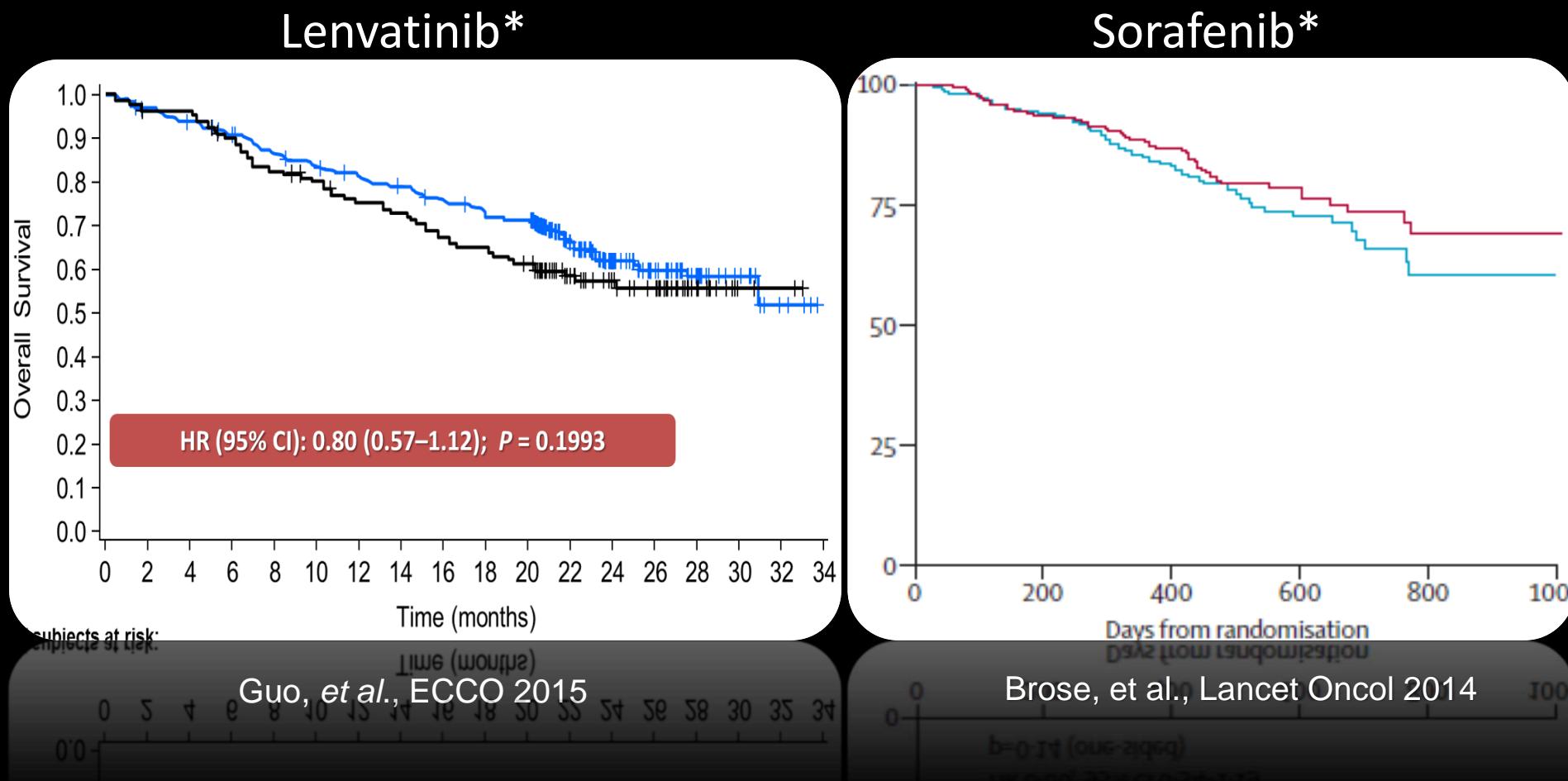
Wells, SA et al. J Clin Oncol, 2011

Cabozantinib



Elisei R et al, J Clin Oncol, 2013

¿Los inhibidores multiquinasas mejoran supervivencia global (overall survival)?



*Cancer diferenciado de tiroides

Efectos adversos



Meta-analysis data from earlier phase trials in thyroid cancer (Thomas L, Lai SY, Dong W, Feng L, Dadu R, Regone RM, Cabanillas ME, the Oncologist, 2014); Schlumberger et al, NEJM 2015

Sorafenib (overall/severe)	Lenvatinib (overall/severe)
Hand-foot (76%/20%)	Hypertension (68/42%) ←
Diarrhea (69%/6%)	Diarrhea (59/8%)
Alopecia (67%/0%)	Fatigue (59/9%)
Arthralgia/myalgia (59%/6%)	Anorexia (50%/5%)
Rash (50%/5%)	Nausea (41%/2%)
Fatigue (50%/6%)	Weight loss (46%/10%)
Weight loss (46%/6%)	Stomatitis (36%/4%)
Hypertension (41%/10%)	Hand-foot (32%/3%)
Anorexia (32%/2%)	Proteinuria (31%/10%)
Mucositis (23%/1%)	Headache (28%/3%)
Pruritus (21%/1%)	Dysphonia (24%/1%)
Nausea (20%/0%)	Arthralgia (18%/0%)
Fever (11%/1%)	Dysgeusia (17%/0%)
	Alopecia (11%/0%)

Contraindicaciones relativos a los Anti-angiogenicos

Poor cardiac function or recent MI

Uncontrollable hypertension

Large, rapidly growing tumors

History of stroke or recent surgery

Tumor-associated bleeding

ANTI-ANGIOGENICS NOT SAFE

FOR EVERYONE:

need alternatives or low doses

Hemoptysis or use of anticoagulants

Very low body weight (may be exacerbated with TKIs)





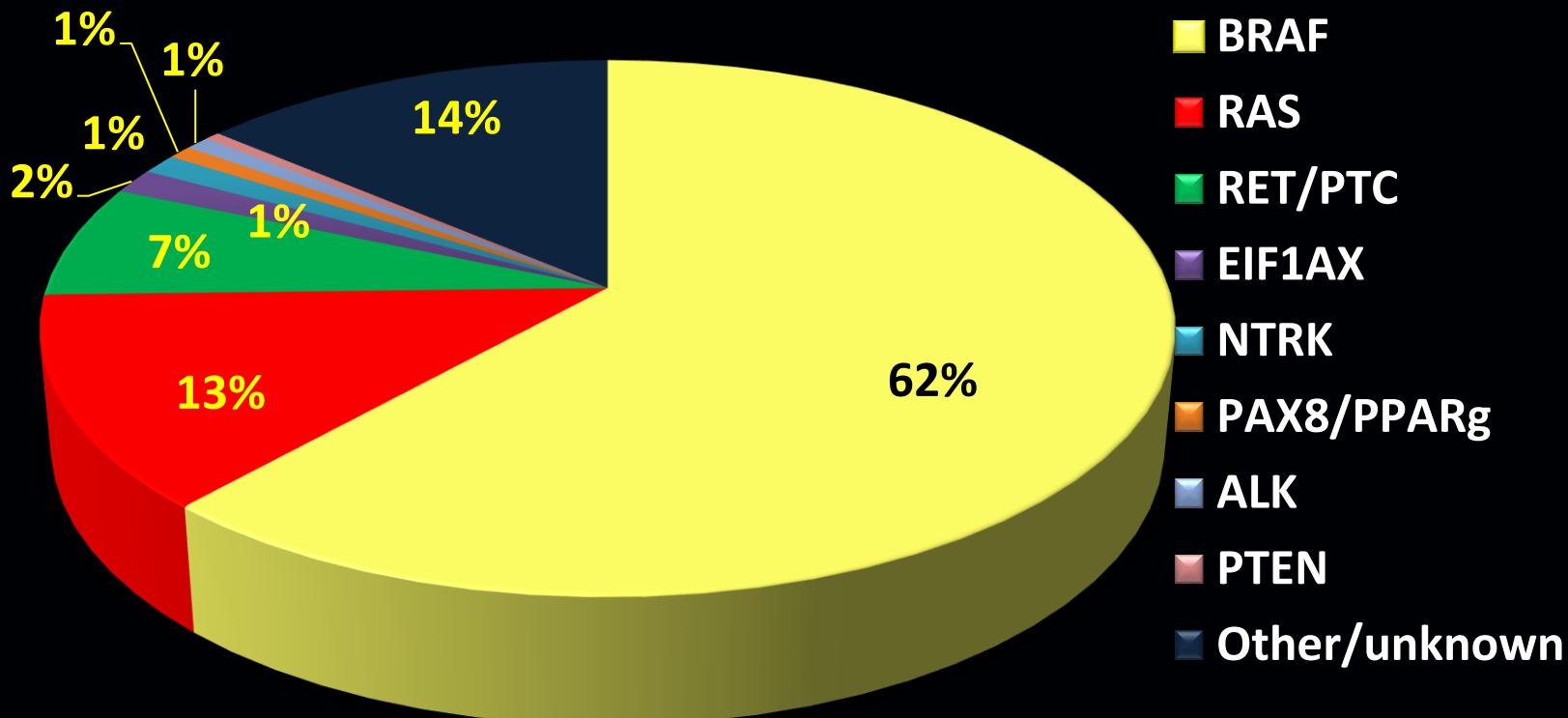
Terapias no-antiangiogénicas

Inhibidores selectivos de BRAF (PTC)

Terapias para re-diferenciación

Inhibidores selectivos de RET y NTRK (PTC)

Mutaciones en cáncer papilar de tiroides



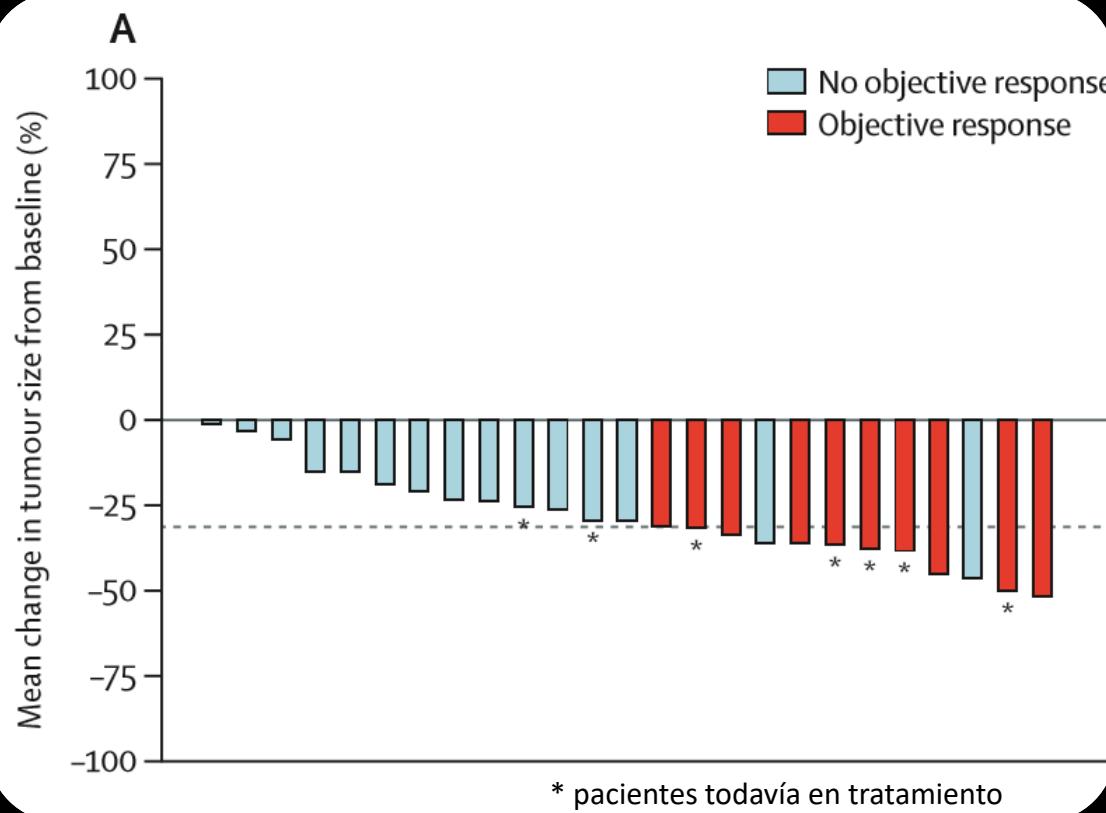
Adapted from Giordano, et al., Cell 2014

Vemurafenib in patients with *BRAF^{V600E}*-positive metastatic or unresectable papillary thyroid cancer refractory to radioactive iodine: a non-randomised, multicentre, open-label, phase 2 trial



Brose MS, Cabanillas ME, Cohen EE, Wirth LJ, Riehl T, Yue H, Sherman SI,
Sherman EJ, 2016

