Rahika® (capmatinib) tablets 150 mg · 200 mg

CAPMATINIB

Unlocking the un**MET** need in **MET**ex14 skipping NSCLC

Presenter: Dr. Ashish Singh
Institution/Hospital: Prof, Medical oncology, CMC, Vellore

Rahika® (capmatinib) tablets 150 mg · 200 mg

DISCLAIMER

The views, opinions, ideas etc. expressed therein are solely those of the author. Novartis does not certify the accuracy, completeness, currency of any information and shall not be responsible or in anyway liable for any errors, omissions or inaccuracies in such information. Novartis is not liable to you in any manner whatsoever for any decision made or action or non-action taken by you in reliance upon the information provided. Novartis does not recommend the use of its products in unapproved indications and recommends to refer to complete prescribing information prior to using any of the Novartis products

Promotional Slide Deck/Rahika/Onco BU/271212/30/07/2021

Issued as a Scientific Service to Healthcare Professionals by

NOVARTIS | Reimagining Medicine

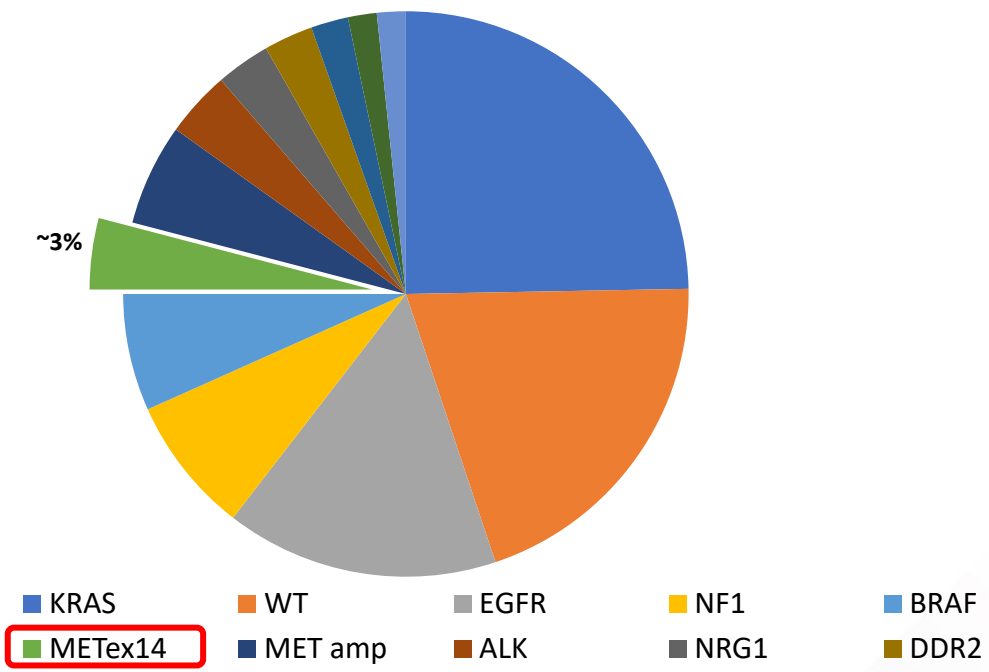
Novartis Healthcare Private Limited
Inspire BKC Part of 601 and 701, Bandra-Kurla Complex,
Bandra (East), Mumbai – 400 051, Maharashtra, India

NOVARTIS | Reimagining Medicine

MET mutations in NSCLC

- *MET* mutation is reported to be mutually exclusive of other established molecular drivers, including *EGFR* mutations or *ALK* translocation[1–3]
- *MET* mutations in the splice site leading to exon 14 skipping result in MET juxta membrane gain-of-function alterations[4–6]
  - Originally discovered in SCLC, and later in NSCLC adenocarcinoma[4,5]
- *MET*ex14 mutations occur in 3% of NSCLC adenocarcinomas and 5–22% of other NSCLC subsets[1,3,7–10]
- *MET*ex14 mutations are linked to early-stage diagnosis and older age[10,11]

Common oncogenic mutations in NSCLC[4–9,12–14]

