# הטיפול בסרטן מתקדם של בלוטת התריס

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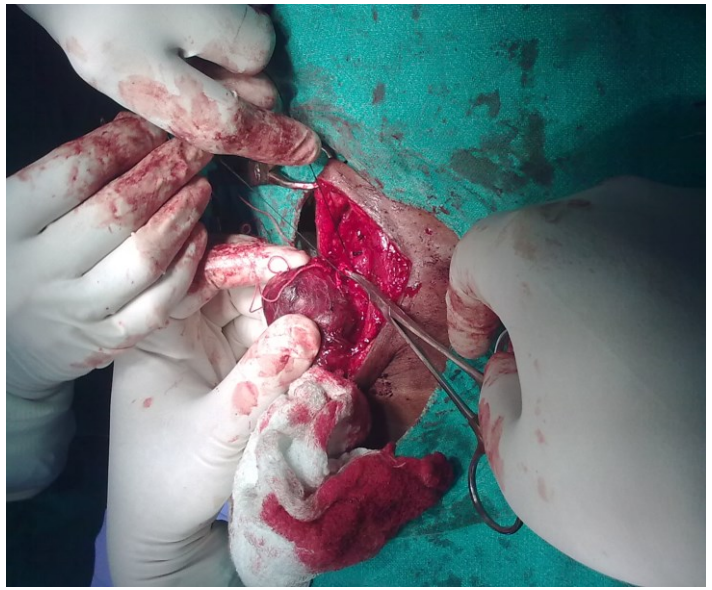
RABIN MEDICAL CENTER
BEILINSON • HASHARON

# Disclosures

- Roche
- Sanofi
- MSD
- Novartis
- Medison
- Neopharm
- Merck
- Elly Lilly

# S.M

- **65 yrs old patient**
- **2013 – Total thyroidectomy in Marroco**



# S.M

- **2014 – 100mci**
- **2015 – Surgery  - lesion adjacent to the trachea**
- **2015- EBRT – after surgery**

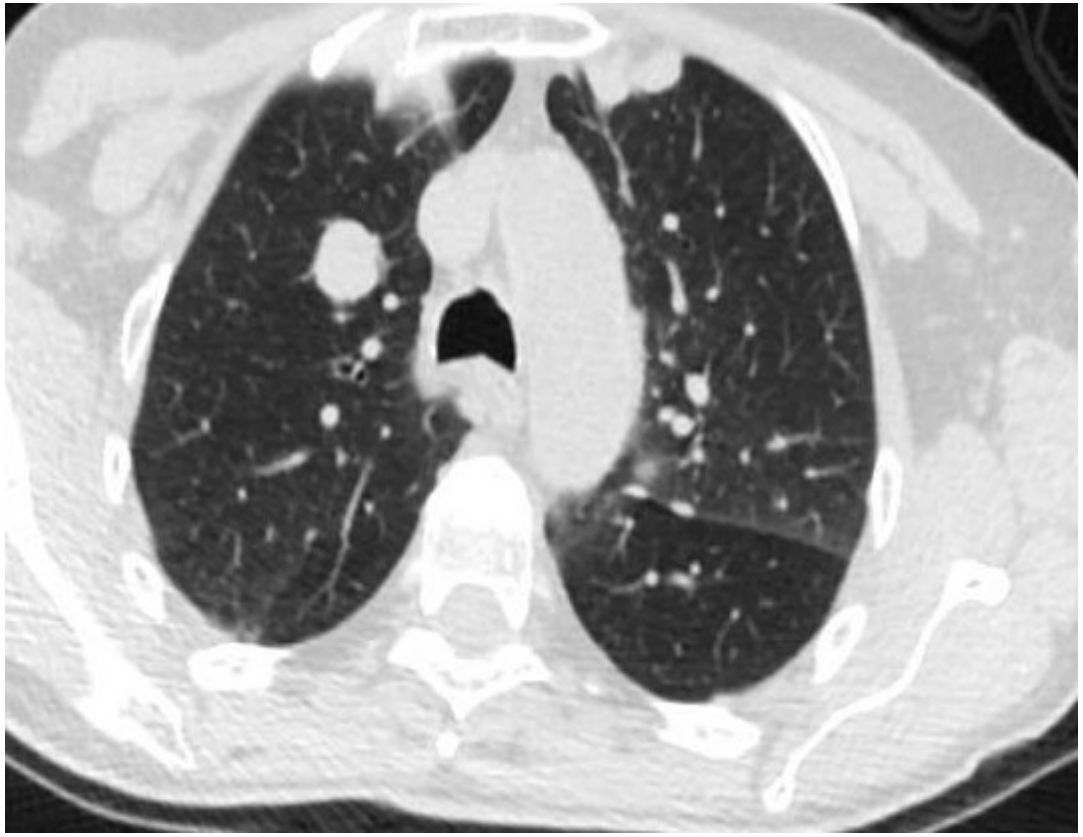
# S.M

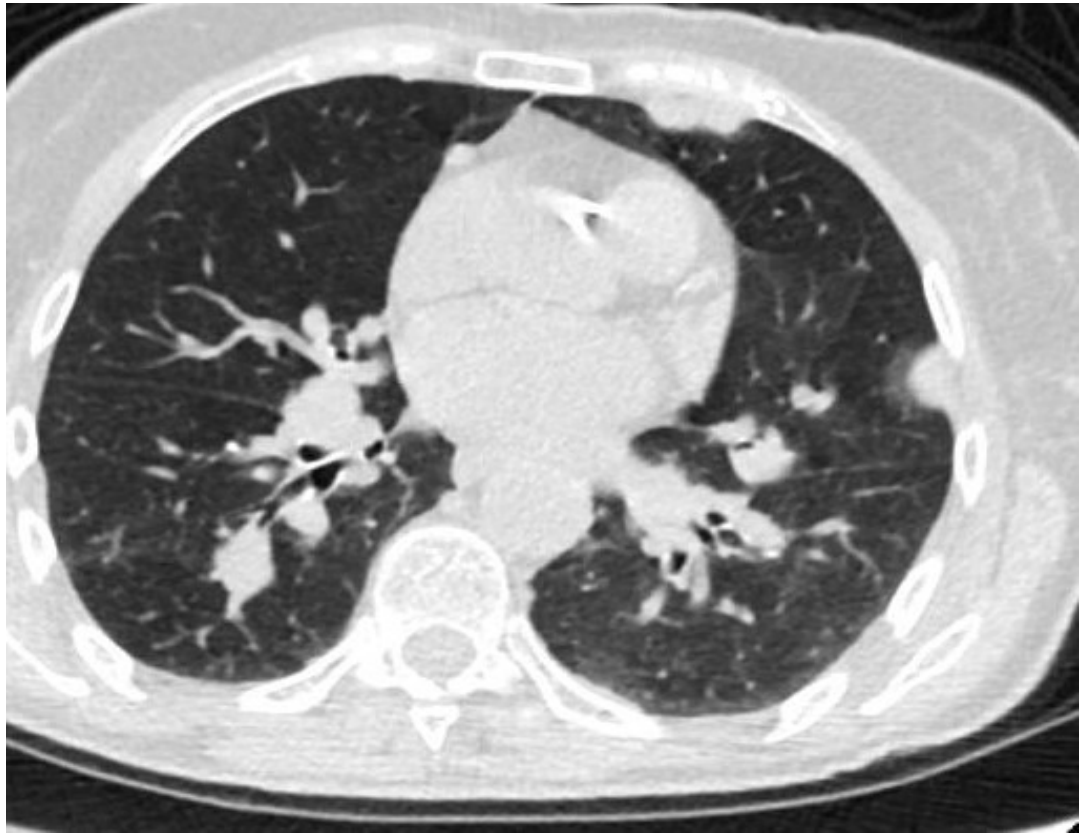
- **1/2018 – 160 mci with no significant enhancement**
- **1/2019 – TG levels – 34 -→ 138**
- **2/2019 – PET CT -Lung nodules and LNs involvement in the mediastinum , Left paraveretebral lesion**

# S.M

- **2/2020 – Significant progression in the lungs – new subpleural lesions till 6.3 cm in diameter**