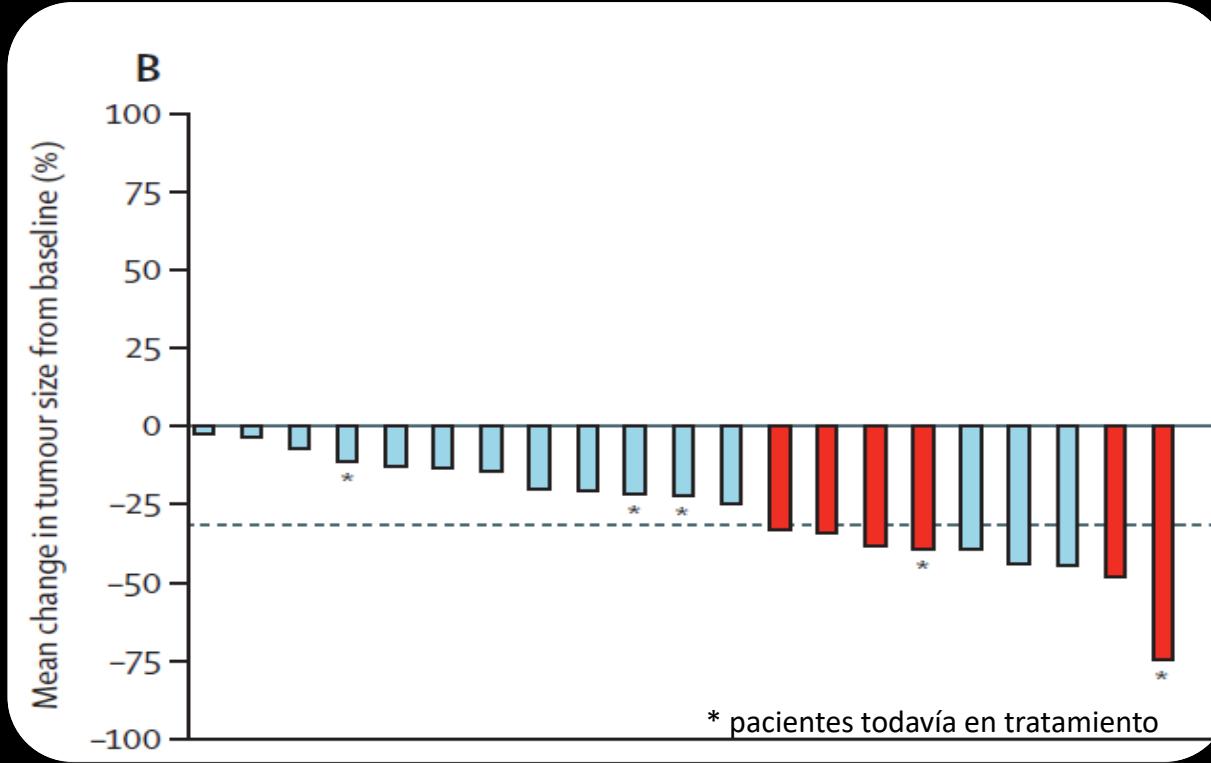
Vemurafenib: nunca antes tratados con inhibidores de VEGFR



- Mediana de supervivencia libre de progresión= 18.2 meses (95% CI 15.5–29.3)
- Mediana de la duración de respuestas= 16.5 meses
- Supervivencia global no alcanzo una mediana

Cohort 1 (n=26)	
Best overall response (confirmed)	
Complete response	0
Partial response	10 (38.5%, 20.2–59.4)
Stable disease	15 (57.7%, 36.9–76.7)
Progressive disease	1 (3.8%, 0.1–19.6)
Unknown	0

Vemurafenib: previamente tratados con inhibidores de VEGFR



- Mediana de supervivencia libre de progresión= 8.9 meses (95% CI 5.5–NE)
- Mediana de la duración de respuestas= 7.4 meses
- Mediana de supervivencia global= 14.4 meses (8.2-29.5)

Cohort 2 (n=22)	
Best overall response (confirmed)	
Complete response	0
Partial response	6 (27.3%, 10.7-50.2)
Stable disease	14 (63.6%, 40.7-82.8)
Progressive disease	1 (4.5%, 0.1-22.8)
Unknown	1 (5%)

Vía de señalización “MAP Kinase”

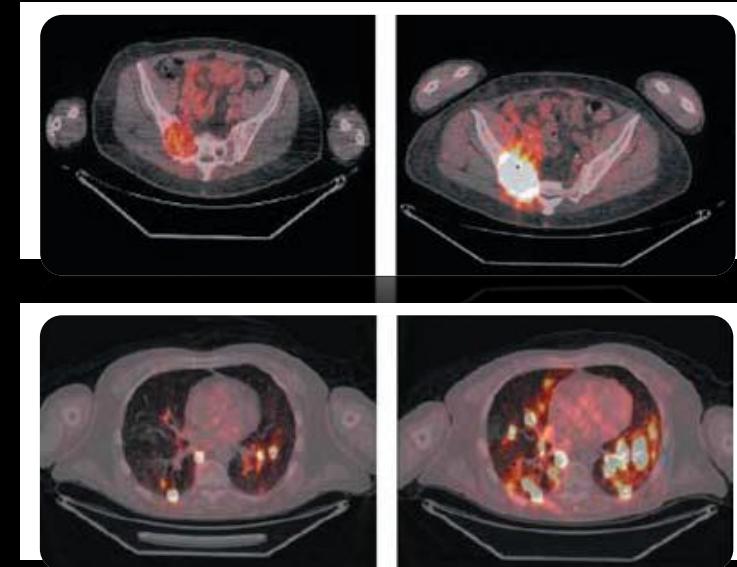
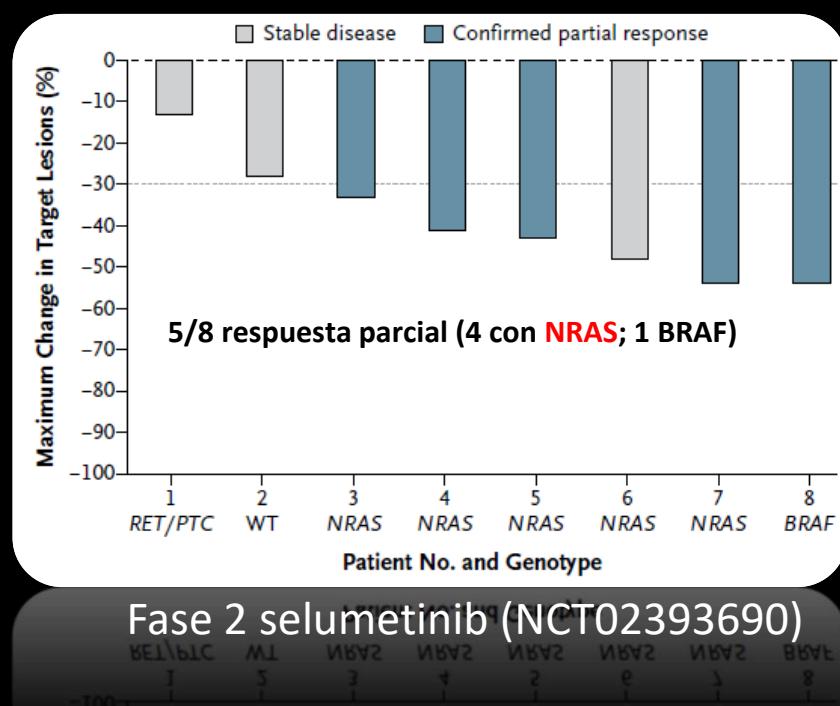


Re-diferenciación: Restaurar la habilidad de captar radioyodo en pacientes refractarios

- ─ Inhibidores de BRAF—para canceres con mutaciones en BRAF (e.g. dabrafenib, vemurafenib)
- ─ Inhibidores de MEK (e.g. selumetinib, trametinib, cobimetinib)

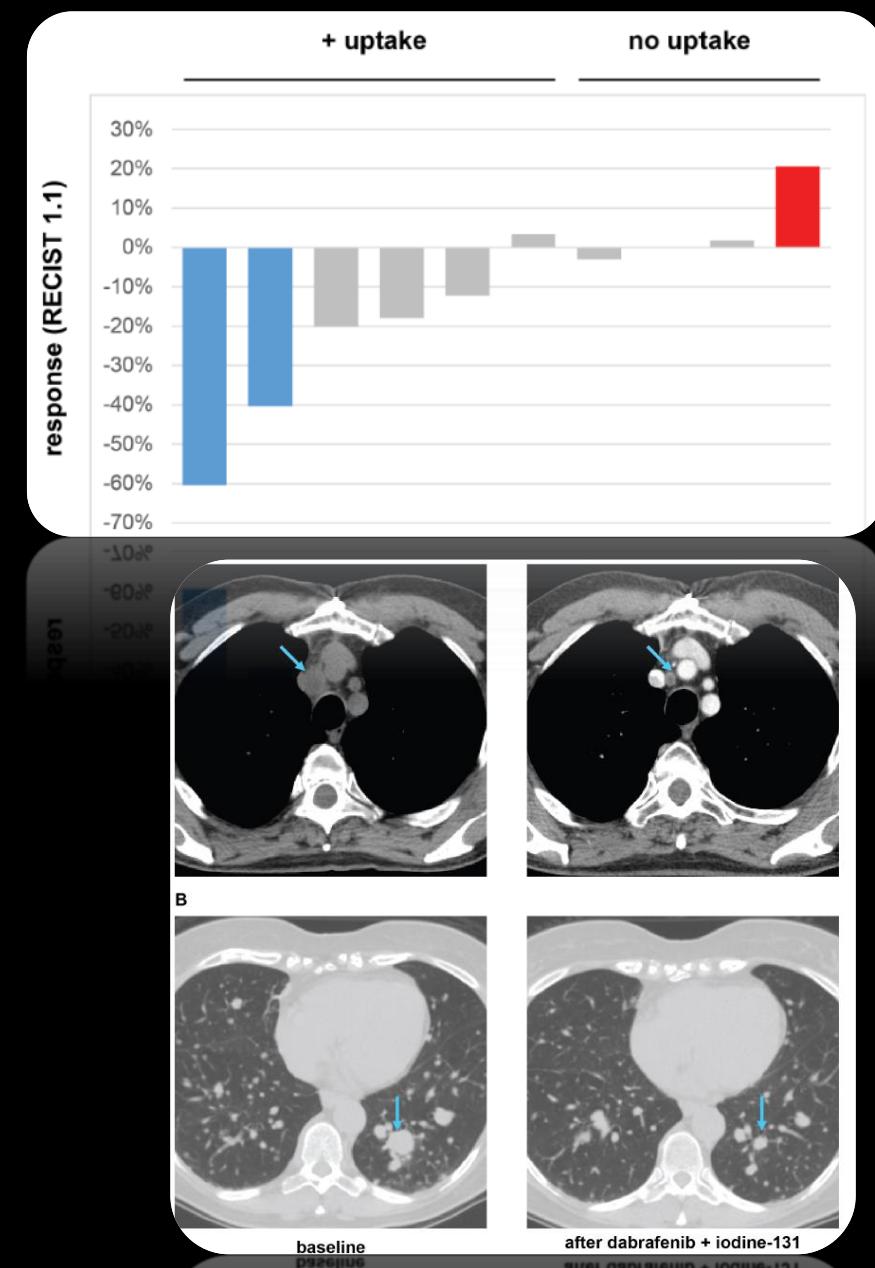
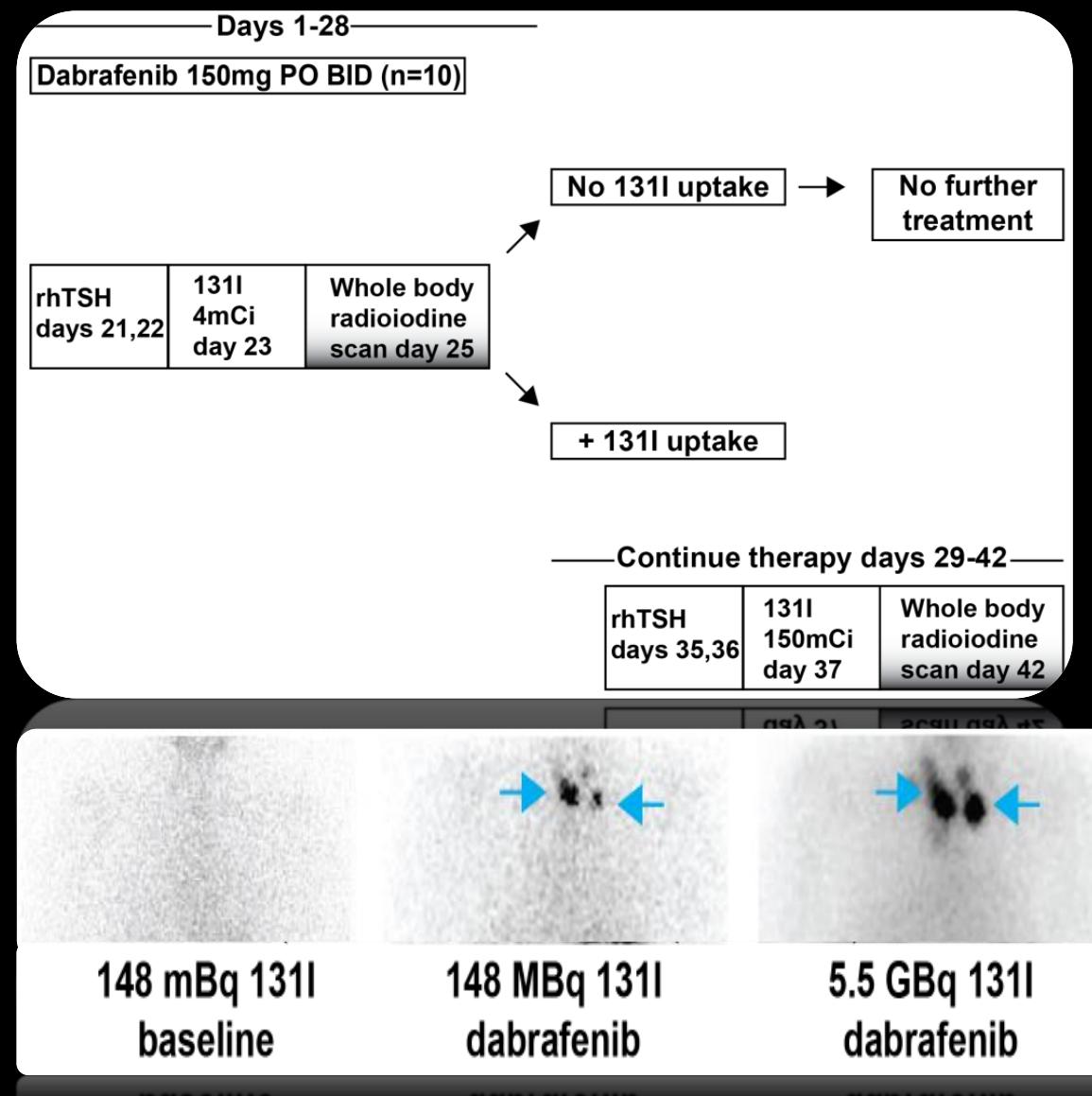
Selumetinib (inhibidor de MEK)