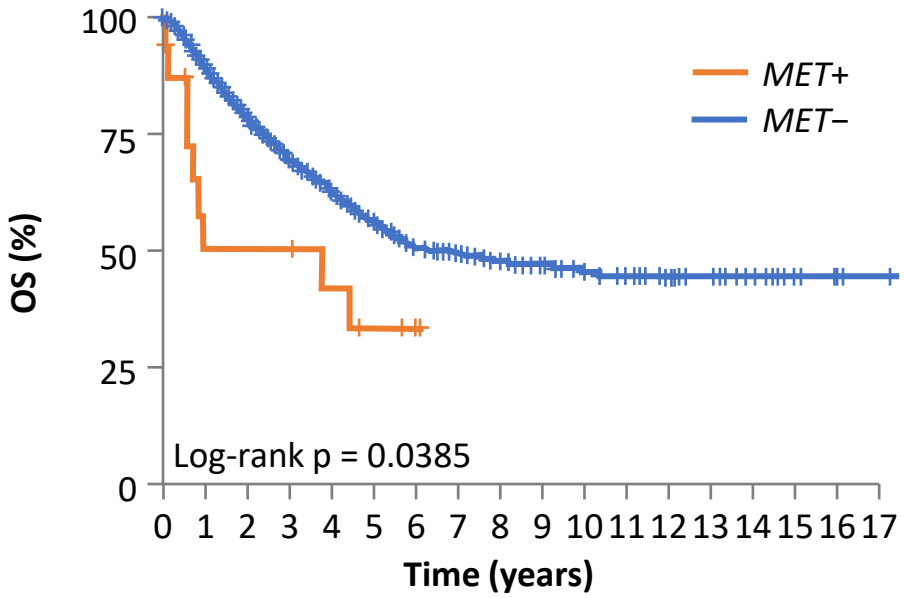


1. Tong JH, et al. Clin Cancer Res. 2016;22:3048-56. 2. Awad MM, et al. Lung Cancer. 2019;133:96-102. 3. Cancer Genome Atlas Research Network. Nature. 2014;511:543-50. 4. Ma PC, et al. Cancer Res. 2003;63:6272-81. 5. Ma PC, et al. Cancer Res. 2005;65:1479-88. 6. Frampton GM, et al. Cancer Discov. 2015;5:850-9. 7. Ou SHI, et al. Poster presented at ASCO 2016; abstract 9021. 8. Heist RS, et al. Oncologist. 2016;21:481-6. 9. Liu X, et al. J Clin Oncol. 2016;34:794-802. 10. Zheng D, et al. Oncotarget. 2016;7:41691-702. 11. Awad MM, et al. J Clin Oncol. 2016;34:721-30. 12. Cappuzzo F, et al. J Clin Oncol. 2009;27:1667-74. 13. Kawakami H, et al. Cancers (Basel). 2014;6:1540-52. 14. Rosell R, Karachaliou N. Lancet. 2016;387:1354-56.

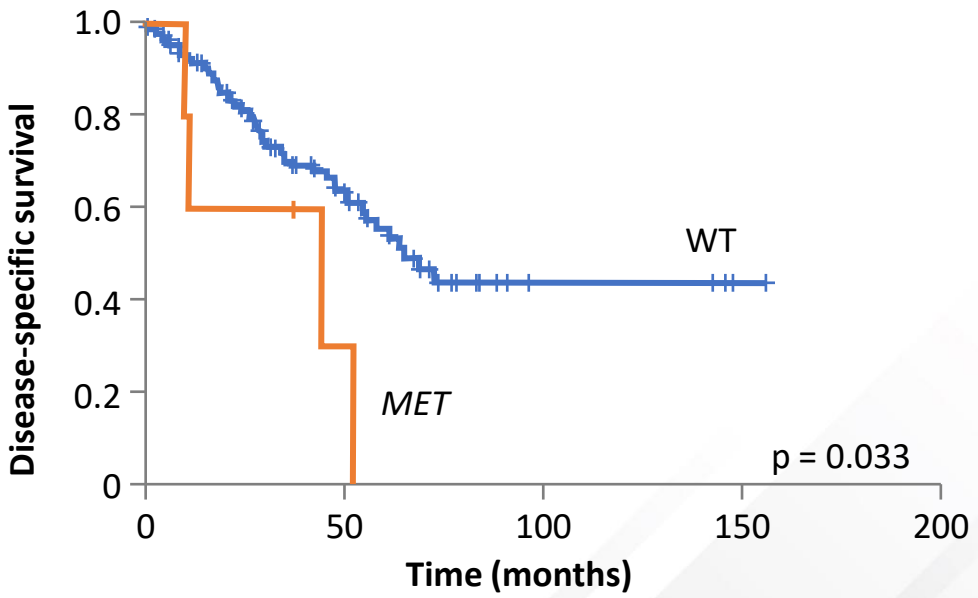
*MET*ex14 Is Associated With Worse Survival

*MET*ex14 was found to be an independent prognostic factor that predicted worse survival compared with patients without *MET* mutation[1,2]

Kaplan–Meier survival curve for OS in NSCLC according to *MET* mutation[1]



Kaplan–Meier survival curve for OS in lung adenocarcinoma according to *MET* mutation[2]