# 2/2020

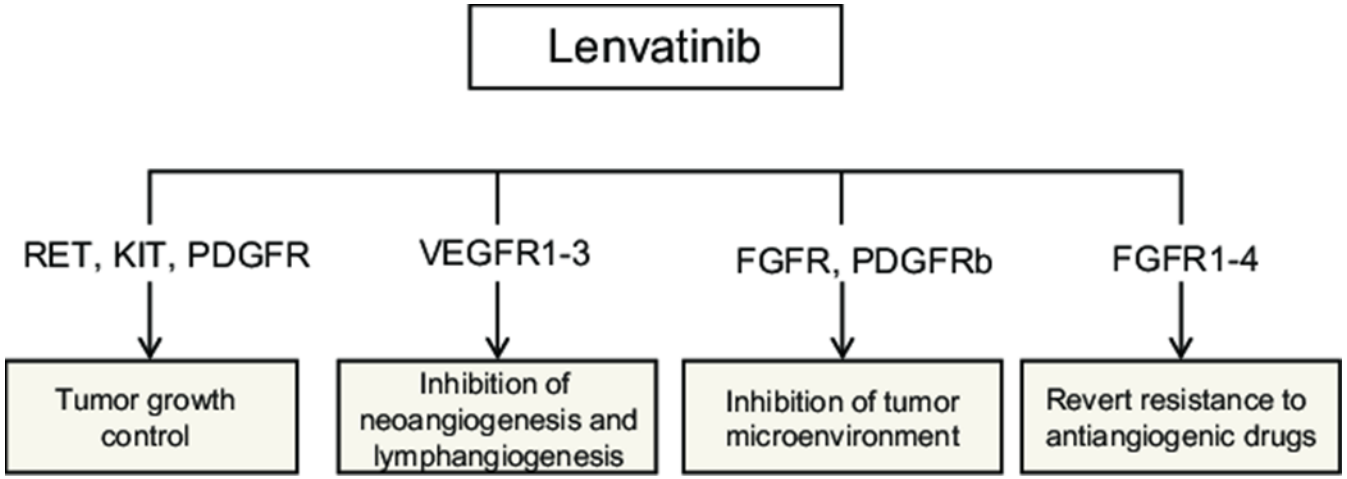




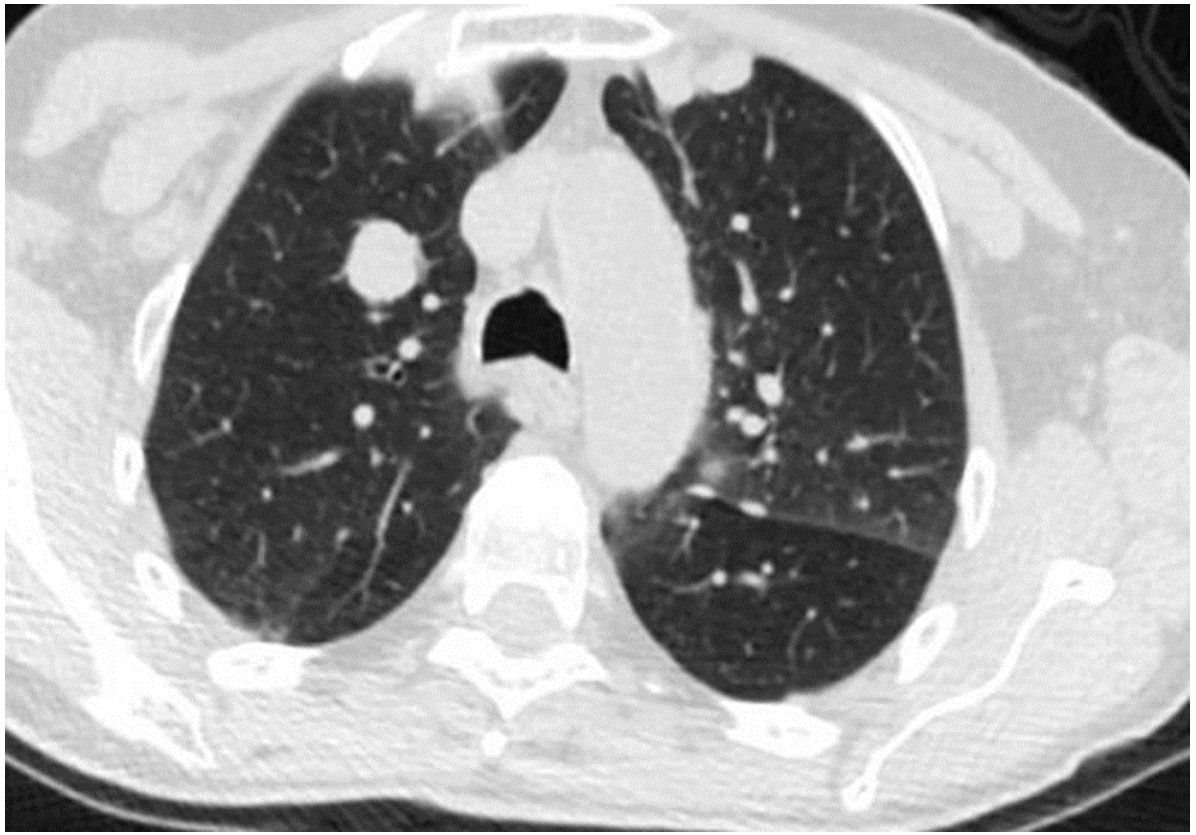
# S.M

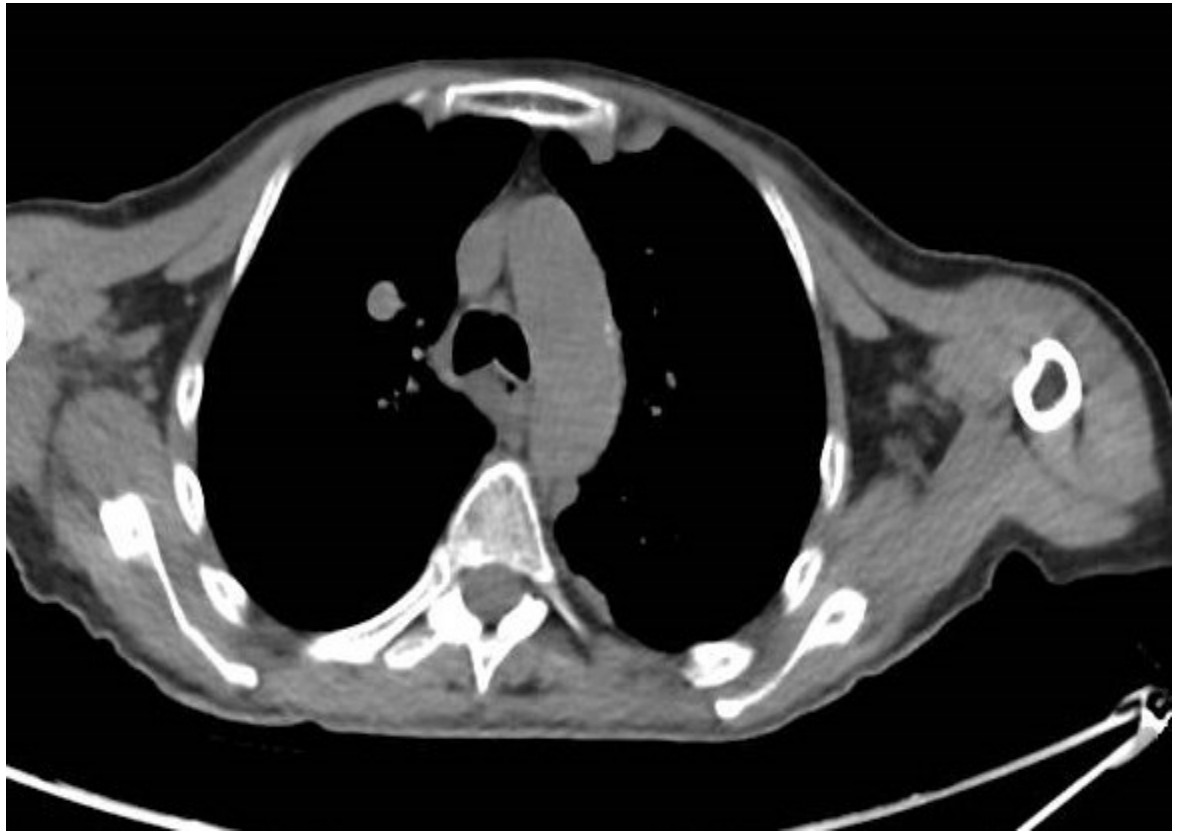
- **3/2020 – Lenvatinib - clinical radiological and laboratory improvement – resolution of respiratory symptoms**

  **Partial response**
- **Partially tolerable , hospitalization due to dehydration and GI S/E**



# 2/2020 -→6/2020





# Phase 3 trial - DECISION

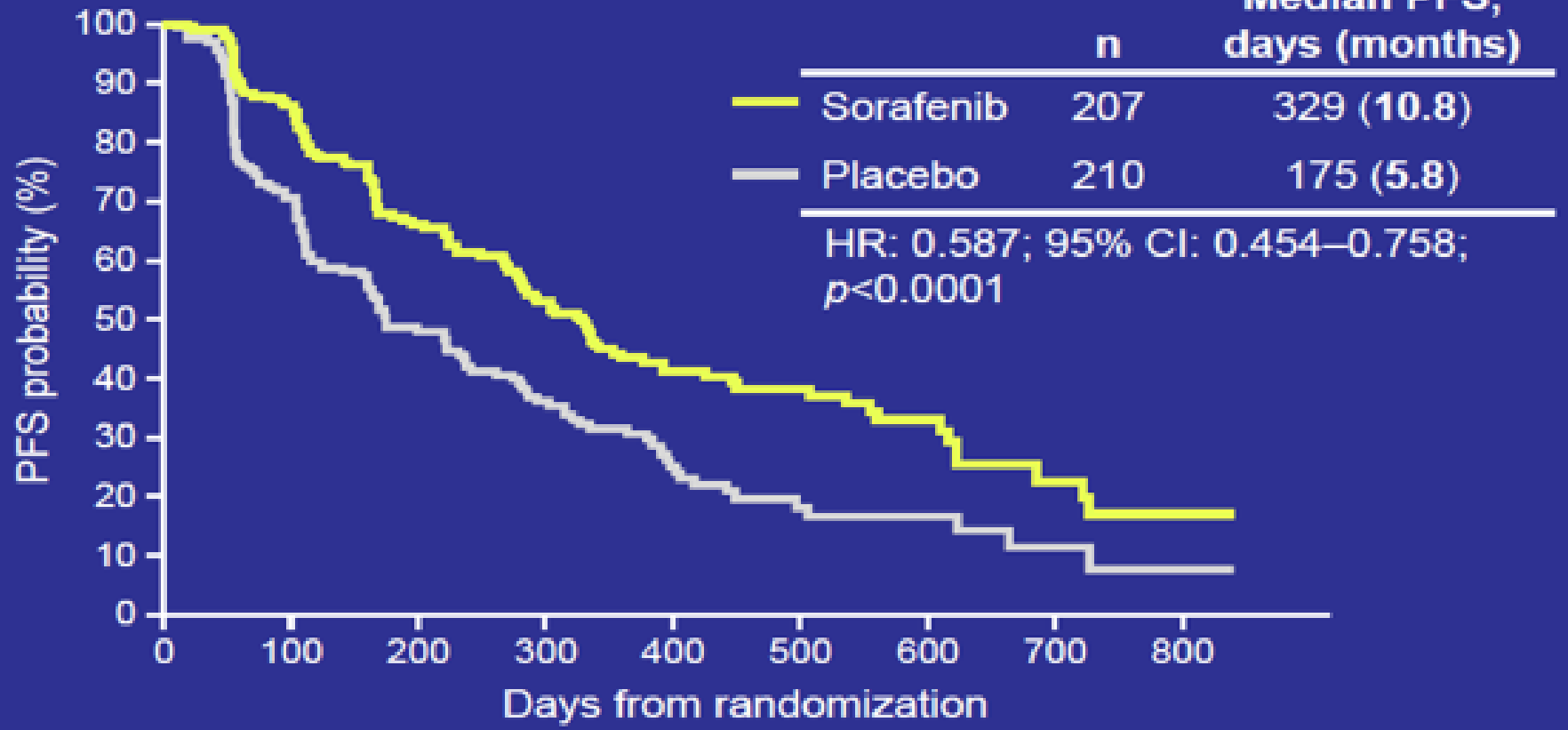
stuDy of sorafEnib in loCally advanced or metastatIc patientS with radioactive Iodine refractory thyrOid caNcer

- **Randomized, double-blind, phase 3**
- **417 חולים שגויסו בין 2009 ל-2011**

1. מחלה עמידה ליוד
2. מחלה גרורתית או אגרסיבית מקומית
3. התקדמות ב-14 חודשים אחרונים (RECIST)
4. ללא טיפולים סיסטמיים קודמים

Brose et al. Lancet 2014

# Progression-free survival
## (by independent central review)




| | n | Median PFS, days (months) |
|---|---|---|
| Sorafenib | 207 | 329 (**10.8**) |
| Placebo | 210 | 175 (**5.8**) |

HR: 0.587; 95% CI: 0.454–0.758; $p<0.0001$

Full analysis set.
CI, confidence interval; HR, hazard ratio; PFS, progression-free survival

# Most common treatment-emergent AEs
## (double-blind period)

| AE*, % | Sorafenib (n=207) | | Placebo (n=209) | |
|---|---|---|---|---|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| Hand–foot skin reaction | 76.3 | 20.3 | 9.6 | 0 |
| Diarrhea | 68.6 | 5.8 | 15.3 | 1.0 |
| Alopecia | 67.1 | 0 | 7.7 | 0 |
| Rash/desquamation | 50.2 | 4.8 | 11.5 | 0 |
| Fatigue | 49.8 | 5.8 | 25.4 | 1.4 |
| Weight loss | 46.9 | 5.8 | 13.9 | 1.0 |
| Hypertension | 40.6 | 9.7 | 12.4 | 2.4 |
| Metabolic – lab (other) | 35.7 | 0 | 16.7 | 0 |
| Anorexia | 31.9 | 2.4 | 4.8 | 0 |
| Oral mucositis | 23.2 | 1.0 | 3.3 | 0 |
| Pruritus | 21.3 | 1.0 | 10.5 | 0 |
| Nausea | 20.8 | 0 | 11.5 | 0 |
| Hypocalcemia | 18.8 | 9.2 | 4.8 | 1.4 |

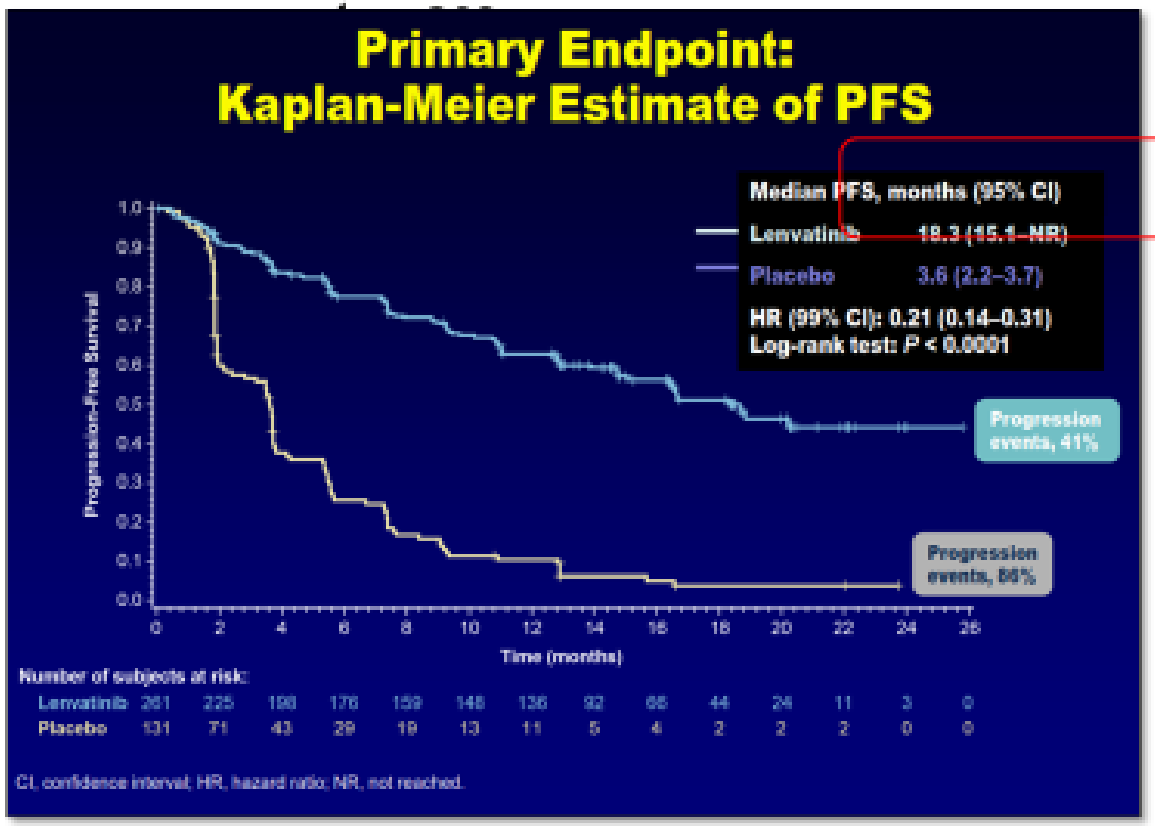
*National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 3.0