- 4 semanas de selumetinib
- Aumento en captación de yodo radioactivo en 12/20 pacientes
 - 4/9 pacientes con mutaciones en *BRAF*
 - 5/5 pacientes con mutaciones *NRAS*
- 8/12 pacientes llegaron al umbral de dosimetría para yodo radioactivo



Ho AL et al. NEJM 2013

Dabrafenib (PTC con mutación en BRAF) n=10

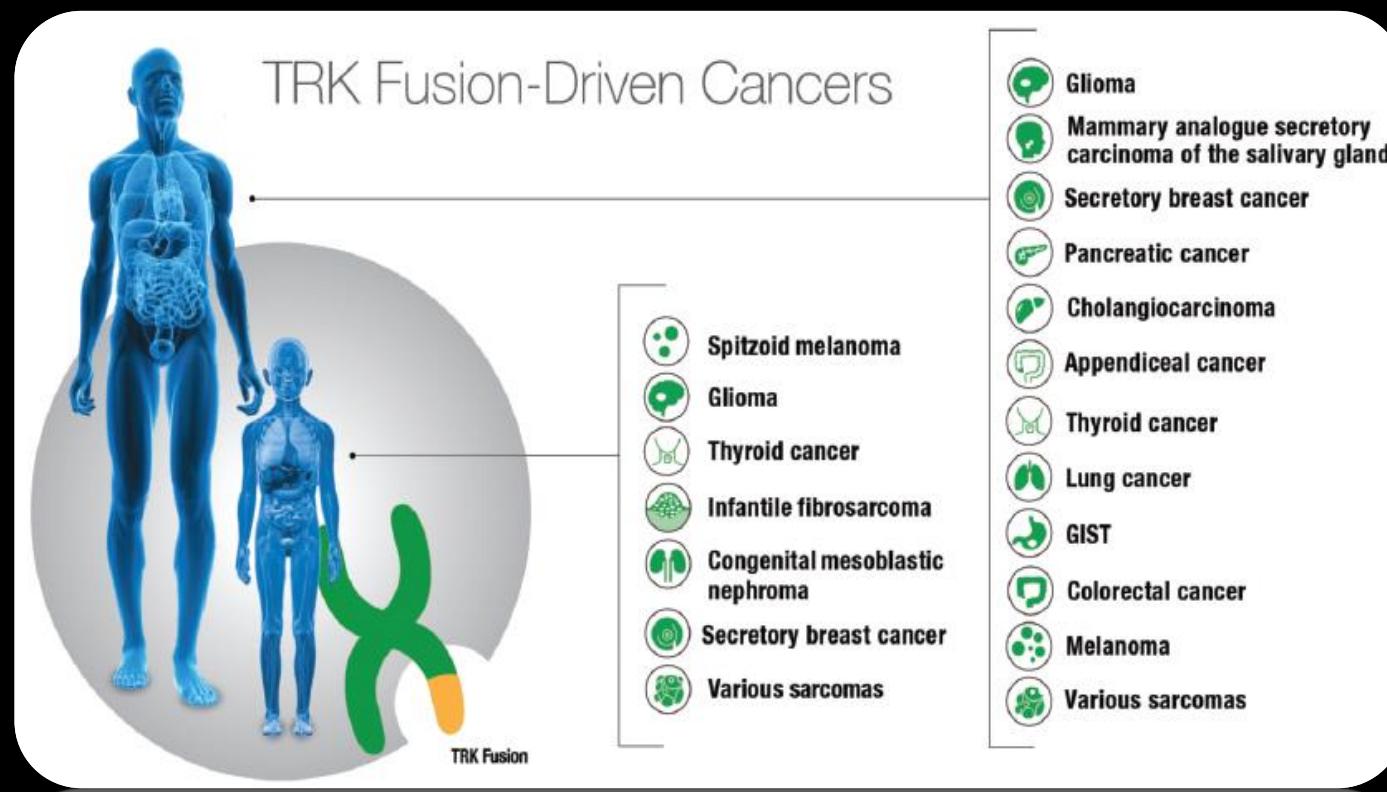


MERAIODE: A Redifferentiation Phase II Trial With Trametinib and Dabrafenib Followed by RAI for Metastatic RAI-Refractory DTC Patients With a BRAFV600E Mutation

- BRAF mutated cohort received dabrafenib/trametinib
- Out of 24 pts, 2 did not receive RAI → 21 pts analyzed.
- 65% had uptake on diagnostic WBS and 95% on post-treatment WBS
- Responses at 6 months:
 - 38% partial response
 - 52% stable disease
 - 10% progression of disease

Reordenamientos en NTRK (“fusiones”)

- Infrecuentes en papilar y anaplasico
- Entrectinib y larotrectinib son inhibidores de NTRK (indicaciones agnósticas)



Larotrectinib treatment of advanced TRK fusion thyroid cancer

Larotrectinib treatment of advanced TRK fusion thyroid cancer

Maria E Cabanillas¹, Alexander Drilon², Anna F Farago³, Marcia S Brose⁴, Ray McDermott⁵, Davendra Sohal⁶, Do-Youn Oh⁷, Mohammed Almubarak⁸, Jessica Bauman⁹, Edward Chu¹⁰, Shivaani Kummar¹¹, Serge Leyvraz¹², Keunchil Park¹³, John A Reeves¹⁴, Laura Dima¹⁵, Patricia Maeda¹⁴, Liana Rodrigues¹⁶, Nicoletta Brega¹⁴, David S Hong¹, Steven G Waguespack¹

¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA; ³Massachusetts General Hospital, Boston, MA, USA; ⁴Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; ⁵St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland; ⁶University of Cincinnati, Cincinnati, OH, USA; ⁷Seoul National University Hospital, Seoul, South Korea; ⁸West Virginia University, Morgantown, WV, USA; ⁹Fox Chase Cancer Center, Philadelphia, PA, USA; ¹⁰UPMC Hillman Cancer Center, Pittsburgh, PA, USA; ¹¹Oregon Health & Science University, Portland, OR, USA; ¹²Comprehensive Cancer Center, Charité Universitätsmedizin, Berlin, Germany; ¹³Samsung Medical Center, Seoul, South Korea; ¹⁴Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; ¹⁵Bayer Consumer Care AG, Basel, Switzerland; ¹⁶Bayer S.A., São Paulo, Brazil

BACKGROUND

- Standard-of-care treatment for unresected (i.e., non-BRAF mutated) patients with radioactive iodine (RAI)-refractory advanced differentiated thyroid cancer (DTC) is limited to targeted therapies, such as tyrosine kinase inhibitors (TKIs), with objective response rates (ORRs) ranging from 12–65%.^{1–3} Recommended treatments for metastatic DTC include targeted therapies and primary chemotherapy, with ORRs of 33–53%.^{1,2}
- Recurrent gene fusions (including ALK, BRAF, PRRG and RET) have been identified in approximately 10% of patients with advanced thyroid cancer.⁴
- Neurotrophic tyrosine receptor kinase (NTRK) gene fusions encode chimeric neurotrophic receptor kinase (NTRK) proteins, which are constitutively active and act as oncogenes in a variety of cancers, including DTC and selected tumors. NTRK gene fusions are found in 5–25% of thyroid cancers.⁵
- Larotrectinib (LRTX) is a first-in-class, orally administered, pan-NTRK inhibitor approved in 40 countries, including the US and EU, for adult and pediatric patients with TRK fusion cancer.⁶
- Amongst patients with advanced TRK fusion thyroid cancer, a 5-month duration of response (DoR) in 159 patients with TRK fusion cancer, regardless of tumor type, was observed. The drug was well tolerated with mainly Grade 1 or 2 adverse events (AEs).⁷
- The objective of this analysis was to assess the efficacy and safety of larotrectinib in a subset of patients with TRK fusion thyroid cancer.

METHODS

- Patients with thyroid harboring an NTRK gene fusion and treated with larotrectinib in two single-arm trials (NCT0222913 and NCT0222913c).
- Patients had to have locally advanced or metastatic disease and have previously received standard therapy (if available).
- Levorotrectinib was administered orally at a dose of 100 mg/m² (liquid formulation) at 100 mg twice daily in adults or 100 mg/m² twice daily in pediatric patients. The primary endpoint was ORR as assessed by investigators using Response Evaluation Criteria in Solid Tumors v.1.1 criteria.
- The data cut-off was 13 July 2018.

RESULTS

- A total of 10 patients with TRK fusion thyroid cancer were identified. Histology included papillary thyroid cancer (Table 1).
- Four patients had CNS metastases at baseline, three of whom had received radiotherapy to the brain.
- None of the patients had received ≥2 prior systemic therapies.

Efficacy

- ORR was 75% (95% confidence interval [CI] 55–95%; Figure 1). Among 10 patients with TRK fusion thyroid cancer, 2 had a complete response (CR) and 8 had a partial response (PR).

- Both patients with follicular thyroid cancer had a PR.

- Among the 7 patients with anaplastic thyroid cancer, 2 had a PR, 1 had a CR and 4 had progressive disease (PD) (Table 1).

- All 4 patients with CNS metastases had a PR.

- Two patients had metastatic intracranial disease, with intracranial tumor reductions of 44% and 50%; both had received radiotherapy ≥1 month prior to starting larotrectinib.

Figure 1 Best change in tumor size

Figure 2 Best response to larotrectinib

Figure 3 Safety

Figure 4 Patient with ET74-NTRK fusion metastatic thyroid cancer

Figure 5 CONCLUSIONS

Figure 6 References

Figure 7 Acknowledgments

Figure 8 Disclosure

Figure 9 Presented by:

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Presented at the ESMO Virtual Congress 2020, 19–21 September 2020.