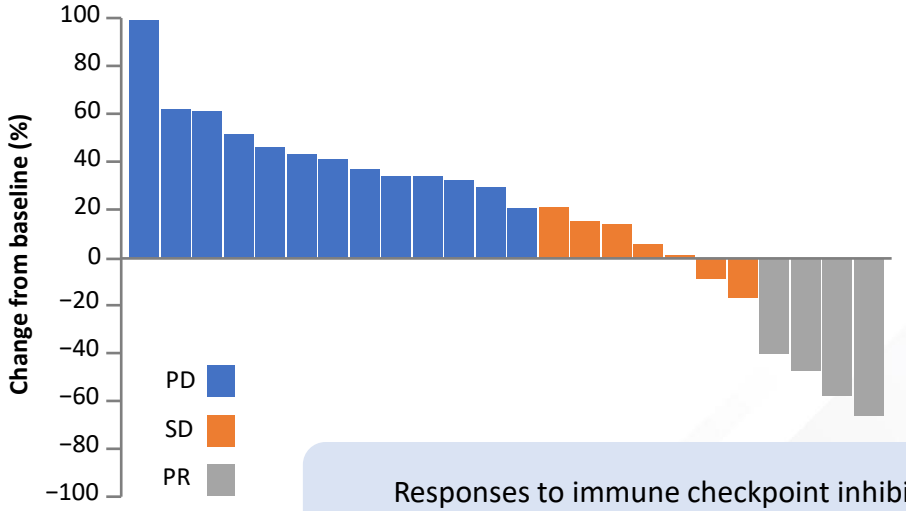
1. Tong JH, et al. Clin Cancer Res. 2016;22:3048-56.
2. Yeung SF, et al. J Thorac Oncol. 2015;10:1292-300.

NOVARTIS | Reimagining Medicine

*MET*ex14: Poor Response To Immunotherapy

- In a retrospective study of 147 patients with *MET*ex14 NSCLC, 24 patients who received immunotherapy were evaluable for response[1]
  - ORR 17% (95% CI 6–36)
  - Median PFS 1.9 months (95% CI 1.7–2.7)
  - Median OS 18.2 months (95% CI 12.9–NR)
- Individual case reports suggest that pembrolizumab might not be effective for NSCLC with high PD-L1 expression and *MET*ex14[2,3]

Immunotherapy	Pembro	Nivo	Nivo	Pembro	Nivo	Nivo	Nivo	Nivo	Nivo	Nivo	Durva	Pembro	Durva	Nivo	Pembro	Nivo	Pembo	Pembro	Atezo	Ipi + N	Ipi + N	Pembro	Pembro	Pembro
Histology	Sarc	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Squam	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Adeno	Sarc	Adeno	Adeno	Adeno
PD-L1	90	80	80	NA	NA	0	0	0	NA	NA	90	60	NA	100	1	0	80	50	100	NA	NA	90	90	0
TMB	7.5	4.8	4.8	12.1	8.2	5.3	0.9	7.5	3.8	5.7	12.1	6.8	3.8	2.8	9.1	0.9	0.8	7.4	6.1	NA	4.9	9.9	8.4	7.3

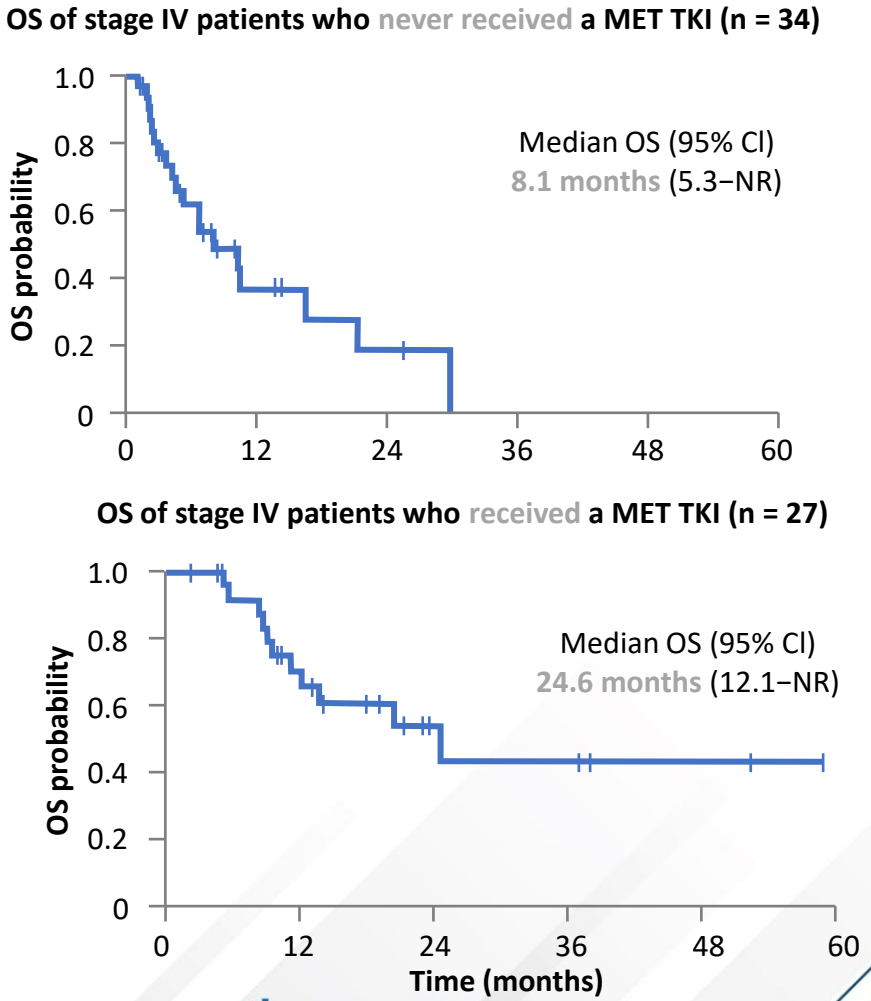


Responses to immune checkpoint inhibition were low regardless of PD-L1 expression status and TMB[1]

1. Sabari JK, et al. Ann Oncol. 2018;29:2085-91.
2. Baba K, et al. Thorac Cancer. 2019;10:369-72.
3. Reis H, et al. Clin Lung Cancer. 2018;19:e441-63.