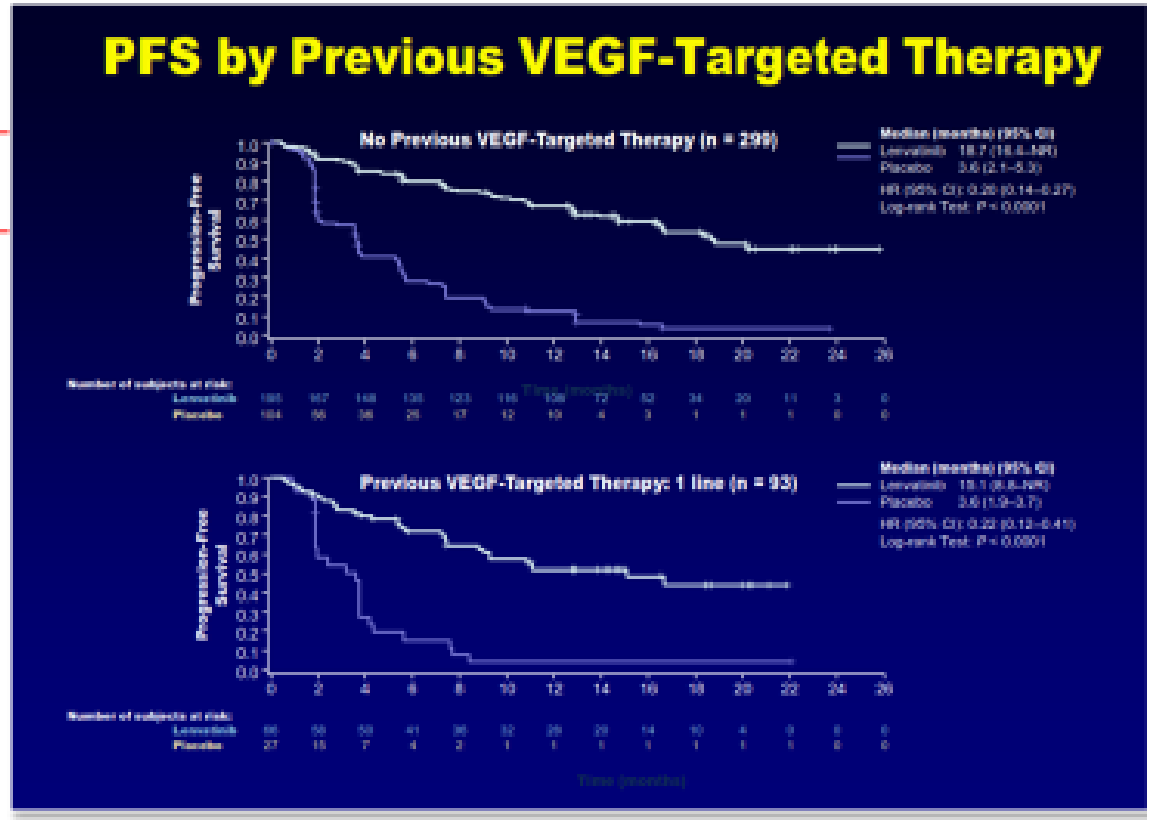
# סיכום המחקר

- **Sorafenib יעיל: הארכת PFS מ-5.8 חודשים ל-10.8 חודשים**
- **אין קורלציה עם מוטציות ב-BRAF או RAS**
- **פרופיל בטיחות: נסבל תחת לווי והתאמת מינון**

**למי להציע: מחלה בגודל משמעותי (מעל 2-1 ס״מ), התקדמות מהירה**

# SELECT trial – phase 3 Lenvatinib




Schlumberger et al. NEJM 2015

# Systemic treatment – All comers

- **תרופות מאושרת FDA – Sorafenib, Lenvatinib**
- **PFS – DECISION - Sorafenib 10.8 לעומת 5.8 חודשים**
- **PFS – SELECT – Lenvatinib 18.3 לעומת 3.6 חודשים**
- **מאפיינים:**
  - **השפעה לשנה-עד שלוש שנים, ואז בד"כ escape**
  - **ברוב החולים partial response, אחוז תגובה 50-70%**
  - **ב-Lenvatinib 2% עם רמיסיה מלאה**
  - **תופעות לוואי משמעותיות , מצריכות ניטור.**


- **להתחיל בזמן הנכון – כאשר המחלה בשלב גדילה מהירה, אבל לא מאוחר מדי**

# Initiation of treatment

- The timing of initiation of systemic therapy is one of the biggest challenges clinicians face when treating patients with RR-DTC.
- For patients with RR-DTC who are asymptomatic and have pulmonary nodules that are small (< 1 cm) and unchanging or slowly progressive (doubling every 5 years), a "watch and wait" approach can be employed as in the short-term they tend to have a good quality of life .
- It is crucial to monitor the disease carefully as progression may occur before patients become symptomatic

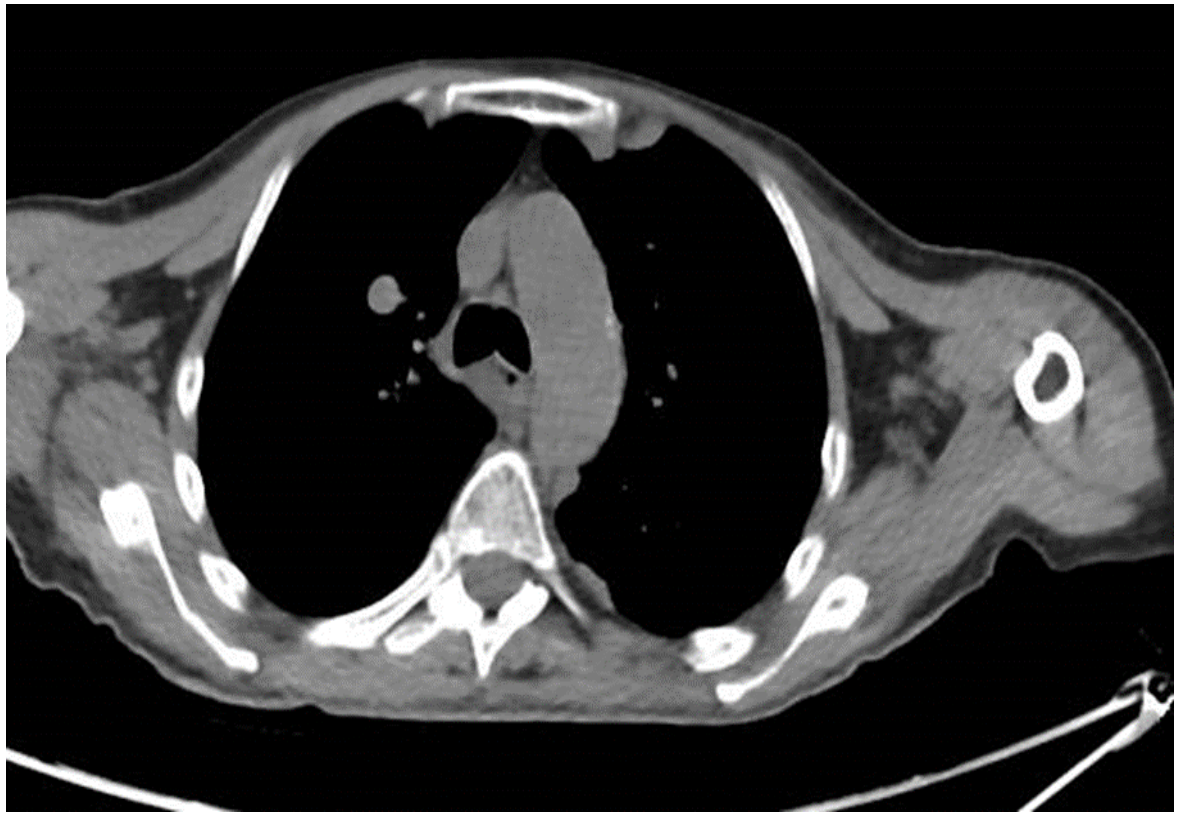
# S.M

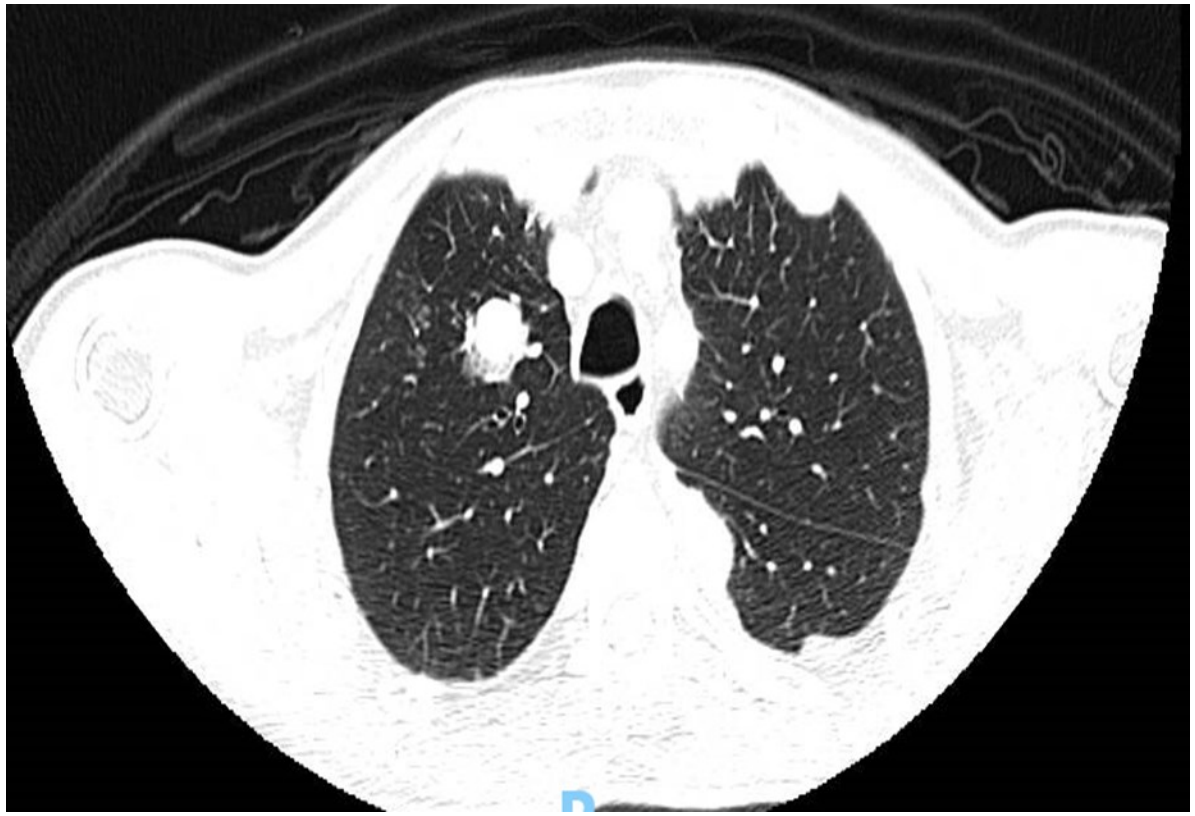
- **Tolerate suboptimal dose**

- **1/2021 – PD**

  **Brain MRI with brain Mets**

# 6/20->1/21





# NGS

## Biomarker Findings

**Microsatellite status** - MS-Stable

**Tumor Mutational Burden** - 0 Muts/Mb

## Genomic Findings

*For a complete list of the genes assayed, please refer to the Appendix.*

***RET*** NCOA4-RET fusion

***CREBBP*** G757fs*17

***NOTCH1*** L1579del

***TERT*** promoter -124C>T

# S.M

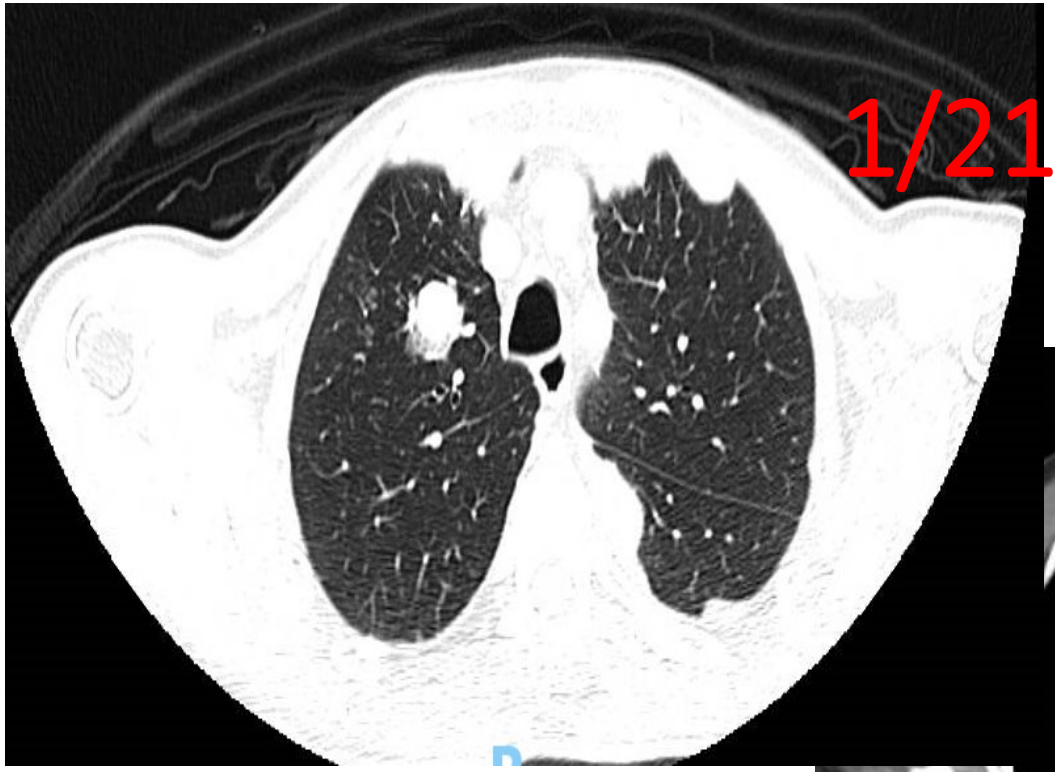
- **3/2021 – Pralsetinib – selective RET fusion inhibitor**