On behalf of:

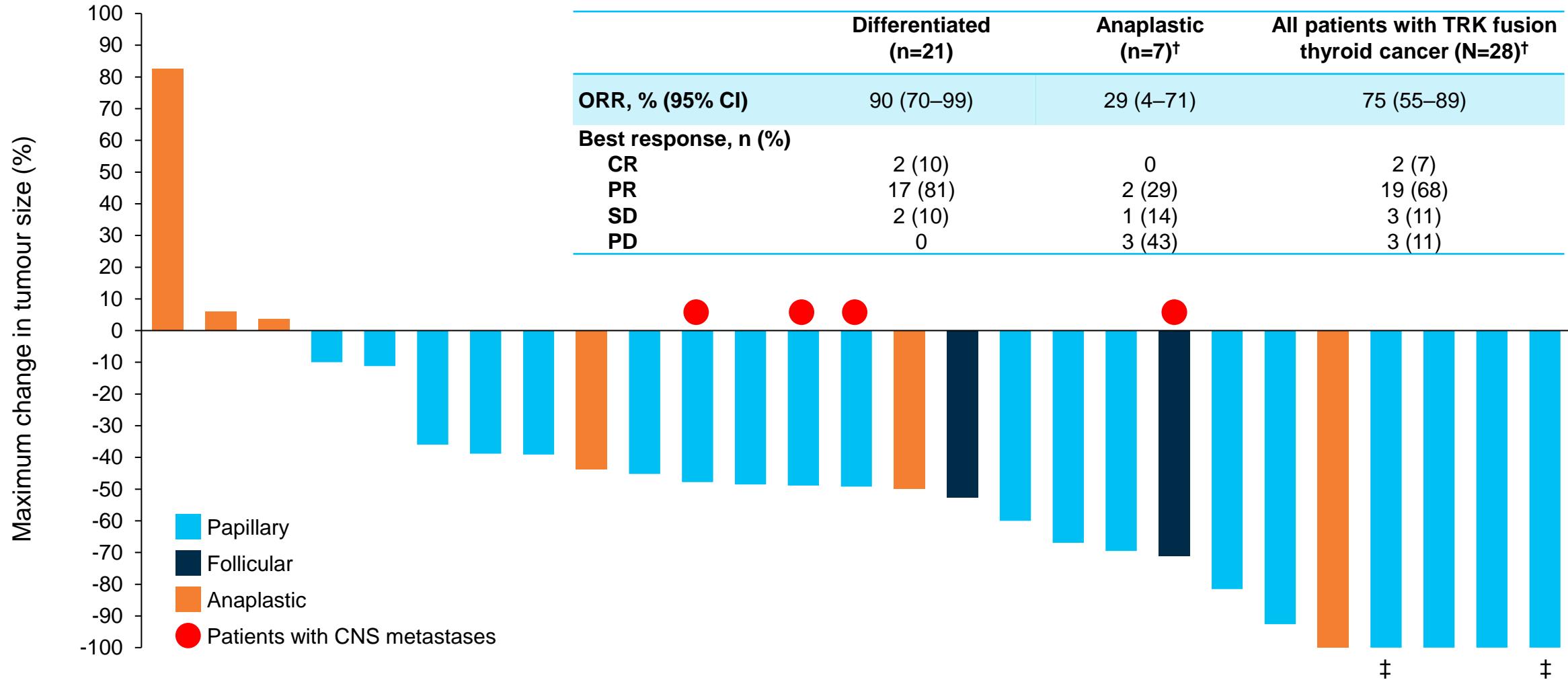
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³Massachusetts General Hospital, Boston, MA, USA; ⁴Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; ⁵St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland; ⁶University of Cincinnati, Cincinnati, OH, USA; ⁷Seoul National University Hospital, Seoul, South Korea; ⁸West Virginia University, Morgantown, WV, USA; ⁹Fox Chase Cancer Center, Philadelphia, PA, USA; ¹⁰UPMC Hillman Cancer Center, Pittsburgh, PA, USA; ¹¹Oregon Health & Science University, Portland, OR, USA;

¹²Comprehensive Cancer Center, Charité Universitätsmedizin, Berlin, Germany; ¹³Samsung Medical Center, Seoul, South Korea; ¹⁴Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; ¹⁵Bayer Consumer Care AG, Basel, Switzerland; ¹⁶Bayer S.A., São Paulo, Brazil

Best response to larotrectinib



[†]One patient with anaplastic thyroid cancer had clinical disease progression prior to the first tumour response assessment. [‡]Paediatric patients (<18 years old).
 CI, confidence interval; CNS, central nervous system; CR, complete response;
 ORR, objective response rate; PD, progressive disease; PR, partial response;
 SD, stable disease; TRK, tropomyosin receptor kinase.

AEs occurring in ≥15% of patients

Preferred term	Treatment-emergent AEs, n (%)				Treatment-related AEs, n (%)		
	Grade 1–2	Grade 3	Grade 4	Any grade	Grade 3	Grade 4	Any grade
Fatigue	10 (36)	0	0	10 (36)	0	0	8 (29)
Constipation	9 (32)	0	0	9 (32)	0	0	5 (18)
Dizziness	8 (29)	1 (4)	0	9 (32)	0	0	8 (29)
ALT increased	8 (29)	0	0	8 (29)	0	0	8 (29)
Anaemia	4 (14)	4 (14)	0	8 (29)	1 (4)	0	2 (7)
AST increased	8 (29)	0	0	8 (29)	0	0	8 (29)
Cough	7 (25)	1 (4)	0	8 (29)	—	—	—
Peripheral oedema	8 (29)	0	0	8 (29)	0	0	3 (11)
Lymphocyte count decreased	3 (11)	3 (11)	1 (4)	7 (25)	1 (4)	0	2 (7)
Myalgia	7 (25)	0	0	7 (25)	0	0	3 (11)
Arthralgia	6 (21)	0	0	6 (21)	0	0	1 (4)
Dyspnoea	5 (18)	1 (4)	0	6 (21)	0	0	1 (4)
Leukocyte count decreased	5 (18)	1 (4)	0	6 (21)	0	0	5 (18)
Nausea	6 (21)	0	0	6 (21)	0	0	2 (7)
Diarrhoea	3 (11)	2 (7)	0	5 (18)	0	0	2 (7)
Headache	5 (18)	0	0	5 (18)	0	0	1 (4)

- AEs were mainly Grade 1 or 2
- Grade 3 AEs occurred in 9 (32%) patients
- Grade 3 treatment-related AEs occurred in 2 (7%) patients
- Grade 4 and 5 AEs occurred in 2 (7%) patients each
 - None were considered treatment related
- Two (7%) patients had dose reductions due to an AE
- No patients experienced AEs leading to permanent treatment discontinuation

Selpercatinib (LOXO-292) en cancer de tiroides con mutación (MTC) o reordenamiento en *RET* (DTC/ATC)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Selpercatinib in *RET*-Altered Thyroid Cancers

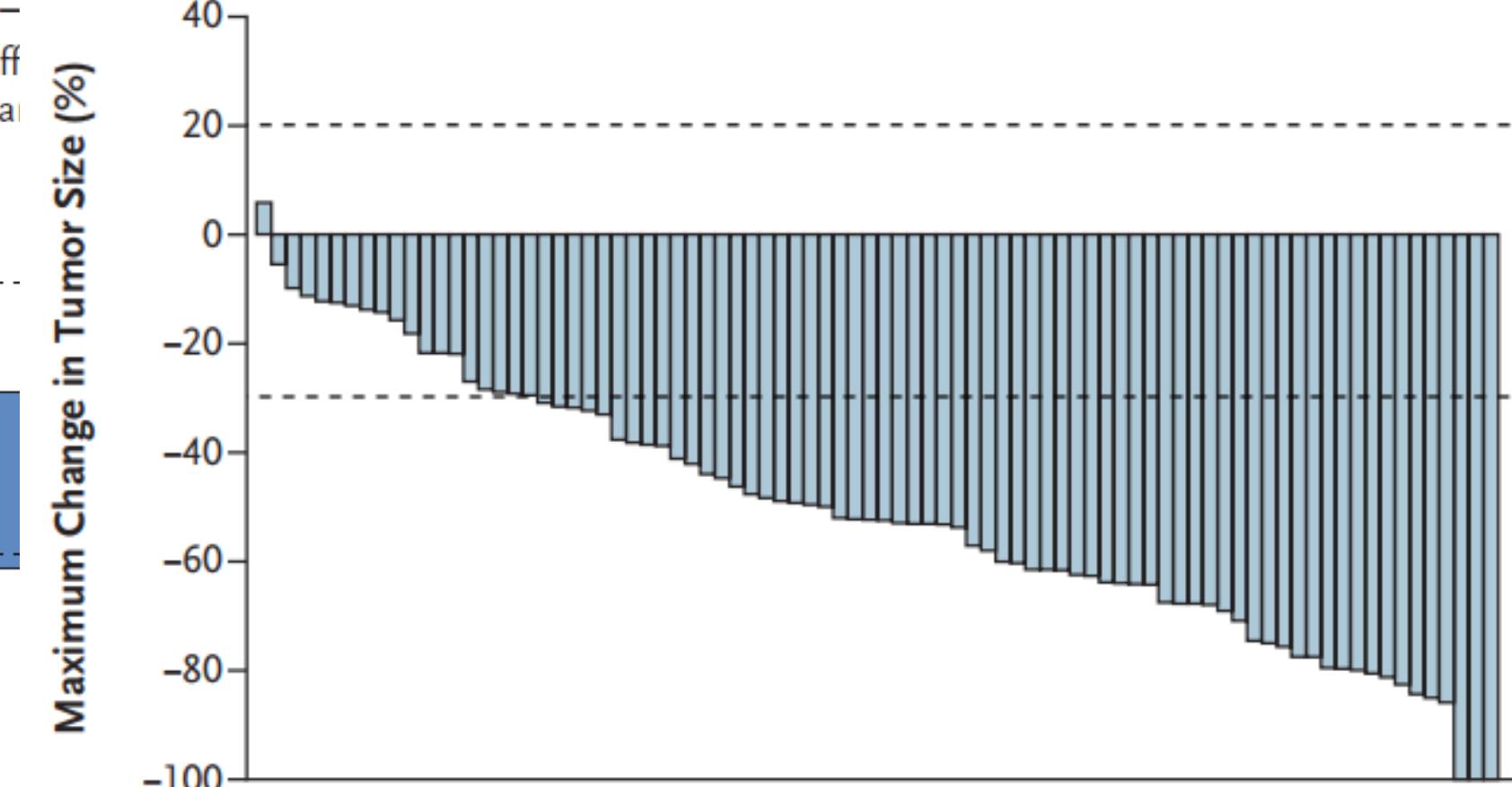
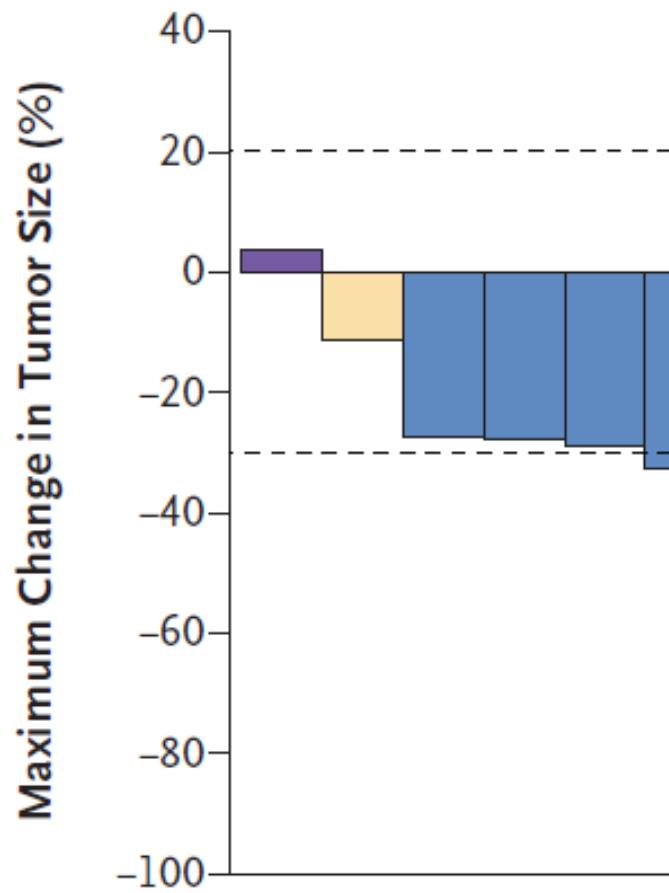
L.J. Wirth, E. Sherman, B. Robinson, B. Solomon, H. Kang, J. Lorch, F. Worden,
M. Brose, J. Patel, S. Leboulleux, Y. Godbert, F. Barlesi, J.C. Morris,
T.K. Owonikoko, D.S.W. Tan, O. Gautschi, J. Weiss, C. de la Fouchardière,
M.E. Burkard, J. Laskin, M.H. Taylor, M. Kroiss, J. Medioni, J.W. Goldman,
T.M. Bauer, B. Levy, V.W. Zhu, N. Lakhani, V. Moreno, K. Ebata, M. Nguyen,
D. Heirich, E.Y. Zhu, X. Huang, L. Yang, J. Kherani, S.M. Rothenberg, A. Drilon,
V. Subbiah, M.H. Shah, and M.E. Cabanillas

Selpercatinib (inhibidor de *RET*)