MET inhibition prolongs survival in *MET*-mutated stage IV NSCLC

- In a retrospective study (N = 148), patients with *MET*-mutated metastatic NSCLC treated with a MET inhibitor had prolonged survival compared with those treated with other therapies
- OS in *MET*-mutated stage IV NSCLC patients was
  - 8.1 months for patients who never received a MET TKI
    - 10.5 months for patients with *MET* mutation only
    - 5.2 months for patients with *MET* mutation and concurrent amplification
- 24.6 months for patients who received a MET TKI (crizotinib, glesatinib, capmatinib)



Awad MM, et al. Lung Cancer. 2019;133:96-102.

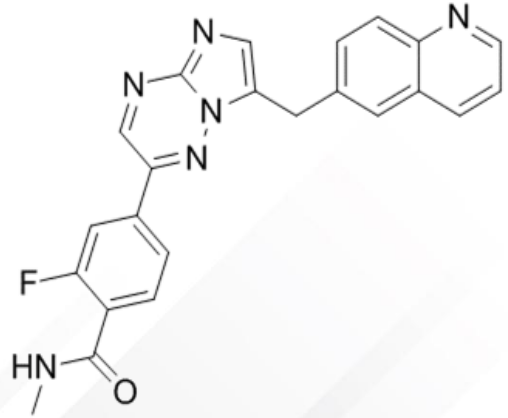
Rahika® (capmatinib) tablets 150 mg · 200 mg

Capmatinib: A Selective MET Inhibitor

- Capmatinib is an oral, ATP-competitive, highly potent, selective, and reversible inhibitor of MET kinase[1]
  - > 10,000-fold selectivity for MET receptor kinase when assessed against a panel of 55 other human kinases[1,2]
  - Crosses the blood–brain barrier showing preliminary brain activity[3,4]
  - Potent blockade of MET activation in cell-based functional and biochemical assays, as well as in in vivo models
- Compared with other agents, capmatinib is the most potent inhibitor against *MET*ex14[5]

	Capmatinib	Savolitinib	Tepotinib	Cabozantinib	Crizotinib
IC_{50} (nM)	**0.6**	2.1	3.0	7.8	22.5

Capmatinib (INC280)[6]