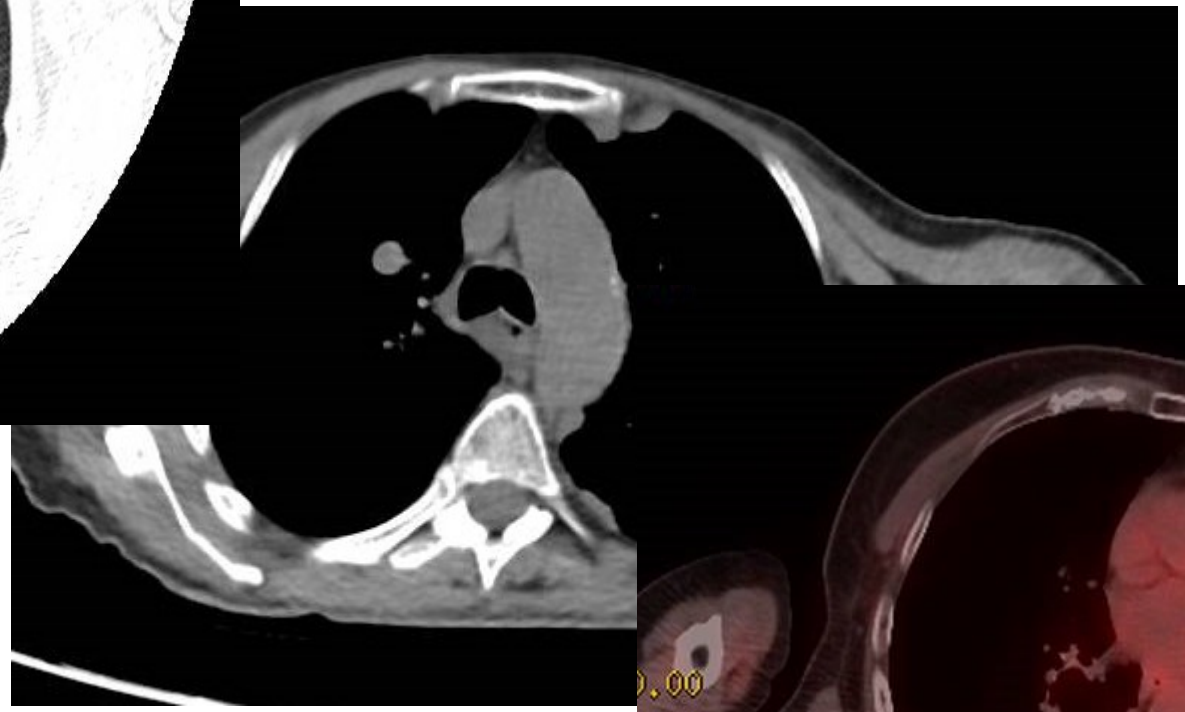
- **10/2021 – Clinical improvement**

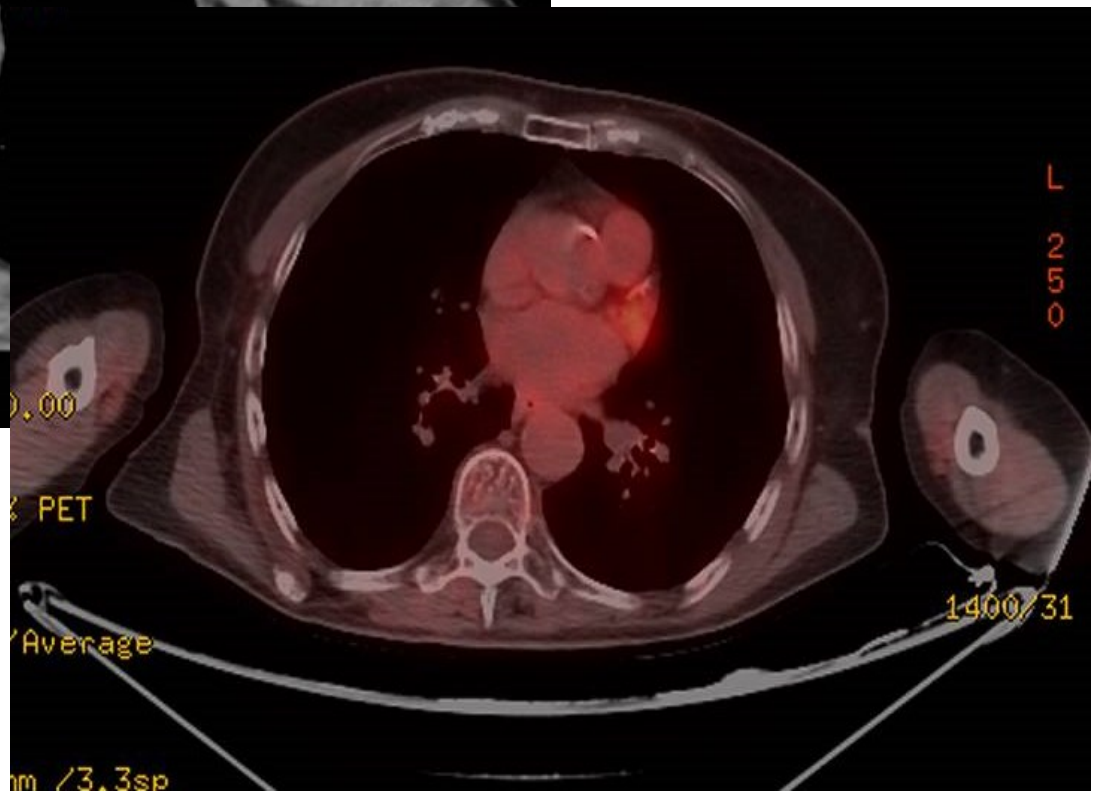
  **laboratory – TG 960 -→13**

  **Radiological – Regression of 98% of the disease almost metabolic CR**

# 1/21->4/21->9/22







# Pralsetinib Phase 1/2 ARROW study

Phase 2 study design

- Advanced solid tumors
- RET-altered (local testing)
- No other driver mutations
- ECOG PS 0-1

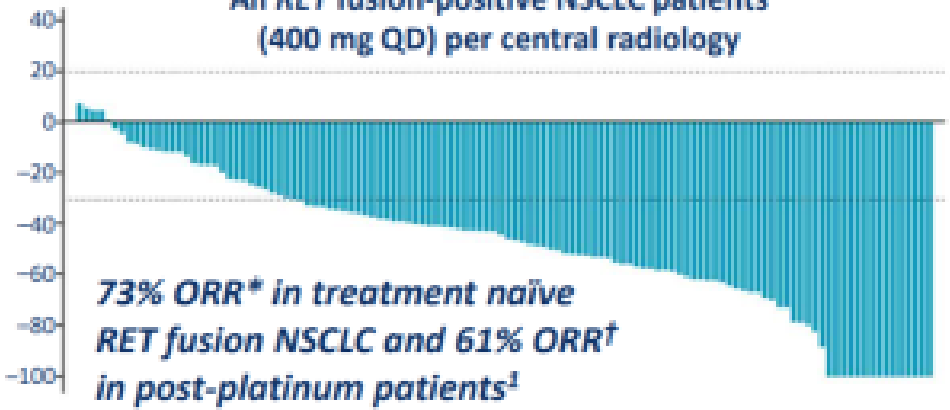
**Pralsetinib dosing: 400 mg PO QD**

- *RET* fusion-positive NSCLC
- *RET* mutation-positive MTC
- *RET* fusion-positive other tumors

**Primary endpoints**

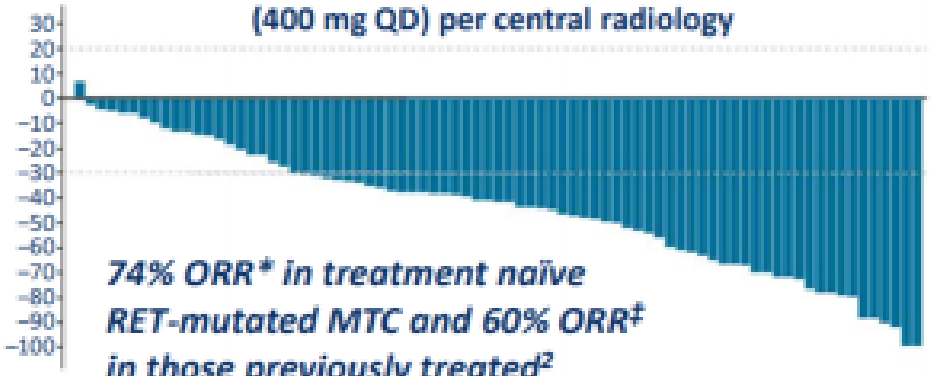
- **Centrally reviewed ORR per RECIST v1.1**
- **Safety**

**All *RET* fusion-positive NSCLC patients (400 mg QD) per central radiology**




***73% ORR* in treatment naïve RET fusion NSCLC and 61% ORR† in post-platinum patients[1]***

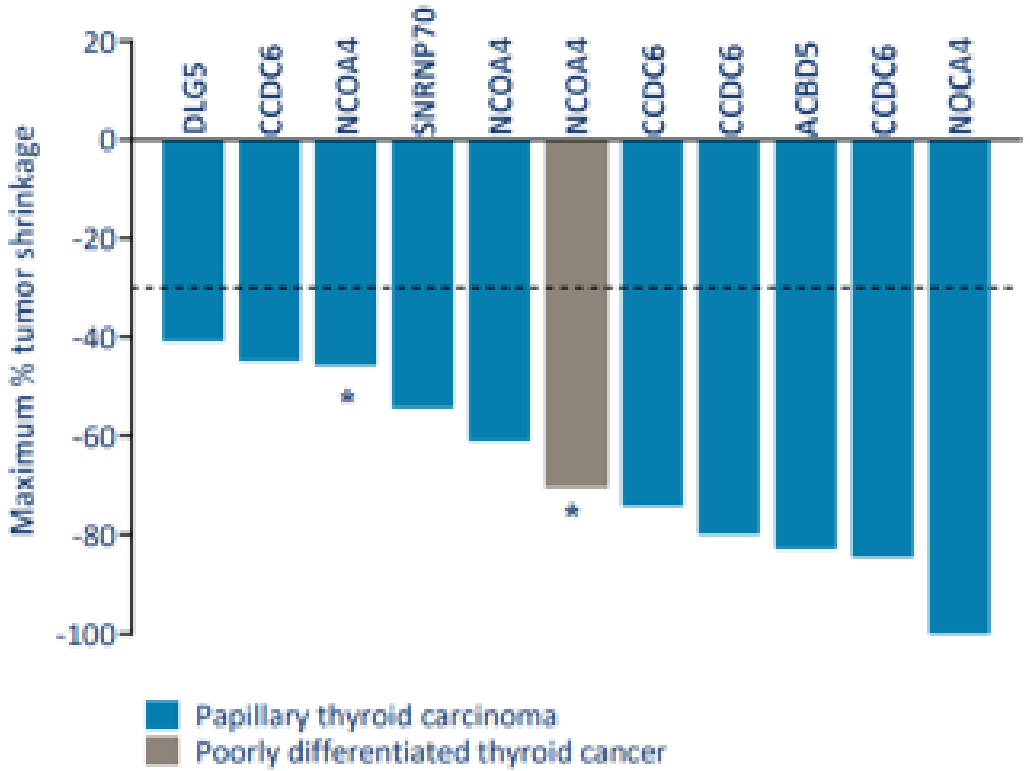
**All *RET* mutant MTC patients (400 mg QD) per central radiology**




***74% ORR* in treatment naïve RET-mutated MTC and 60% ORR‡ in those previously treated[2]***

ARROW is registered with clinicaltrials.gov (NCT03037385). Data cutoff: November 18, 2019. AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance score;