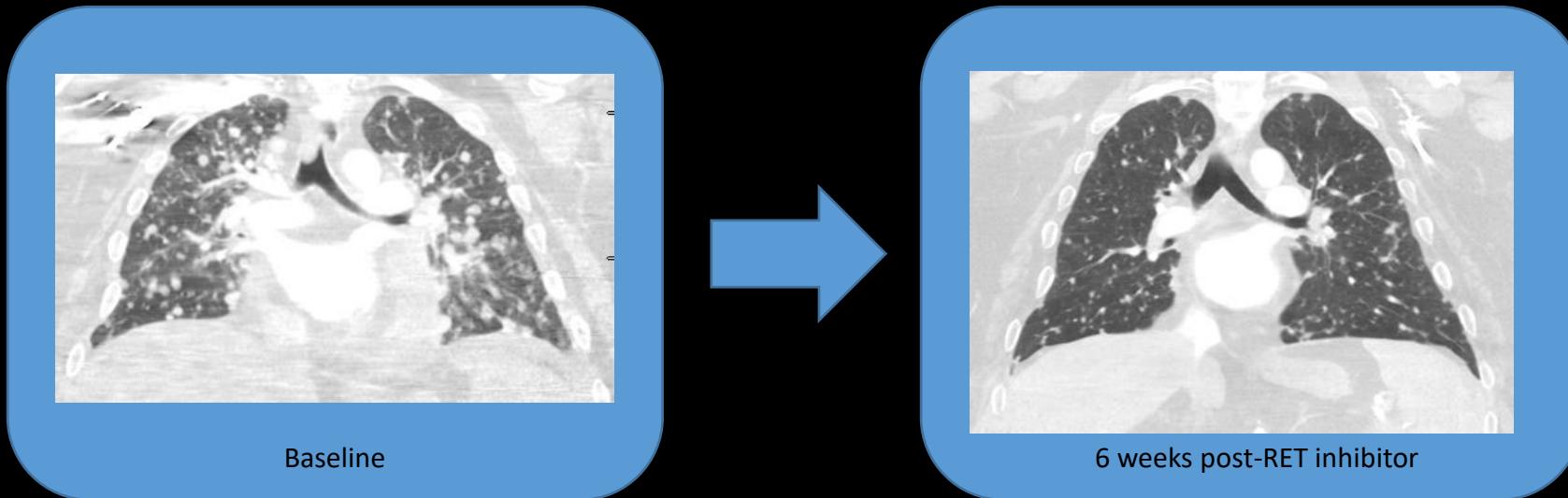
B RET-Mutant MTC Not Previously Treated with Vandetanib or Cabozantinib

C Previously Treated *RET* Fusion-

Papillary thyroid cancer Poorly diff thyroid ca



55 y.o. man with papillary thyroid cancer



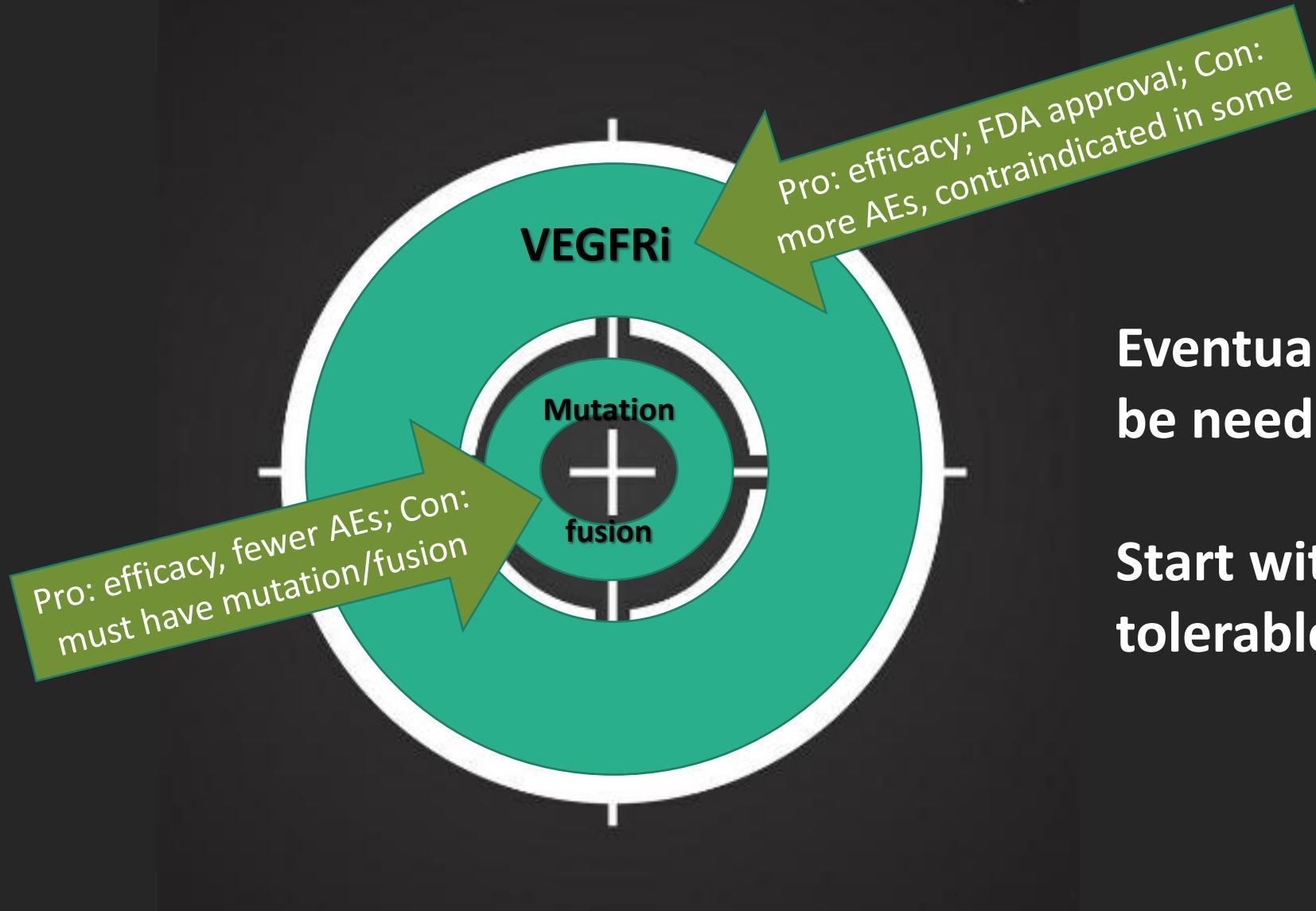
- Patient started on selpercatinib (selective RET inhibitor)
 - After 6 weeks of therapy, patient no longer requires oxygen
 - Able to ambulate normally
 - Tg dropped from 907 to 467

Table 3. Adverse Events in 162 Patients with RET-Mutant MTC or RET Fusion–Positive Thyroid Cancer Who Received Selpercatinib.*

Adverse Event	Adverse Events, Regardless of Attribution					Treatment-Related Adverse Events		
	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade number of patients (percent)	Grade 3	Grade 4	Any Grade
	Grade 1	Grade 2	Grade 3	Grade 4		Grade 3	Grade 4	
Any adverse event	9 (6)	42 (26)	95 (59)	11 (7)	162 (100)	45 (28)	3 (2)	153 (94)
Dry mouth	69 (43)	5 (3)	0	0	74 (46)	0	0	63 (39)
Hypertension	10 (6)	25 (15)	34 (21)	0	69 (43)	19 (12)	0	49 (30)
Diarrhea	44 (27)	8 (5)	9 (6)	0	61 (38)	4 (3)	0	27 (17)
Fatigue	35 (22)	24 (15)	2 (1)	0	61 (38)	1 (1)	0	41 (25)
Increased aspartate aminotransferase level	37 (23)	6 (4)	13 (8)	1 (1)	57 (35)	12 (7)	1 (1)	45 (28)
Nausea	44 (27)	13 (8)	0	0	57 (35)	0	0	25 (15)
Constipation	44 (27)	11 (7)	1 (1)	0	56 (35)	0	0	26 (16)
Increased alanine aminotransferase level	26 (16)	7 (4)	17 (10)	1 (1)	51 (31)	16 (10)	1 (1)	42 (26)
Headache	36 (22)	11 (7)	4 (2)	0	51 (31)	1 (1)	0	21 (13)
Peripheral edema	42 (26)	5 (3)	1 (1)	0	48 (30)	0	0	29 (18)
Increased blood creatinine level	27 (17)	12 (7)	0	0	39 (24)	0	0	22 (14)
Abdominal pain	25 (15)	8 (5)	5 (3)	0	38 (23)	0	0	6 (4)
Arthralgia	25 (15)	10 (6)	0	0	35 (22)	0	0	8 (5)
Vomiting	26 (16)	8 (5)	1 (1)	0	35 (22)	0	0	12 (7)
Hypocalcemia	14 (9)	13 (8)	6 (4)	1 (1)	34 (21)	0	0	5 (3)
Back pain	19 (12)	10 (6)	2 (1)	0	31 (19)	0	0	1 (1)
QT interval prolonged on electrocardiography	11 (7)	16 (10)	4 (2)	0	31 (19)	3 (2)	0	21 (13)
Cough	25 (15)	4 (2)	0	0	29 (18)	0	0	2 (1)
Rash	25 (15)	3 (2)	0	0	28 (17)	0	0	13 (8)
Dizziness	25 (15)	2 (1)	0	0	27 (17)	0	0	9 (6)
Abdominal distension	18 (11)	7 (4)	0	0	25 (15)	0	0	12 (7)
Hypothyroidism	14 (9)	11 (7)	0	0	25 (15)	0	0	12 (7)
Weight increased	11 (7)	9 (6)	5 (3)	0	25 (15)	1 (1)	0	8 (5)

increased LFTs

In DTC/MTC: How do we choose which treatment first?



Eventually, 2nd line therapy will be needed

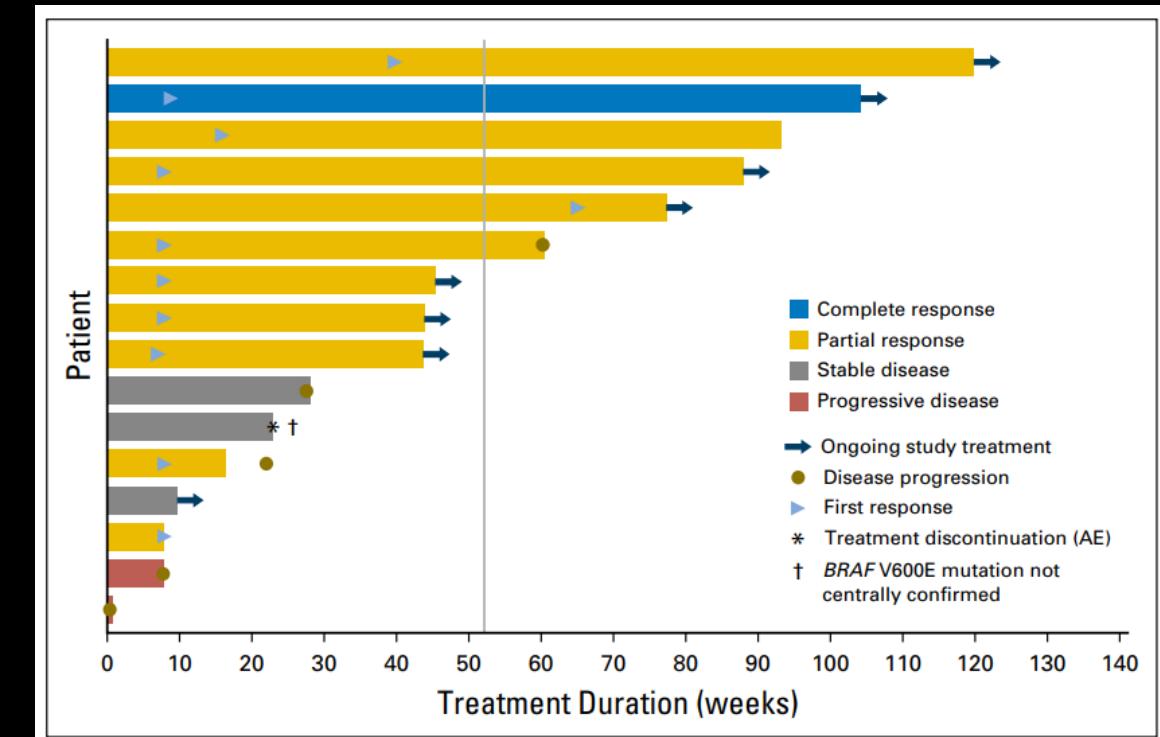
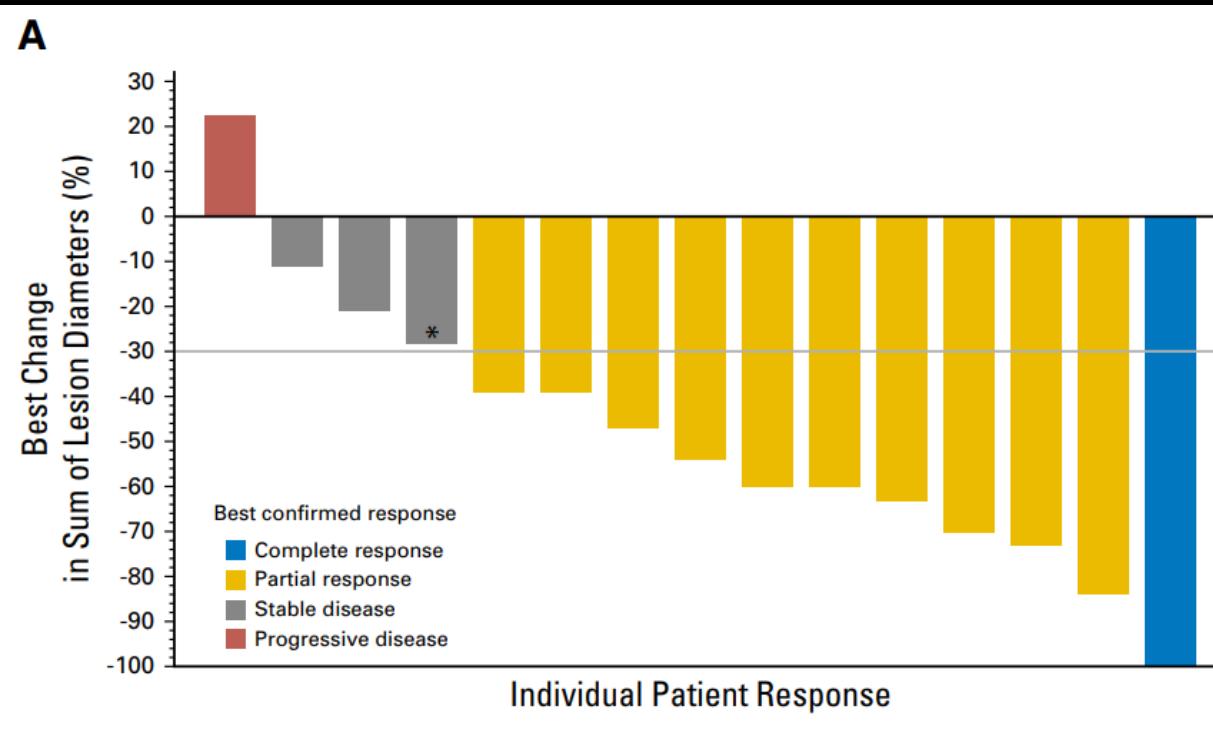
Start with the safest and most tolerable drug