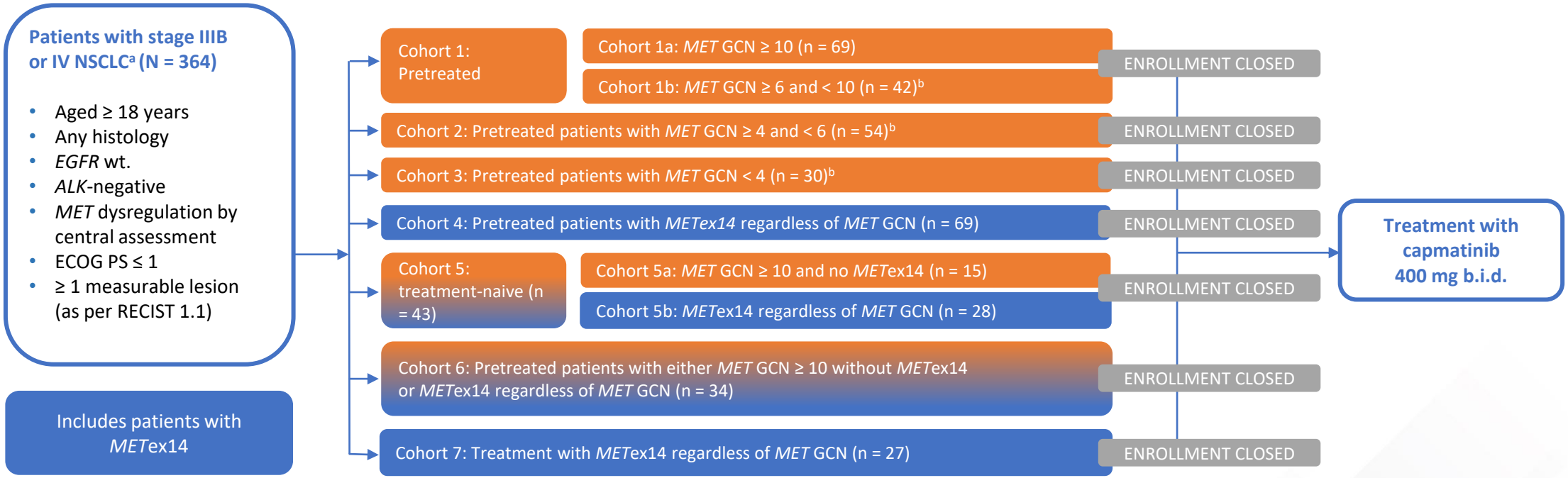


1. Liu X, et al. Clin Cancer Res. 2011;17:7127-38. 2. Lara MS, et al. Clin Lung Cancer. 2017;18:281-5. 3. Wu YL, et al. Presented at WCLC 2017; abstract P1.01-97. 4. Wu Y-L, et al. J Clin Oncol. 2018;36:3101-9. 5. Fujino T, et al. Presented at WCLC 2018; abstract P1.13-41.
6. Salgia R. Mol Cancer Ther. 2017;16:555-65.

NOVARTIS | Reimagining Medicine

GEOMETRY mono-1: Study Design

Multicenter, open-label, phase 2 trial evaluating the efficacy and safety of single-agent capmatinib in adults



[a] Patients were allocated based on *MET* central molecular prescreening.
[b] Cohorts 1b, 2, and 3 included patients with lower amplifications; these cohorts were closed for futility but continue to be evaluated for safety within the full data set.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Study Objectives and Endpoints

Objectives	Endpoints
Primary objective	
• Demonstrate antitumor activity of capmatinib	• ORR[a] assessed by BIRC, by cohort or Cohort
Key secondary objective	
• Evaluate the DoR to capmatinib	• DoR[a] assessed by BIRC, by cohort or Cohort
Other secondary objectives	
• Evaluate antitumor efficacy endpoints for capmatinib	• ORR and DoR[b] assessed by investigator, by cohort or Cohort • TTR, DCR, and PFS[c] assessed by investigator and BIRC, by cohort or Cohort
• Evaluate OS	• OS by cohort or Cohort
• Evaluate the safety profile of capmatinib	• AEs, vital signs, ECGs, and laboratory abnormalities
• Characterize the PK of capmatinib and metabolite CMN288	• Plasma concentration–time profiles and PK parameters

[a] BIRC-assessed using RECIST 1.1 criteria.
[b] Investigator-assessed using RECIST 1.1 criteria.
[c] BIRC- and investigator-assessed using RECIST 1.1 criteria.

INC280 (capmatinib). Clinical Trial Protocol CINC280A2201. Version 6, 28 Feb 2019. Internal data on file.
Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – Baseline Patient Characteristics

Rahika® (capmatinib) tablets 150 mg · 200 mg

Characteristic		*MET*ex14	
		Pretreated Cohort 4 (N = 69)	Treatment-naive Cohort 5b (N = 28)
Age	Median (range), years	71 (49–90)	71 (57–86)
	≥ 65 years, n (%)	55 (79.7)	25 (89.3)
Female, n (%)		40 (58.0)	18 (64.3)
ECOG PS, n (%)	0	16 (23.2)	7 (25.0)
	≥ 1	53 (76.8)[a]	21 (75.0)
Smoking history, n (%)	Never smoker	40 (58.0)	18 (64.3)
	Ex-smoker	27 (39.1)	9 (32.1)
	Current smoker	2 (2.9)	1 (3.6)
Histology, n (%)	Adenocarcinoma	53 (76.8)	25 (89.3)
	Squamous cell carcinoma	6 (8.7)	2 (7.1)
	Large cell carcinoma	1 (1.4)	0
	Other	9 (13.0)	1 (3.6)
Brain metastases at baseline[b], n (%)		11 (15.9)	3 (10.7)
Concurrent *MET* amplification, n (%)	GCN < 4	18 (26.1)	4 (14.3)
	GCN ≥ 4 and < 6	15 (21.7)	10 (35.7)
	GCN ≥ 6 and < 10	17 (24.6)	3 (10.7)
	GCN ≥ 10	11 (15.9)	4 (14.3)
	Missing	8 (11.6)	7 (25.0)

Data cut-off date: 6 January 2020.

[a] One patient in cohort 4, who had undergone randomization in error (protocol deviation), had an ECOG performance-status score of 2.

[b] For *MET*ex14 patients, 12 were identified from their medical history and 2 identified at baseline CT scan.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – Prior Therapies

Prior therapies		*MET*ex14	
		Pretreated Cohort 4 (N = 69)	Treatment-naive Cohort 5b (N = 28)
Prior lines of therapy, n (%)	1	51 (73.9)	NA
	2	16 (23.2)	
	3	2 (2.9)	
Prior therapies (any line), n (%)	Chemotherapy	65 (94.2)	NA
	Platinum-based chemotherapy	61 (88.4)	
	First line	57 (82.6)	
	Second line	5 (7.2)	
	Single-agent chemotherapy	9 (13.0)	
	Immunotherapy	19 (27.5)	NA
	First line	9 (13.0)	
	Second/third line	10 (14.5)	
	Targeted therapy (bevacizumab)	3 (4.3)	NA