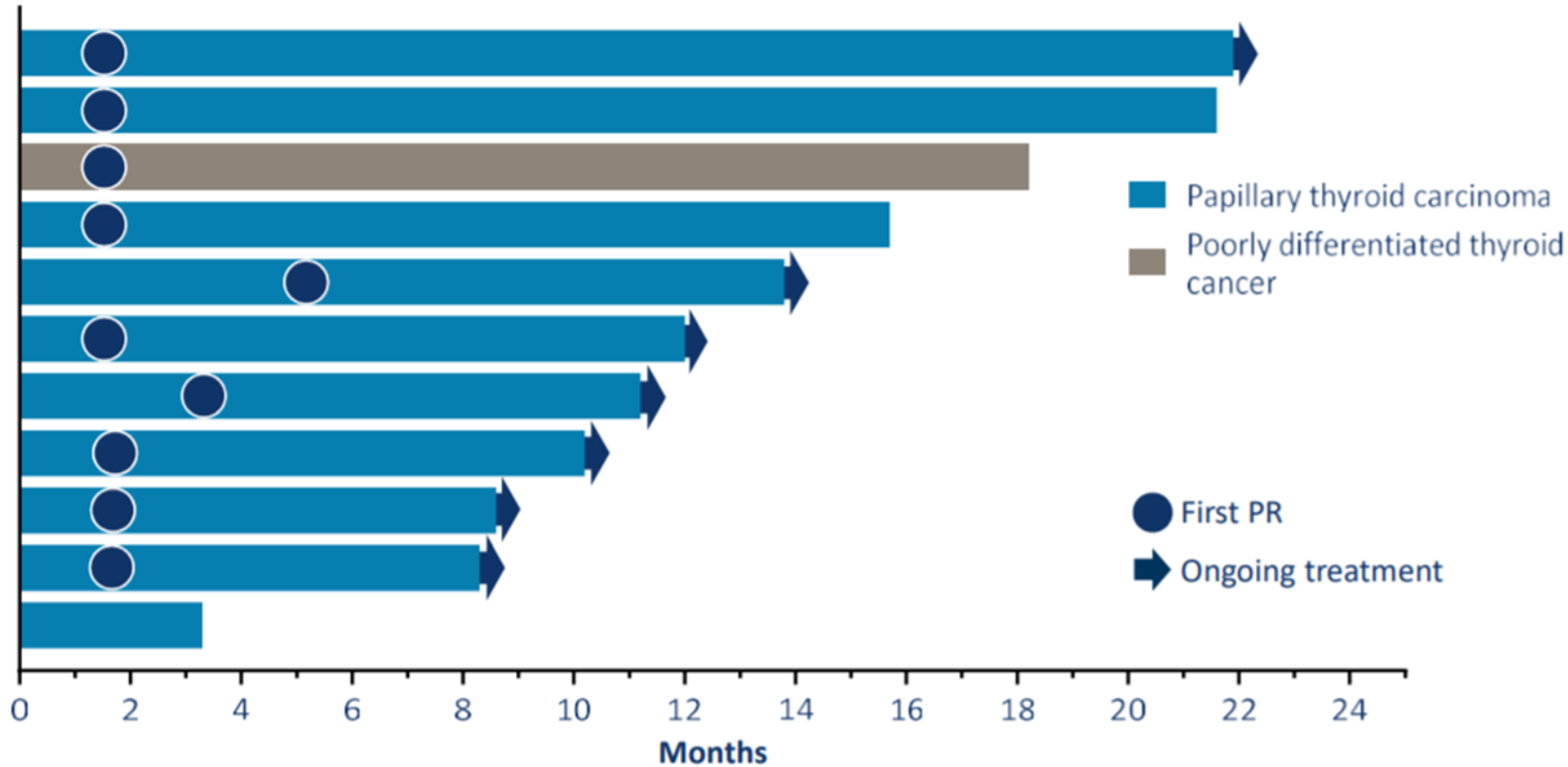
# Activity of pralsetinib in *RET* fusion-positive thyroid tumors




| Best response, (response evaluable), % | RET fusion-positive thyroid cancer (n=11)† |
|---|---|
| ORR (95% CI) | 91 (59–100) |
| PR | 91 |
| SD | 9 |
| PD | 0 |
| DCR (95% CI) | 100 (72–100) |

Blinded independent central review of tumor response; response-evaluable patients enrolled by Jul 11, 2019, as of a data cut-off Feb 13, 2020. *Patients initially received alternate pralsetinib starting doses in the dose-escalation study portion, but subsequently transitioned to 400 mg QD. †Response-evaluable population excludes two patients with papillary thyroid carcinoma without measurable disease at baseline per blinded central review. These two patients were assessed with CR and SD, and continue treatment at 12.9 and 23.3 months, respectively. CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, overall response rate; PD, progressive disease; PR, partial response; RET, rearranged during transfection; SD, stable disease.

# Pralsetinib treatment duration in patients with *RET* fusion-positive thyroid cancer




Blinded independent central review of tumor response; response-evaluable patients enrolled by Jul 11, 2019, as of a data cut-off Feb 13, 2020. PR, partial response.

# Conclusions

- Pralsetinib has broad and durable antitumor activity with multiple advanced solid tumor types
  - 91% ORR and 100% DCR in RET fusion thyroid cancer
  - 50% ORR* and 92% DCR across various other RET fusion-positive solid tumors
    - Including responses in RET fusion-positive cholangiocarcinoma, pancreatic tumors, and neuroendocrine tumors
- Pralsetinib was well-tolerated, and its safety profile was consistent across the overall population treated
- The ARROW study is still ongoing and currently continues to enroll patients with various RET fusion-positive solid tumors

VIRTUAL 2020 ESMO congress

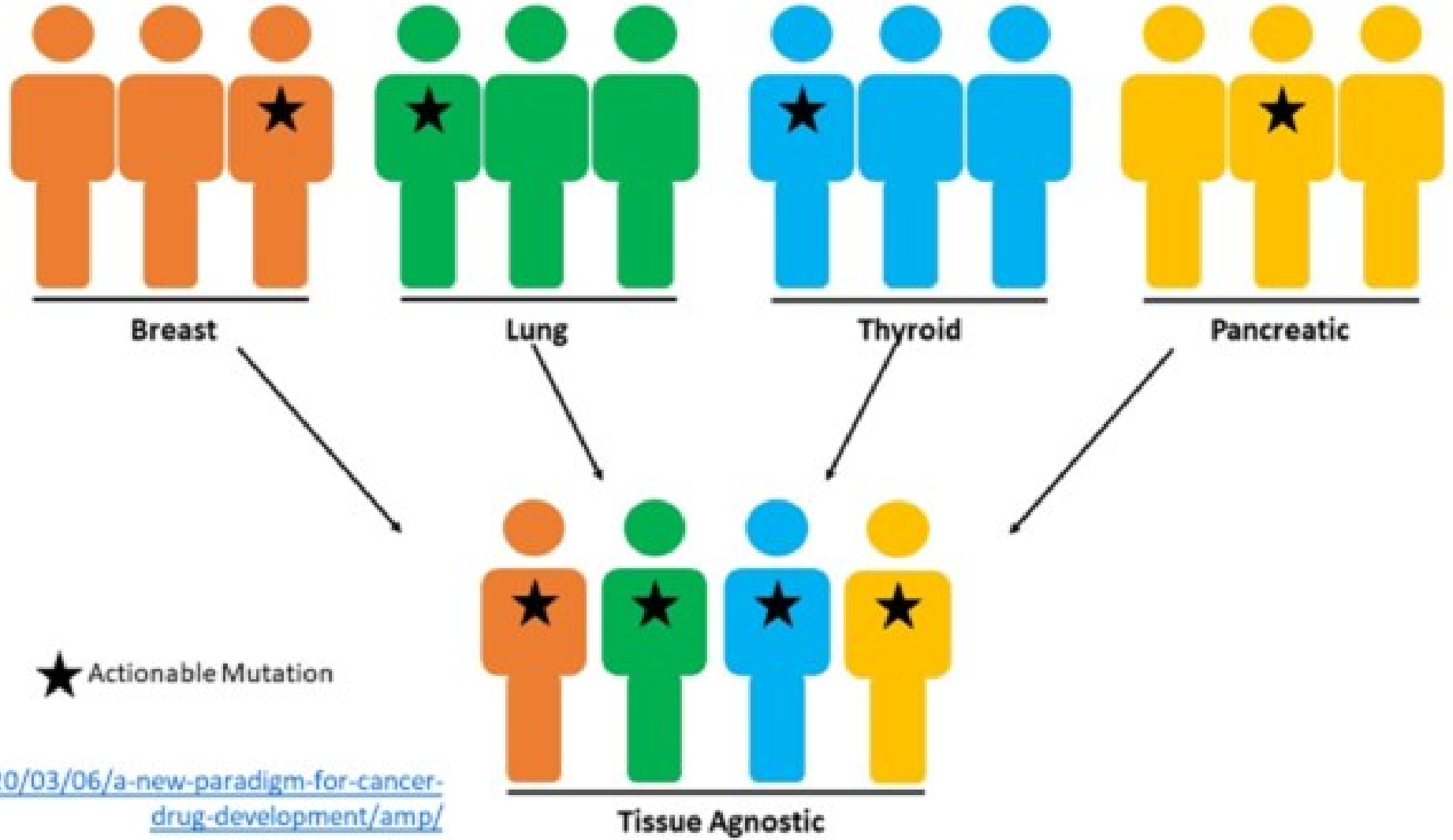
# Pralsetinib safety profile (all tumor types)

| TRAEs in ≥15% of patients | Pralsetinib 400 mg QD (N=438) | |
|---|---|---|
| | All grades | Grade ≥3 |
| Aspartate aminotransferase increased | 34% | 2% |
| Anemia | 24% | 8% |
| Alanine aminotransferase increased | 23% | 2% |
| Constipation | 23% | 1% |
| Hypertension | 22% | 11% |
| White blood cell count decreased | 18% | 3% |
| Neutropenia | 18% | 10% |
| Neutrophil count decreased | 16% | 6% |
| Hyperphosphatemia | 15% | 1% |

- Pralsetinib was well tolerated
- TRAEs were primarily Grade 1–2 and reversible
- 4% of patients discontinued due to TRAEs
- Median dose intensity was 92% (range 18–100)

Data cut-off February 12, 2020. TRAE, treatment-related adverse event

# A paradigm shift: Some (different) tumors may be “the same”




https://oncobites.blog/2020/03/06/a-new-paradigm-for-cancer-drug-development/amp/

MUNICH 2018 ESMO congress

# Efficacy and safety of entrectinib in patients with *NTRK* fusion-positive tumours: pooled analysis of STARTRK-2, STARTRK-1 and ALKA-372-001

Demetri GD[1], Paz-Ares L[2], Farago AF[3], Liu SV[4], Chawla SP[5], Tosi D[3], Kim ES[6], Blakely C[7], Krauss JC[8], Sigal D[9], Bazhenova L[10], John T[11], Besse B[12], Wolf J[13], Seto T[14], Chow-Maneval E[15], Multani PS[15], Johnson A[15], Simmons B[16], Doebele RC[17]

[1]Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [2]Hospital Universitario Virgen del Rocio, Sevilla, Spain; [3]Massachusetts General Hospital, Boston, MA, USA; [4]Georgetown University, Washington, DC, USA; [5]University of California Los Angeles, Los Angeles, CA, USA; [6]Carolinas Healthcare System, Charlotte, NC, USA; [7]University of California San Francisco, San Francisco, CA, USA; [8]University of Michigan, Ann Arbor, MI, USA; [9]Scripps Clinic, La Jolla, CA, USA; [10]University of California San Diego, San Diego, CA, USA; [11]Olivia Newton-John Cancer Research Institute, Austin Health, Heidelberg, Victoria, Australia; [12]Gustave Roussy Cancer Campus, Villejuif Cedex, France; [13]University Hospital of Cologne, Cologne, Germany; [14]National Kyushu Cancer Center, Fukuoka, Japan; [15]Ignyta, Inc., San Diego, CA, USA; [16]Genentech, South San Francisco, CA, USA; [17]University of Colorado, Aurora, CO, USA

esmo.org

# Integrated efficacy and safety analysis of entrectinib: *NTRK* fusion-positive solid tumours

**Integrated analysis**

**Efficacy population**[§]

54 adult patients with *NTRK* fusion-positive, TRK inhibitor-naïve solid tumours

**Safety population**

355 patients overall have received entrectinib (all tumour types and gene rearrangements)