TRATAMIENTOS MODERNOS PARA CÁNCER DE TIROIDES ANAPLÁSICO (ATC)

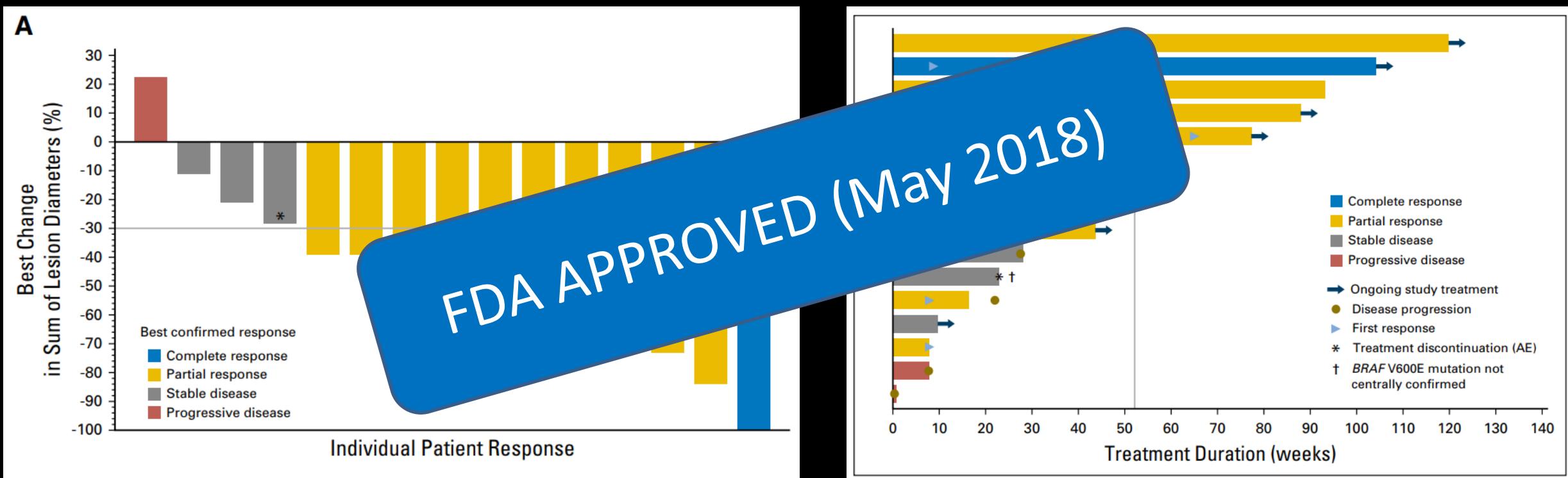
ATC: Dabrafenib (BRAFi) + trametinib (MEKi) basket trial

- 16 *BRAFV600E* mutated ATC patients
- Key entry criteria: Good PS, ability to swallow and normal organ function, chemoRT wash-out 14 days
- 69% response rate; OS 80% at 1 year



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ATA Guidelines on Anaplastic Thyroid Cancer

RECOMMENDATION 4

Once ATC diagnosis is considered, assessment of *BRAF^{V600E}* mutation should be expeditiously performed by IHC and confirmed/expeditiously assessed by molecular testing.

Strength of recommendation: strong

Quality of evidence: moderate

RECOMMENDATION 5

Molecular profiling should be performed at the time of ATC diagnosis to inform decisions related to the use of targeted therapies, especially as there are now Food and Drug Administration-approved mutation-specific therapies in this context.