GEOMETRY mono-1: Best Overall Response in Cohort 4

Clinically meaningful responses were observed in pretreated patients with *MET*ex14 advanced NSCLC

		***MET*ex14**	
		Pretreated Cohort 4 (N = 69)	
		BIRC	**Investigator**
Best OR, n (%)	CR	0	1 (1.4)
	PR	28 (40.6)	29 (42.0)
	SD	25 (36.2)	21 (30.4)
	Non-CR/non-PR	1 (1.4)	2 (2.9)
	PD	6 (8.7)	7 (10.1)
	NE[a]	9 (13.0)	9 (13.0)
ORR, % (95% CI)		**40.6 (28.9–53.1)**	**43.5 (31.6–56.0)**
DCR, % (95% CI)		**78.3 (66.7–87.3)**	**76.8 (65.1–86.1)**

Data cut-off date: 6 January 2020.

[a] Not qualifying for confirmed CR or PR and without SD after > 6 weeks or progression within the first 12 weeks.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Best Overall Response in Cohort 5b

Clinically meaningful responses were observed in treatment-naive patients with *MET*ex14 advanced NSCLC

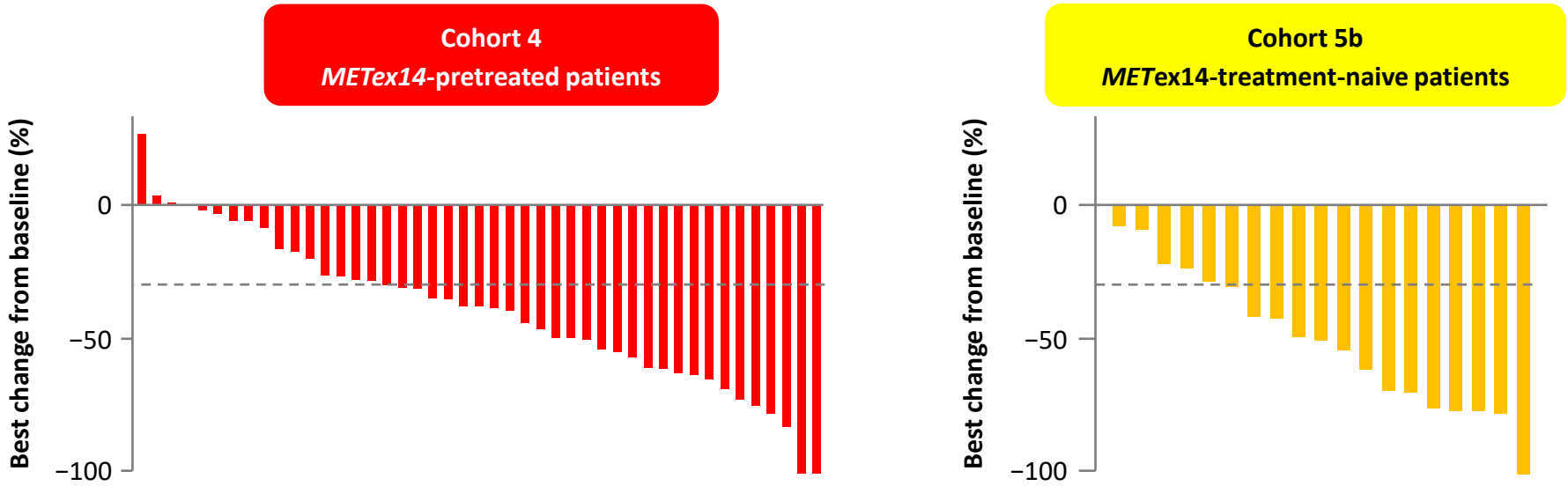
		***MET*ex14**	
		Treatment-naive Cohort 5b (N = 28)	
		BIRC	**Investigator**
Best OR, n (%)	CR	1 (3.6)	0
	PR	18 (64.3)	17 (60.7)
	SD	7 (25.0)	10 (35.7)
	Non-CR/non-PR	1 (3.6)	0
	PD	1 (3.6)	1 (3.6)
ORR, % (95% CI)		**67.9 (47.6–84.1)**	**60.7 (40.6–78.5)**
DCR, % (95% CI)		**96.4 (81.7–99.9)**	**96.4 (81.7–99.9)**

Data cut-off date: 6 January 2020.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – tumor shrinkage per BIRC

Deep responses were observed in the majority of patients across both Cohort 4 and Cohort 5b