**STARTRK-2**[1]
Phase II, multicentre, global basket study 600mg QD, 28-day cycle
**n=51 *NTRK*+ patients**

**STARTRK-1**[2]
Phase I dose escalation
**n=2 *NTRK*+ patients**

**ALKA-372-001**[2]
Phase I dose escalation
**n=1 *NTRK*+ patient**

**Primary endpoints***
ORR and DoR

**Secondary endpoints***
PFS and OS

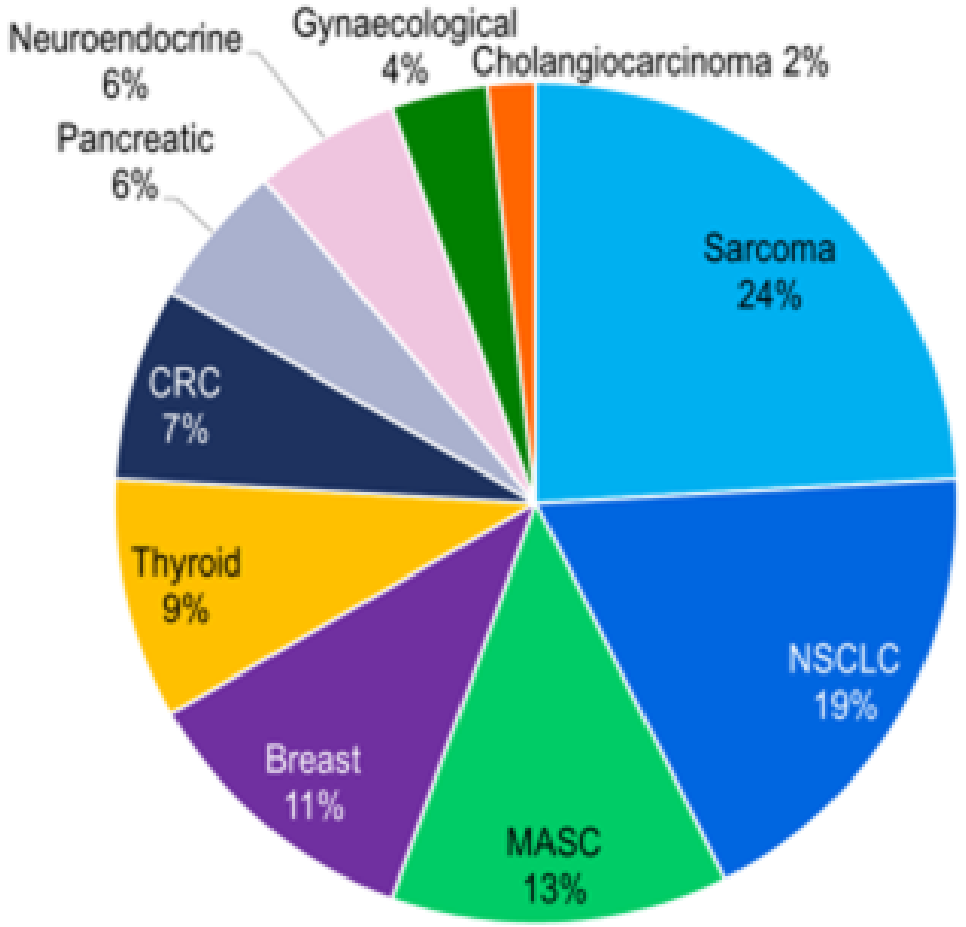
Intracranial ORR and DoR[†]

Safety and tolerability

Data cut-off 31 May 2018

# Baseline characteristics: Adult patients with *NTRK* fusion-positive solid tumours

| Baseline characteristics | | *NTRK*+ patients (n=54) |
|---|---|---|
| Age, years | Median (range) | 57.5 (21–83) |
| Sex, % | Female | 59.3 |
| | Male | 40.7 |
| Race, % | White | 79.6 |
| | Asian | 13.0 |
| ECOG PS, % | 0 | 42.6 |
| | 1 | 46.3 |
| | 2 | 11.1 |
| **Prior lines of systemic therapy, %** | **0** | **37.0** |
| | **1** | **20.4** |
| | **≥2** | **42.6** |
| **CNS mets at baseline, %** | | **22.2** |

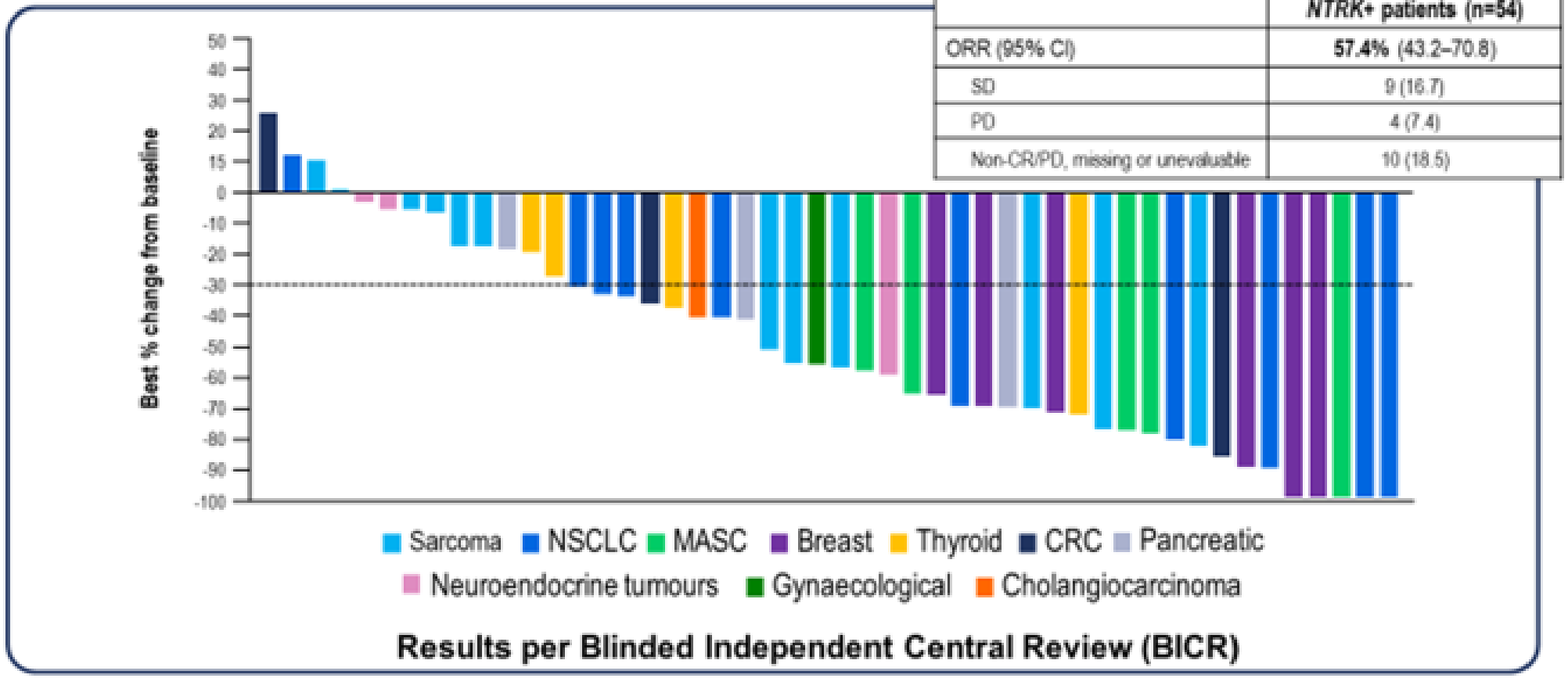



Data cut-off date: 31 May 2018

CRC: colorectal cancer; ECOG PS: Eastern Cooperative Oncology Group performance status;

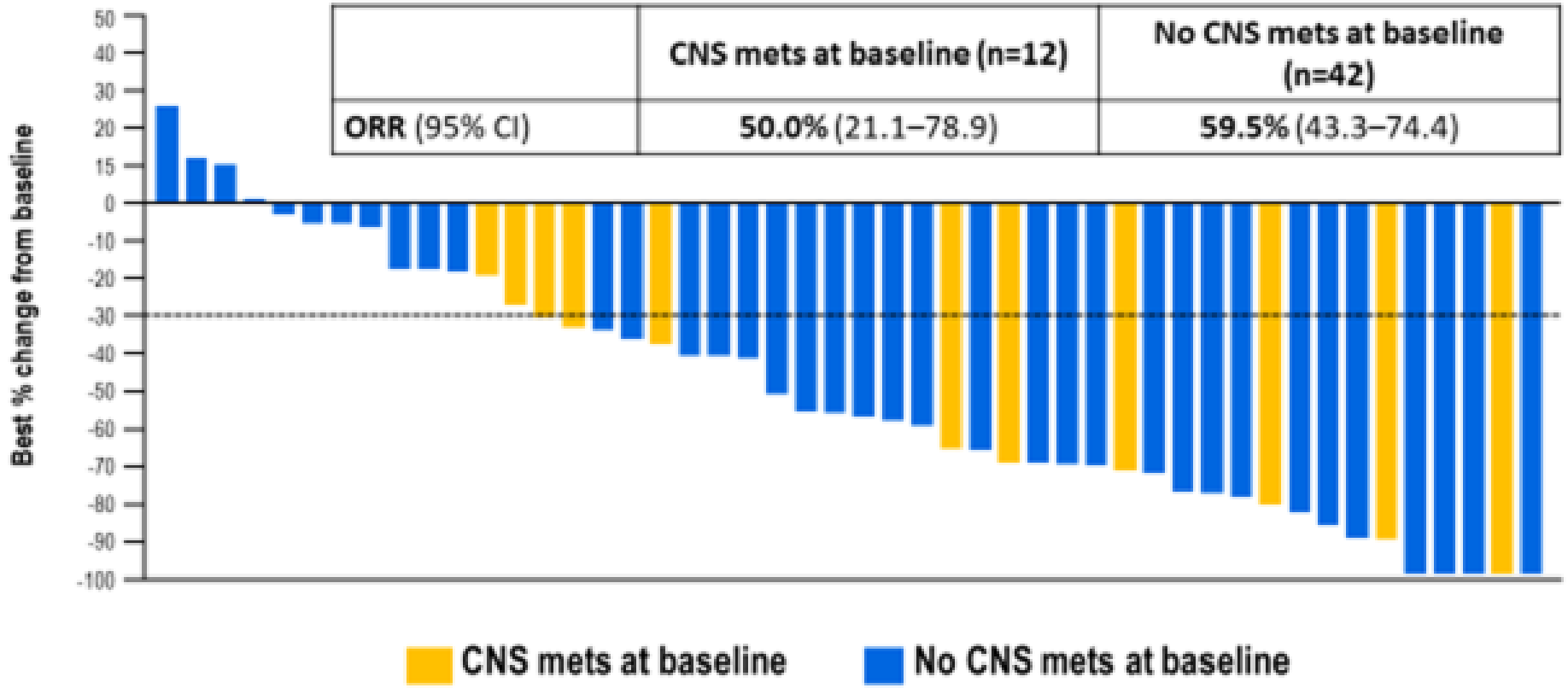
# Entrectinib activity in *NTRK* fusion-positive solid tumours: individual patient responses by tumour type

| | *NTRK*+ patients (n=54) |
|---|---|
| ORR (95% CI) | **57.4%** (43.2–70.8) |
| SD | 9 (16.7) |
| PD | 4 (7.4) |
| Non-CR/PD, missing or unevaluable | 10 (18.5) |



# Entrectinib activity in *NTRK* fusion-positive solid tumours: Individual patient responses by CNS mets status at baseline

| | CNS mets at baseline (n=12) | No CNS mets at baseline (n=42) |
|---|---|---|
| **ORR** (95% CI) | **50.0%** (21.1–78.9) | **59.5%** (43.3–74.4) |