Strength of recommendation: strong

Quality of evidence: moderate

68 y/o BRAF V600E mutated ATC patient treated with dabrafenib + trametinib

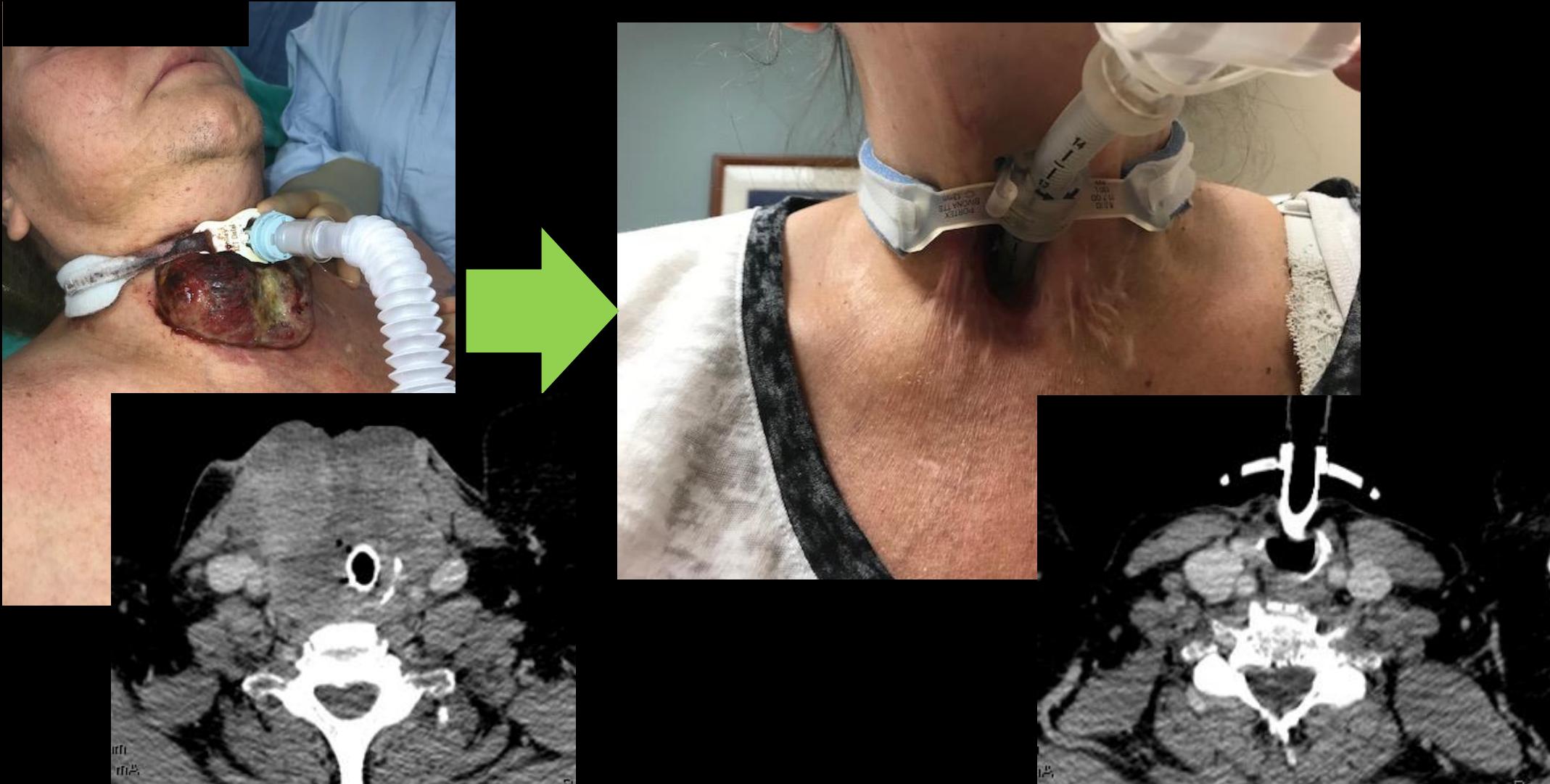


Before dabrafenib/trametinib



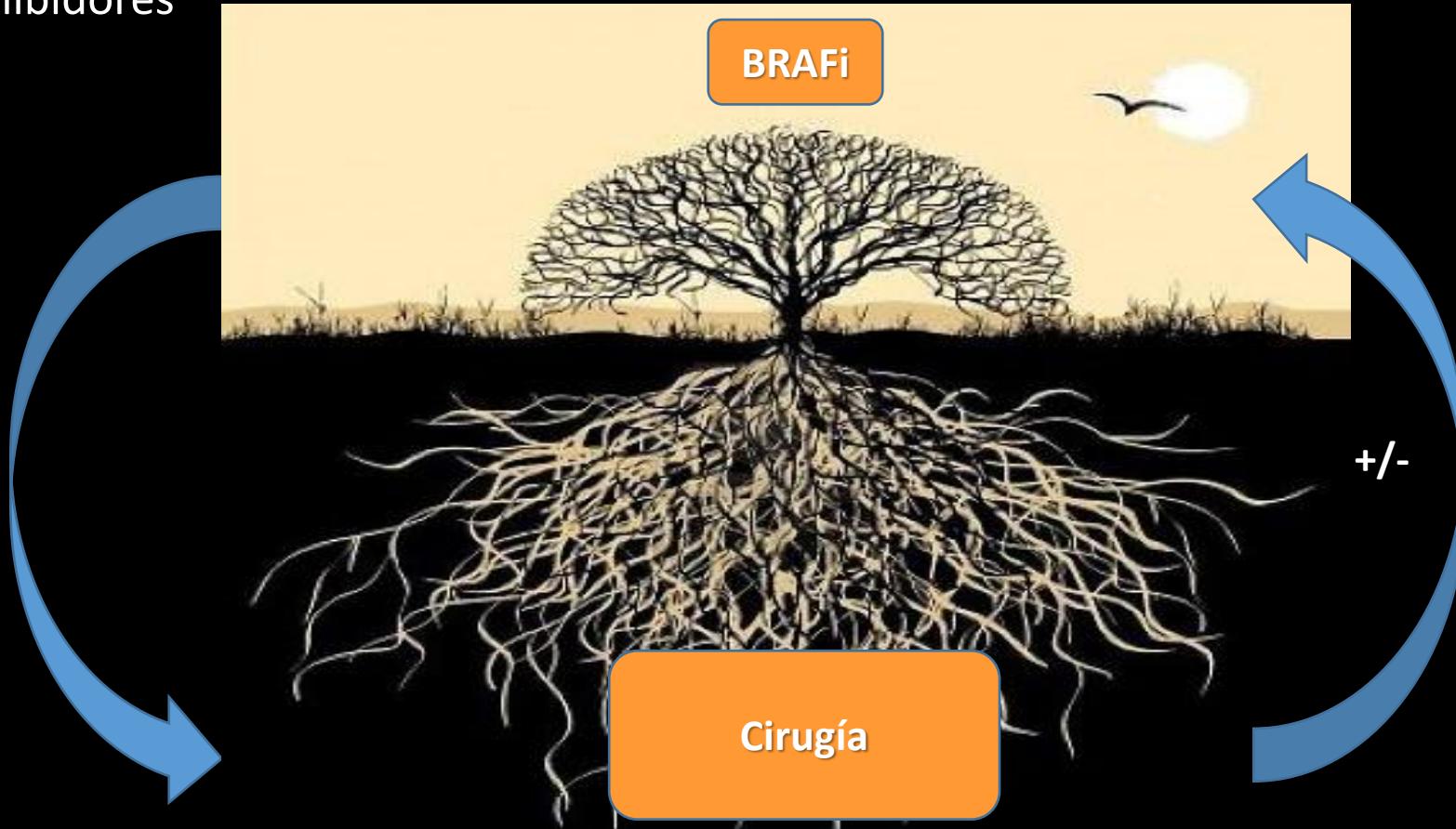
5 weeks later

Anaplásico con mutación en BRAF: Después de 4 semanas de dabrafenib/trametinib



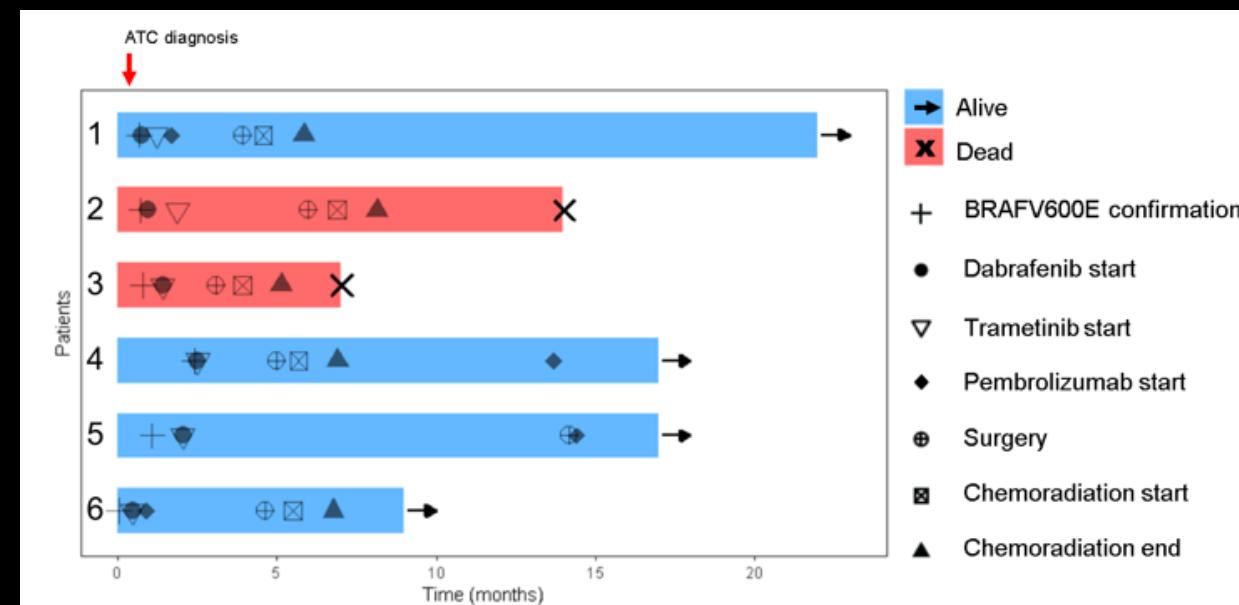
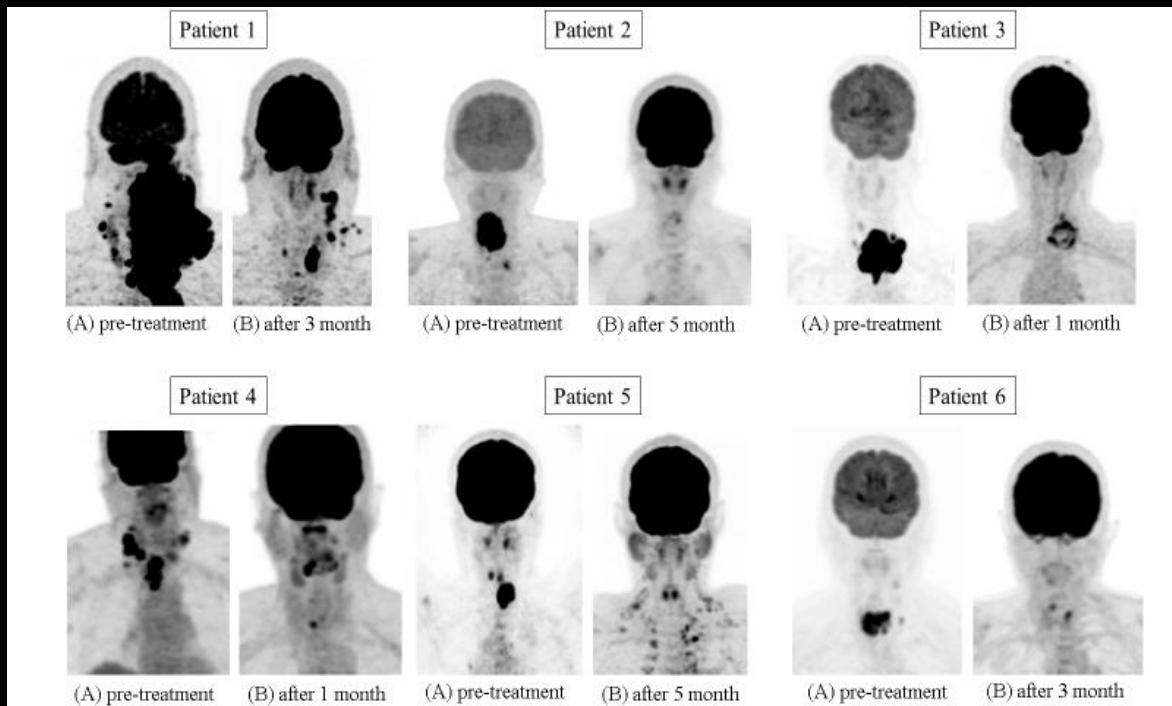
Neoadyuvante con inhibidores de BRAF

Todo paciente desarrolla resistencia a los inhibidores de kinasa



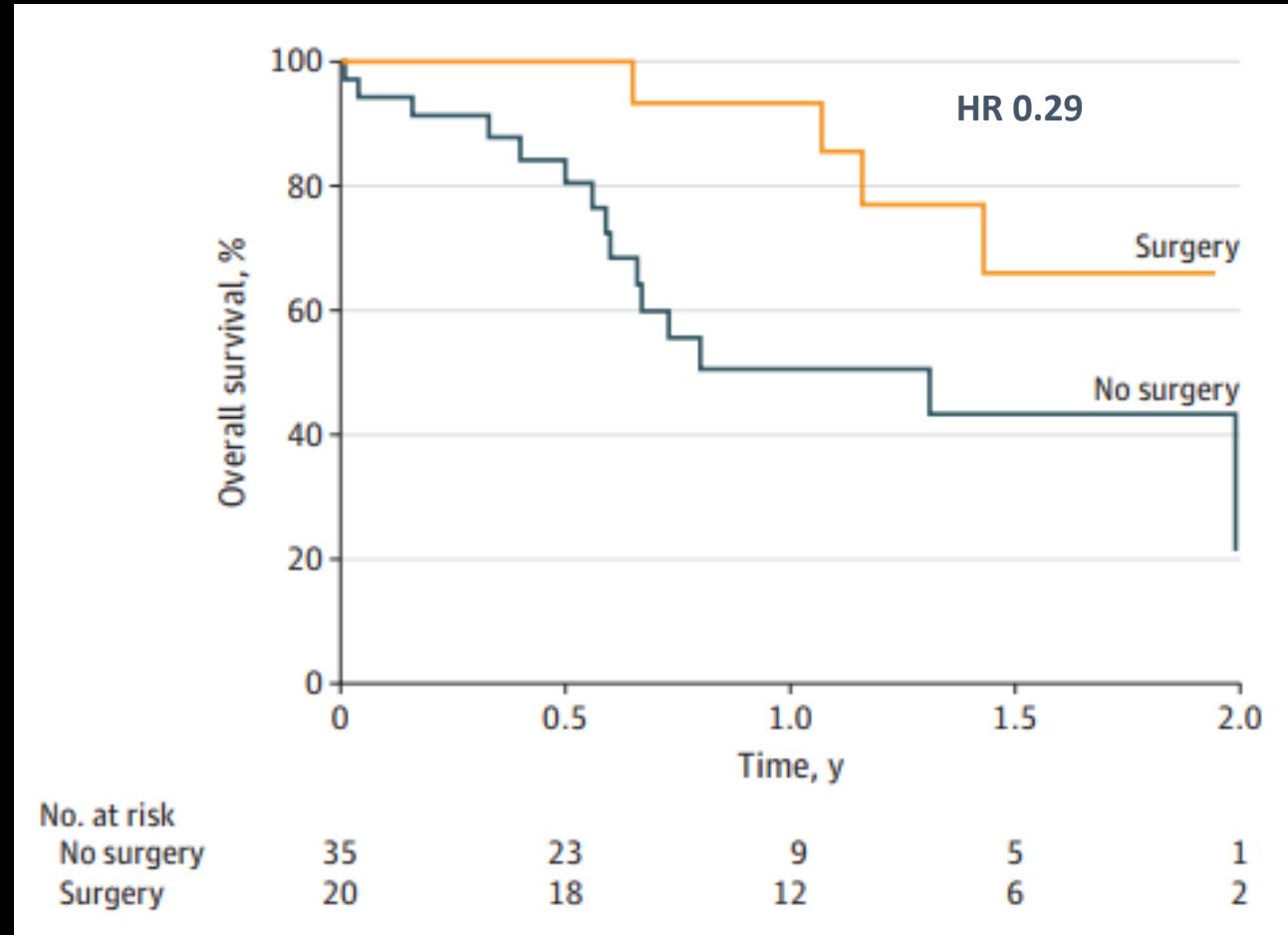
*Administración de un agente terapeútico antes de cirugía

Resección completa después de neoadyuvante con dabrafenib + trametinib en anaplásico con mutación en *BRAFV600E*



- Supervivencia a los 12 meses 83.3%; a los 18 meses 62.5%

Neoadjuvant therapy followed by surgery in $BRAF^{V600E+}$ patients (2017-present)