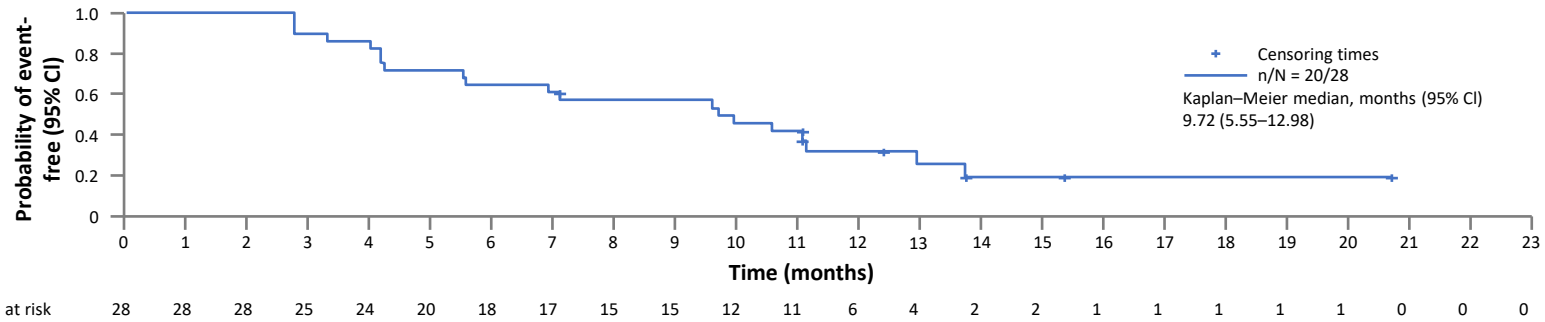


Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – Duration of Response per BIRC

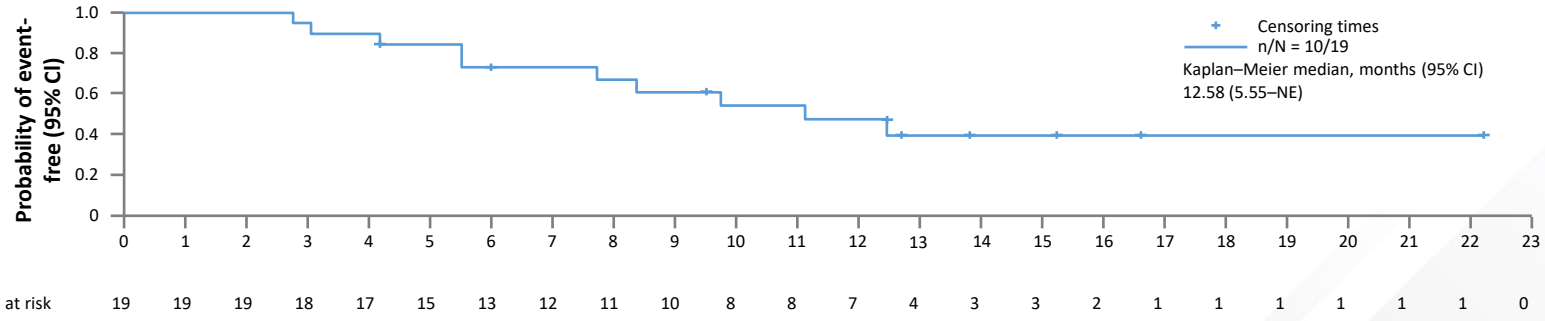
Median DoR was 9.7 months in Cohort 4 and 12.6 months in Cohort 5b[1,2]

Cohort 4
***METex14*-pretreated patients[1]**



No. of patients still at risk	28	28	28	25	24	20	18	17	15	15	12	11	6	4	2	2	1	1	1	1	1	0	0	0

Cohort 5b
***METex14*-treatment-naive patients[1]**



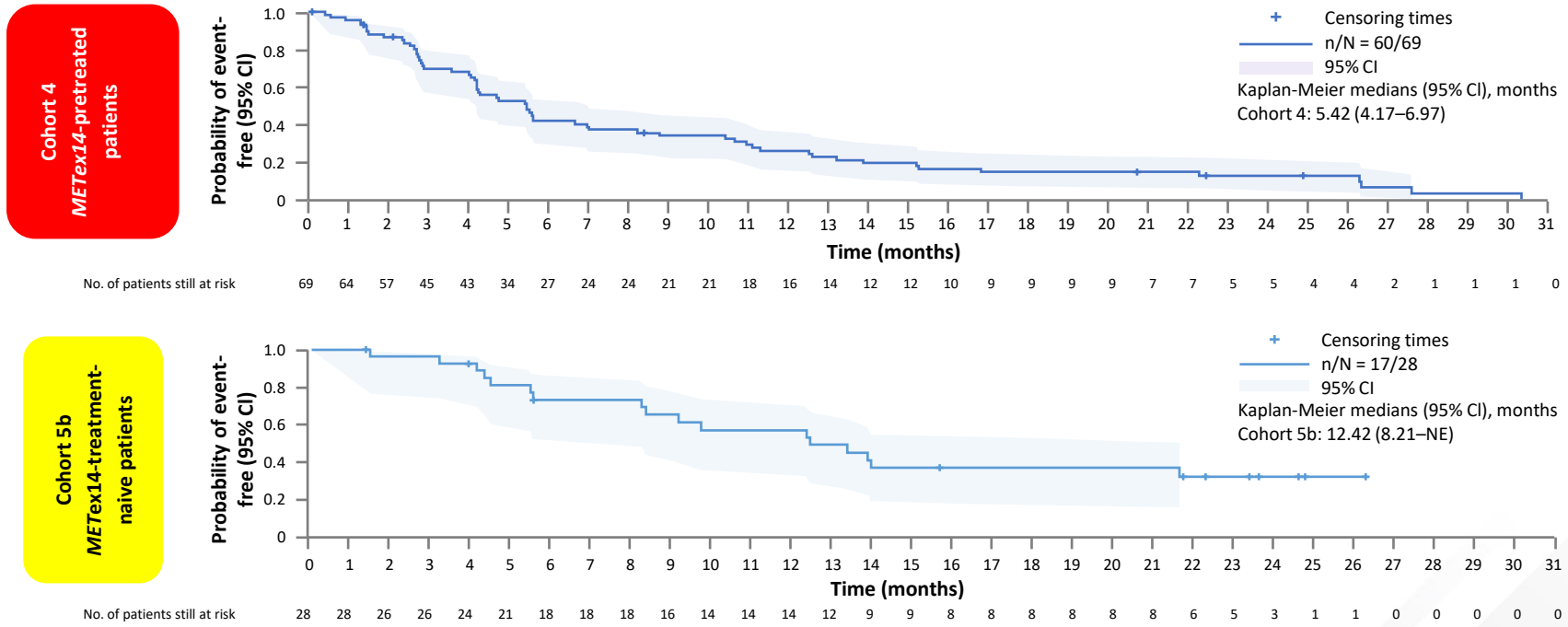
No. of patients still at risk	19	19	19	18	17	15	13	12	11	10	8	8	7	4	3	3	2	1	1	1	1	1	1	0