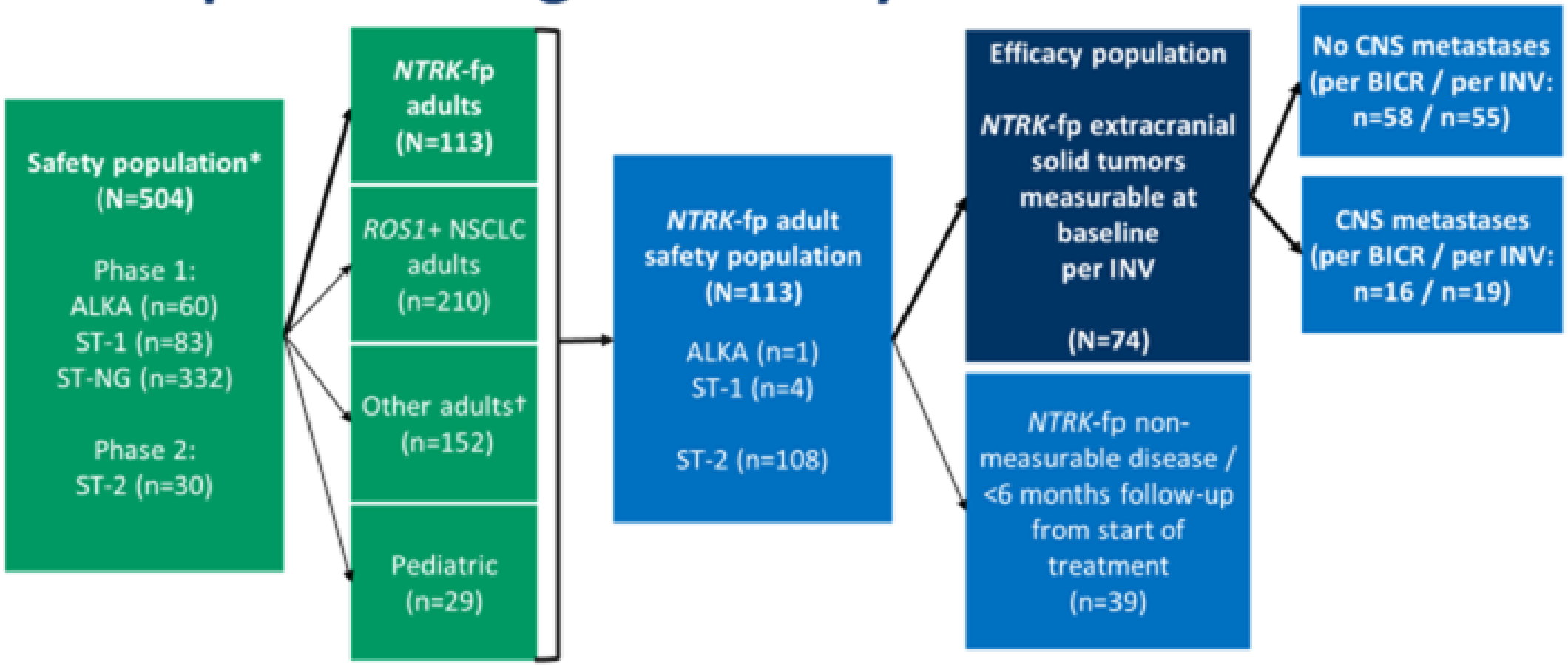



Cut-off date: 31 May 2018

# Efficacy and Safety of Entrectinib in Patients (pts) with NTRK Fusion-Positive (NTRK-fp) Solid Tumors: An Updated Integrated Analysis

Rolfo C, De Braud F, Doebele RC, Drilon A, Siena S, Patel MR, Cho BC, Liu SV, Ahn MJ, Chiu CH, Farago AF, Goto K, Lee J, Bazhenova L, John T, Fakih M, Simmons B, Pitcher B, Huang X, Demetri GD

# Efficacy and safety populations enrolled in the updated integrated analysis



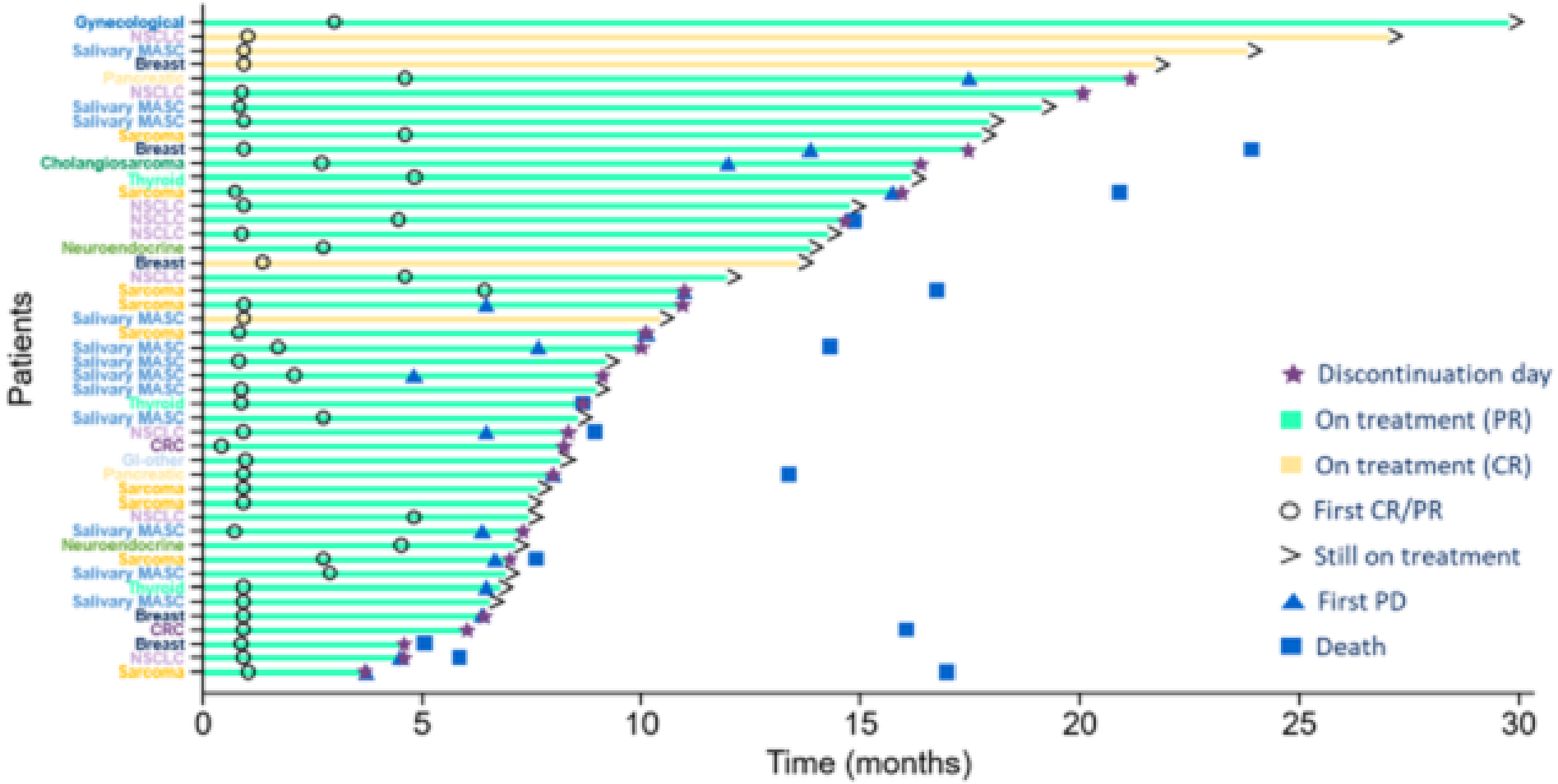

*Received ≥1 entrectinib dose. †*ROS1*+ non-NSCLC, *ALK* fusion-positive, no gene fusion. INV, investigator; BICR, blinded independent central review. CNS, central nervous system.

# Systemic efficacy per BICR in patients with NTRK-fp solid tumors

| Parameter | Efficacy population (N=74) | Baseline CNS metastases‡ (n=16) | No baseline CNS metastases‡ (n=58) |
|---|---|---|---|
| **ORR***, n (%) | 47 (**63.5**) | 10 (**62.5**) | 37 (**63.8**) |
| Complete response, n (%) | 5 (6.8) | 0 | 5 (8.6) |
| Partial response, n (%) | 42 (56.8) | 10 (62.5) | 32 (55.2) |
| **DoR*** | | | |
| Median, months | 12.9 | 6.0 | 12.9 |

*BICR assessed, RECIST v1.1. ‡CNS metastases status determined by BICR. NE, not estimable.

# Time on treatment: responders



# Entrectinib in patients with NTRK-fp solid tumors

**Clinically meaningful responses** in *NTRK*-fp solid tumors



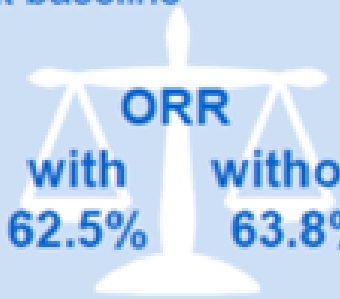
**ORR 63.5%**

**Durable disease control**

**DoR 12.9 months**
vs previous 10.4



Systemic efficacy **irrespective** of presence or absence of CNS metastases at baseline




**Strong intracranial efficacy** in patients with CNS metastases at baseline



**Intracranial ORR 50.0%**

2020 ASCO ANNUAL MEETING

Rolfo, et al. ASCO 2020. Poster P335

approval received June 22 FDA

# Novartis Tafinlar + Mekinist receives FDA approval for first tumor-agnostic indication for BRAF V600E solid tumors

Jun 23, 2022

- *Tafinlar + Mekinist, the worldwide targeted therapy leader in BRAF/MEK-inhibition, is the first and only therapy to be approved with a tumor-agnostic indication for adult and pediatric patients with solid tumors that have a BRAF V600E mutation*[1,2]
- *Approval supported by results from Phase II ROAR and NCI-MATCH studies demonstrating overall response rates up to 80% in patients with BRAF V600E solid tumors*[1,2]
- *BRAF mutations drive tumor growth across more than 20 tumor types, including thyroid, brain and gynecologic cancers*[3,4]

**Wording:** Treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Limitations of Use: TAFINLAR is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition.

# Prevalence of *BRAF* V600 mutation across diverse cancers

**Select Haematologic Cancers***

**CLL:** ≈ 3%
**HCL:** ≈ 100%
**MM:** ≈ 6%

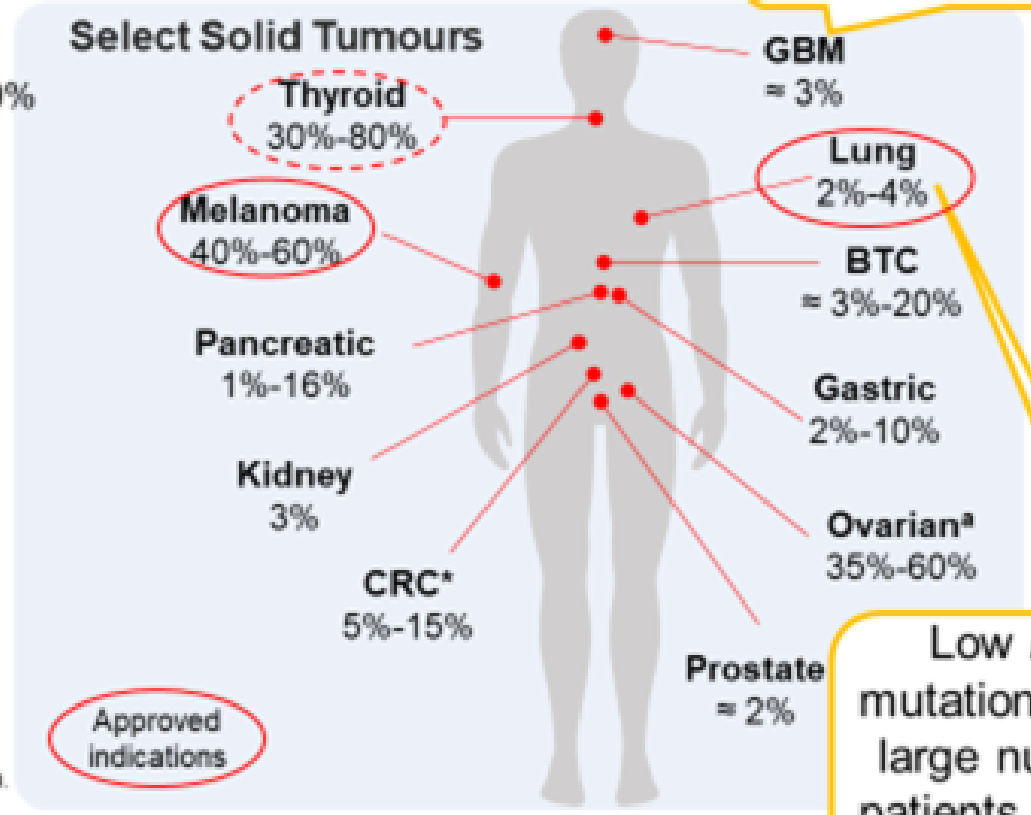
**LCH:** 25%-≈ 40%

High *BRAF* mutation rate

Rare tumour type: Phase III recruitment is challenging

* **US/Japan:** Tumour-agnostic indication will be sought for patients with rare solid tumours. CRC (US) and haematologic malignancies will not be included

**Select Solid Tumours**




Limited effective treatment options

Low *BRAF* mutation rate, but large number of patients who may benefit

BTC, biliary tract cancer; CLL, chronic lymphocytic leukaemia; CRC, colorectal cancer; GBM, glioblastoma; HCL, hairy cell leukemia; LCH, Langerhans cell histiocytosis; MM, multiple myeloma.
[a] Serous borderline and low-grade serous subtypes.
1. Turski ML, et al. *Mol Cancer Ther.* 2016;15:533-547; 2. Pratilas C, et al. *Curr Top Microbiol Immunol.* 2012;355:82-98.