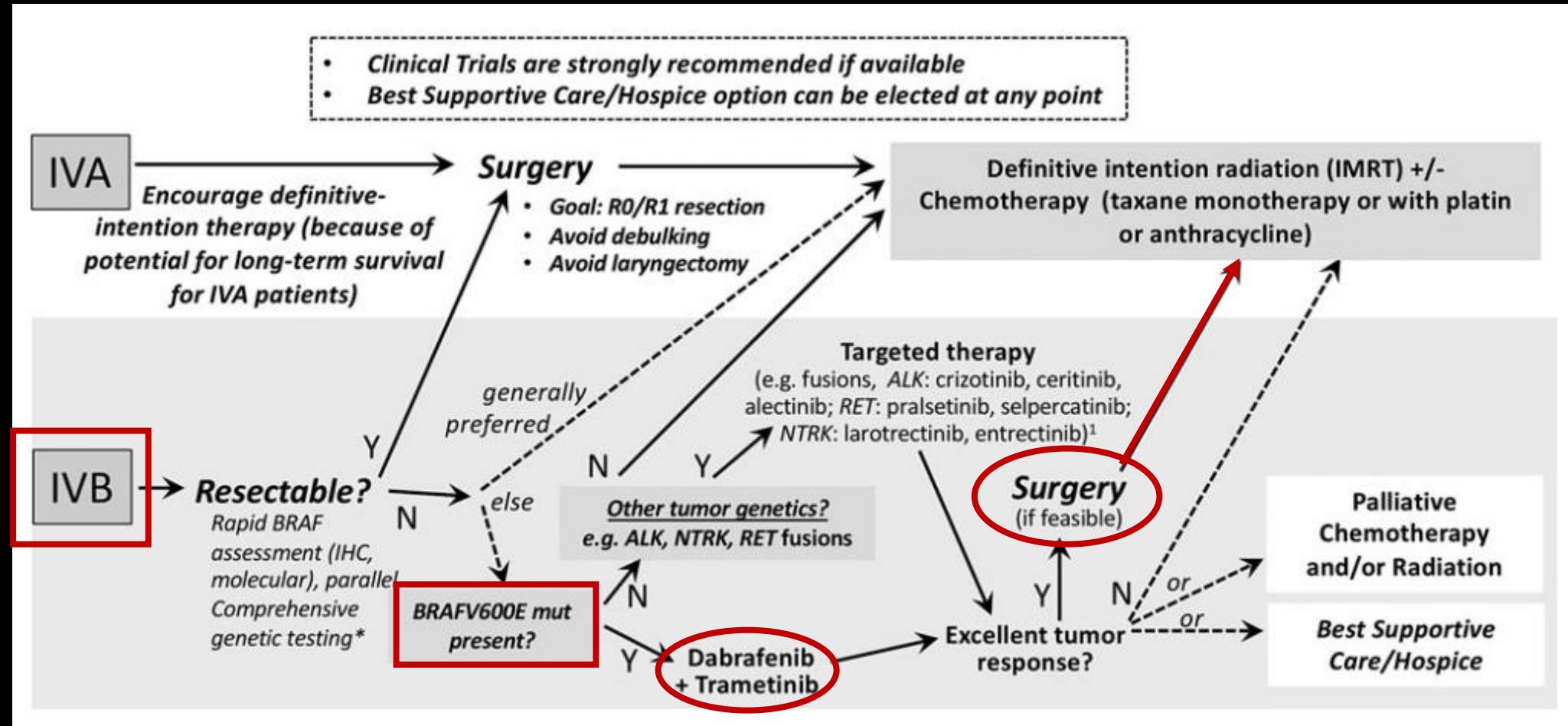


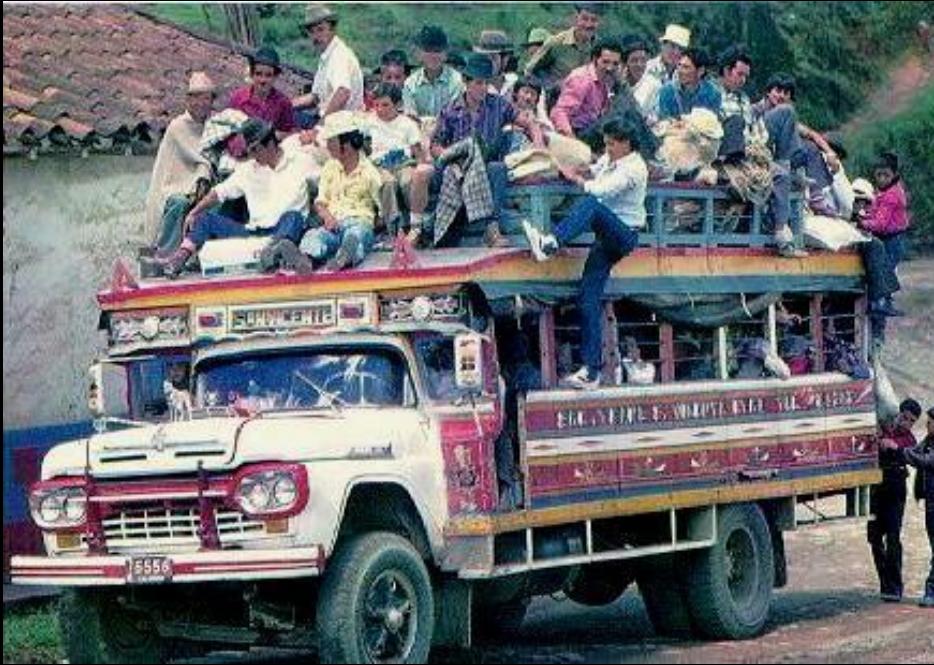
- N=20 (32%) $BRAF^{V600E+}$ patients operated
- Median follow-up from diagnosis=1.21 years
- 16 remain alive

Median overall survival
Surgery=not reached (1 year survival 94%)
No surgery=0.8 years

Clinical trial with neoadjuvant dabrafenib/trametinib/pembro opening 2021

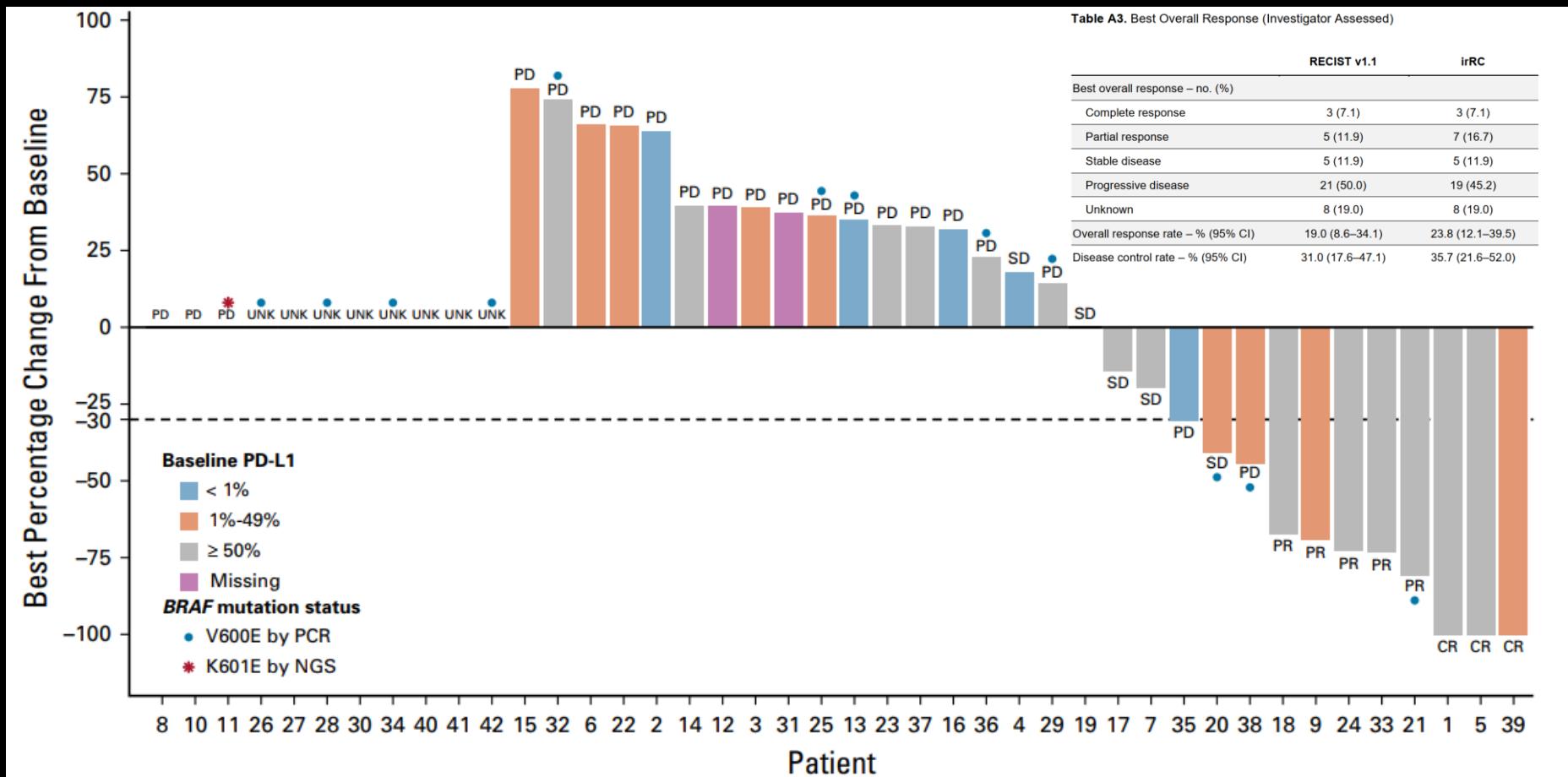
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Immunoterapia para cáncer de tiroides anaplásico

Spartalizumab (anti-PD1/PD2)

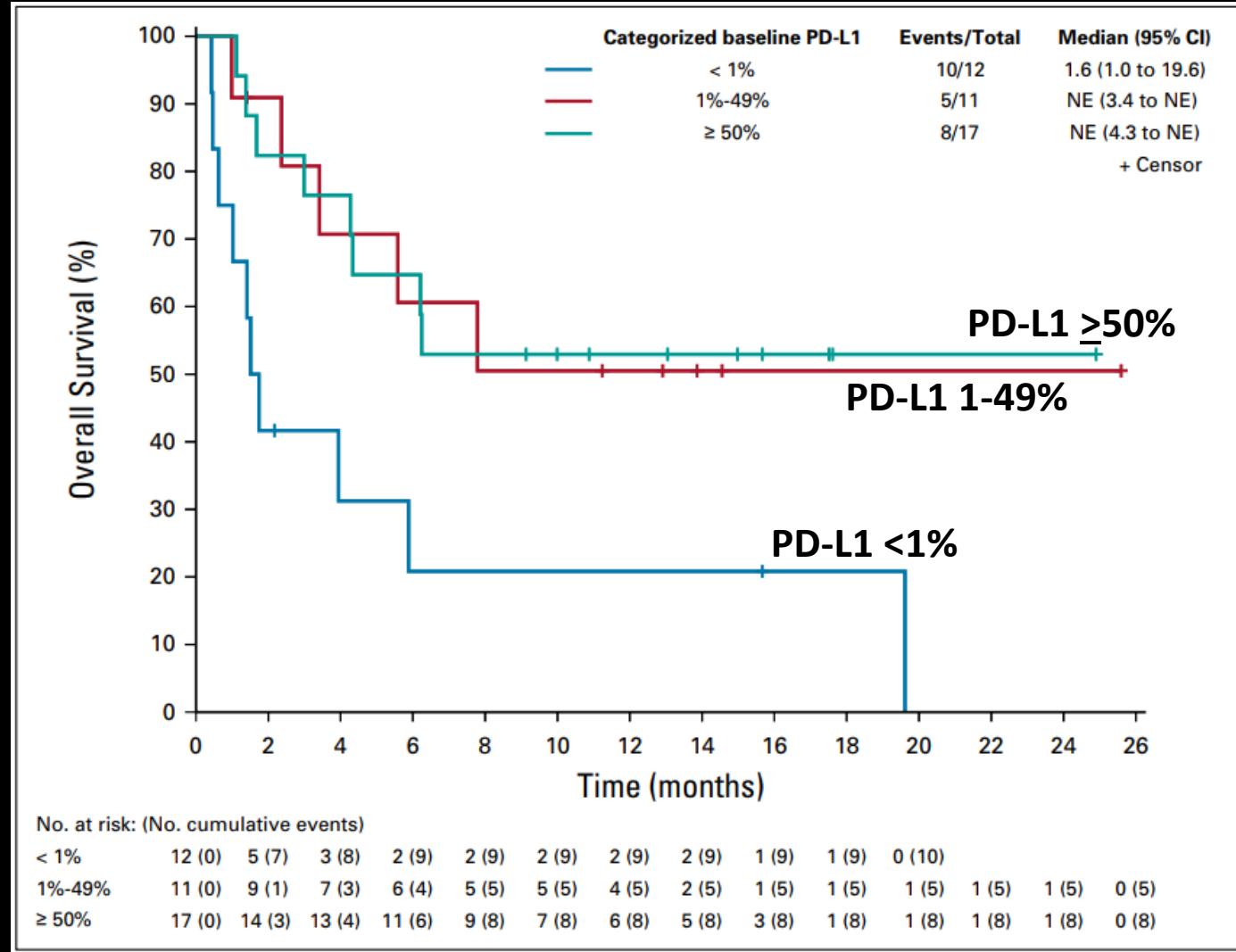


- 42 pacientes con ATC
- Respuestas: 19% (8/41; solo un paciente de 8 con BRAF respondió)

Spartalizumab (anti-PD1/2) en ATC

- Median PFS was 1.7 months
- Median OS was 5.9 months with 40% of patients alive at 1 year
- In patients with high PD-L1, 52% alive at 1 year (RR 29%)

Biomarker status	ORR – % (n/N) [95% CI]
PD-L1-positive cells by IHC	
<1%	0 (0/12) [0, 26.5]
1–49%	18.2 (2/11) [2.3, 51.8]
$\geq 50\%$	35.3 (6/17) [14.2, 61.7]
Missing	0 (0/2) [0, 84.2]



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RECOMMENDATION 24

In IVC ATC patients with high PD-L1 expression, checkpoint (PD-L1, PD1) inhibitors can be considered first-line therapy in the absence of other targetable alterations or as later line therapy, preferably in the context of a clinical trial.

Strength of recommendation: conditional

Quality of evidence: low

Resumen

- No todo paciente con cáncer de tiroides (DTC/MTC) requiere tratamiento sistémico
- Hay varias opciones para pacientes con todo tipo de cáncer de tiroides avanzado
 - Entender la genética del tumor es importante para seleccionar tratamientos
- Anaplásico:
 - Todo paciente con mutación en BRAF se debería tratar
 - Los otros se deberían tratar en ensayos clínicos

Muchas gracias

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