# Evidence in differentiated Thyroid Cancer

THYROID
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BRAF Inhibitor Dabrafenib in Patients with Metastatic *BRAF*-Mutant Thyroid Cancer

Gerald S. Falchook,[1,*] Michael Millward,[2] David Hong,[3] Aung Naing,[3] Sarina Piha-Paul,[3] Steven G. Waguespack,[4] Maria E. Cabanillas,[4] Steven I. Sherman,[4] Bo Ma,[5] Martin Curtis,[5] Vicki Goodman,[5] and Razelle Kurzrock[6]

*Lancet Oncol* 2016 September ; 17(9): 1272–1282. doi:10.1016/S1470-2045(16)30166-8.

**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**

**Marcia S Brose, MD,**

**Dabrafenib vs dabrafenib + trametinib in *BRAF*-mutated radioactive iodine refractory differentiated thyroid cancer – results of a randomized, phase 2, open-label, multicenter trial**

**Running Title:** Dabrafenib vs dabrafenib + trametinib in DTC

*Naifa L. Busaidy, MD[1], *Bhavana Konda, MD, MPH[2], Lai Wei, PhD[3], Lori J. Wirth, MD[4],

# Vemurafenib for RAIR PTC

- Phase II, non randomized
- Two cohorts : cohort 1: naïve to TKI ( treated with taxanes and anthracyclines )
  cohort 2: previously treated with aaTKI
- Cohort 1: median PFS 18.2 mo
  median DOR – 16.5 mo
  median OS – NR
- Cohort 2: median PFS 8.9 mo
  median DOR – 7.4 mo
  median OS – 14.4 mo

2021 ESMO congress

# Cabozantinib Versus Placebo in Patients With Radioiodine-Refractory Differentiated Thyroid Cancer (DTC) Who Have Progressed After Prior VEGFR-Targeted Therapy: Updated Results From the Phase 3 COSMIC-311 Trial (NCT03690388)

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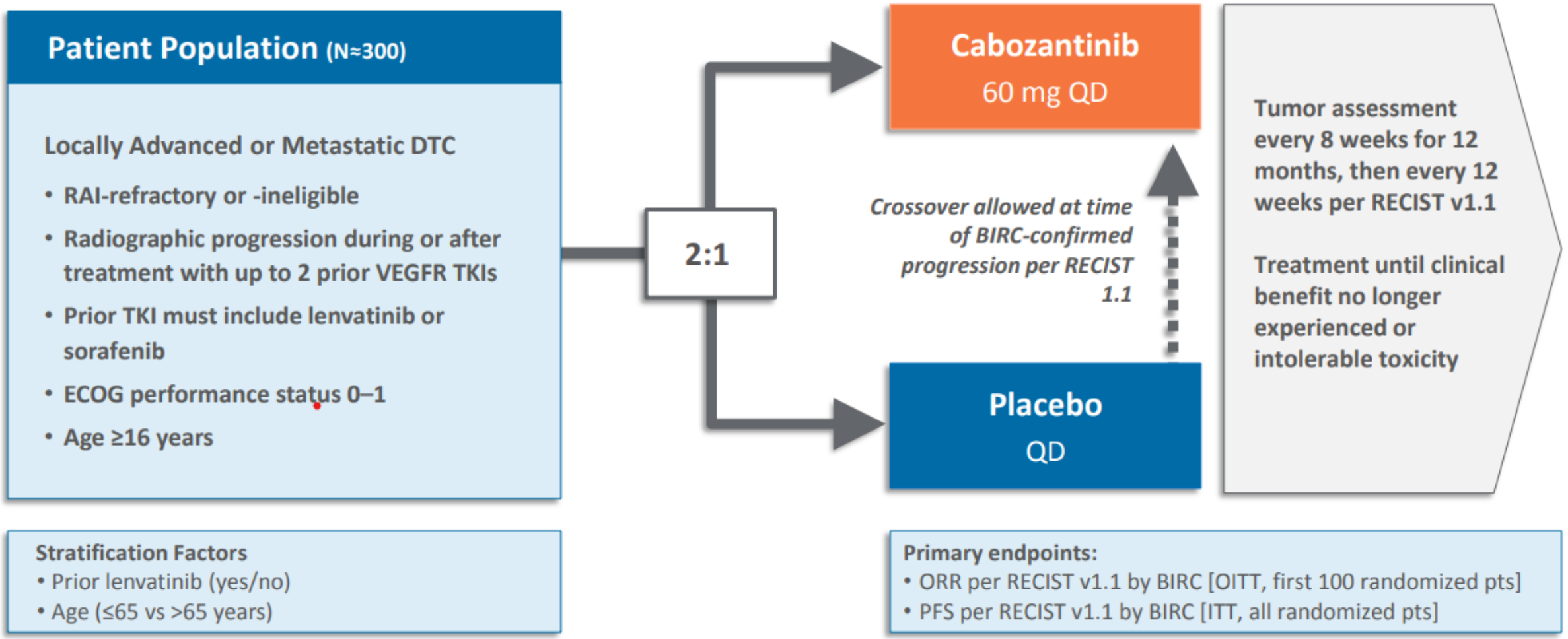
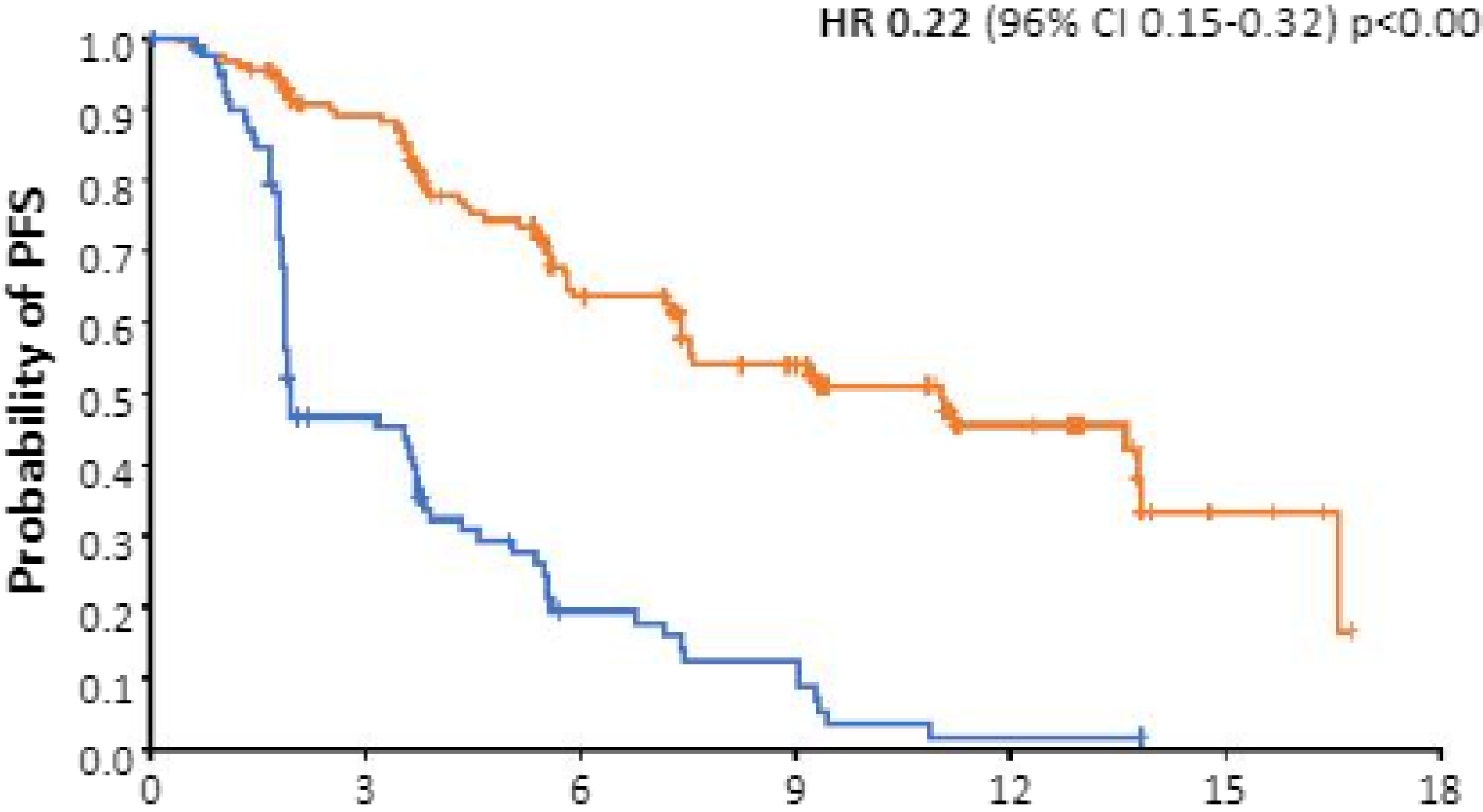
# COSMIC-311 Study Design




C, blinded independent radiology committee; ECOG, Eastern Cooperative Oncology Group; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors;




| Number at Risk | | | | | | | Nu |
|---|---|---|---|---|---|---|---|
| Cabozantinib | 170 | 117 | 59 | 41 | 20 | 4 | 0 |
| Placebo | 88 | 33 | 11 | 7 | 1 | 0 | 0 |

# COSMIC-311 Final Analysis: PFS, ORR

| Outcome | Cabozantinib (n = 170) | Placebo (n = 88) | HR |
|---|---|---|---|
| Median PFS by BIRC, mo | 11.00 | 1.9 | 0.22 (96% CI: 0.15-0.32; *P* <.0001) |
| Median OS, mo | 19.4 | NE | 0.76 (95% CI: 0.45-1.31) |
| ORR by BIRC, % | 11* | 0 | -- |

*Includes 1 CR.

- Trial continued to demonstrate significant improvement in primary endpoint of median PFS with cabozantinib vs placebo (*P* <.0001)

Capdevila. ESMO 2021. Abstr LBA67.

Slide credit: clinicaloptions.com

# COSMIC-311 Final Analysis: PFS by Prior Therapy

| Median PFS, Mo | Cabozantinib | Placebo | HR (95% CI) |
|---|---|---|---|
| Prior sorafenib/no lenvatinib | n = 63<br>16.6 | n = 33<br>3.2 | 0.13 (0.06-0.26) |
| Prior lenvatinib/no sorafenib | n = 68<br>5.8 | n = 34<br>1.9 | 0.28 (0.16-0.48) |
| Prior lenvatinib and sorafenib | n = 39<br>7.6 | n = 21<br>1.9 | 0.27 (0.13-0.54) |

- PFS improvement with cabozantinib vs placebo consistent across subgroups defined by prior exposure to sorafenib and/or lenvatinib

Capdevila. ESMO 2021. Abstr LBA67.

# COSMIC-311 Final Analysis: Safety

| AEs in ≥15% of Patients, % | Cabozantinib (n = 170) | | Placebo (n = 88) | |
|---|---|---|---|---|
| | Any Gr | Gr 3/4 | Any Gr | Gr 3/4 |
| Any | 98 | 62 | 85 | 28 |
| Diarrhea | 62 | 8 | 3 | 0 |
| Hand-foot skin reaction | 47 | 10 | 1 | 0 |
| Hypertension | 32 | 12 | 3 | 2 |
| Decreased appetite | 31 | 3 | 13 | 0 |
| Fatigue | 29 | 9 | 8 | 0 |
| Nausea | 28 | 2 | 2 | 0 |
| ALT increase | 25 | 1 | 2 | 1 |
| AST increase | 25 | 0 | 2 | 0 |

| AEs in ≥15% of Patients, % | Cabozantinib (n = 170) | | Placebo (n = 88) | |
|---|---|---|---|---|
| | Any Gr | Gr 3/4 | Any Gr | Gr 3/4 |
| Hypocalcemia | 25 | 8 | 3 | 2 |
| Weight decrease | 22 | 2 | 2 | 0 |
| Vomiting | 18 | 2 | 8 | 0 |
| Stomatitis | 18 | 4 | 2 | 0 |
| Asthenia | 17 | 2 | 14 | 0 |
| Mucosal inflammation | 17 | 2 | 0 | 0 |
| Hypomagnesemia | 16 | 1 | 3 | 0 |
| Proteinuria | 16 | 2 | 2 | 0 |

- Dose reductions due to AEs: cabozantinib, 67%; placebo, 5%
- No grade 5 TRAEs
- Treatment discontinuations due to AEs unrelated to DTC: cabozantinib, 8.8%; placebo, 0%

Capdevila. ESMO 2021. Abstr LBA67.

# Treatment approach

- For patients with metastatic unresponsive DTC (tumors >1 to 2 cm and growing by at least 20 percent/year) or symptomatic metastatic disease
- Specific kinase inhibitor (a US Food and Drug Administration - approved selective TRK or RET inhibitor, or off-label use of a BRAF inhibitor), or an oral antiangiogenic multitargeted kinase inhibitor (aaMKI).
- Among the FDA-approved aaMKIs, we prefer lenvatinib, and sorafenib is our next preferred option.


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
спасибо
dank je
gracias
dziękuję
obrigado
sukriya
kop khun krap
go raibh maith agat
merci
grazie
arigato
dakujem
mochchakkeram
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감사합니다
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