Median DoR per investigator was 8.31 months (95% CI 5.45–12.06) in Cohort 4 and 13.83 months (95% CI 4.27–25.33) in Cohort 5b.

1. Wolf J, et al. Oral presentation at ASCO 2019. J Clin Oncol. 2019;37(Suppl 15): abstract 9004.
2. Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – Progression-Free Survival per BIRC

Median PFS was 5.42 months in Cohort 4 and 12.42 months in Cohort 5b



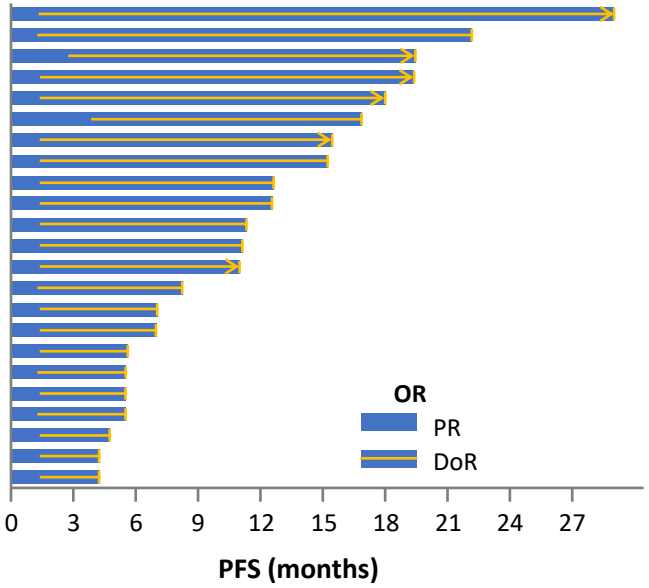
Median PFS per investigator was 4.80 months (95% CI 4.11–7.75) in Cohort 4 and 11.99 months (95% CI 5.52–16.92) in Cohort 5b.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

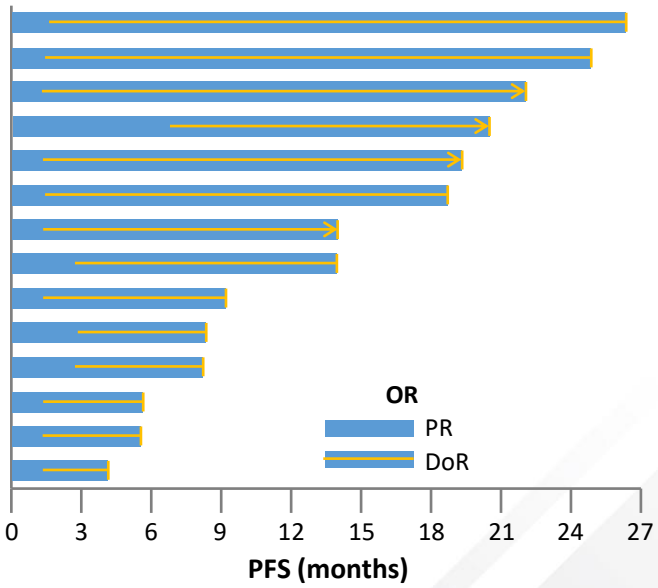
GEOMETRY mono-1: Cohort 4 and Cohort 5b – Swimmer Plots for Responders

Rapid and durable responses across both Cohort 4 and Cohort 5b, with onset occurring at first tumor evaluation after initiating capmatinib in 82.1% of patients in Cohort 4 and 68.4% in Cohort 5b

Cohort 4
***MET*ex14-pretreated patients**



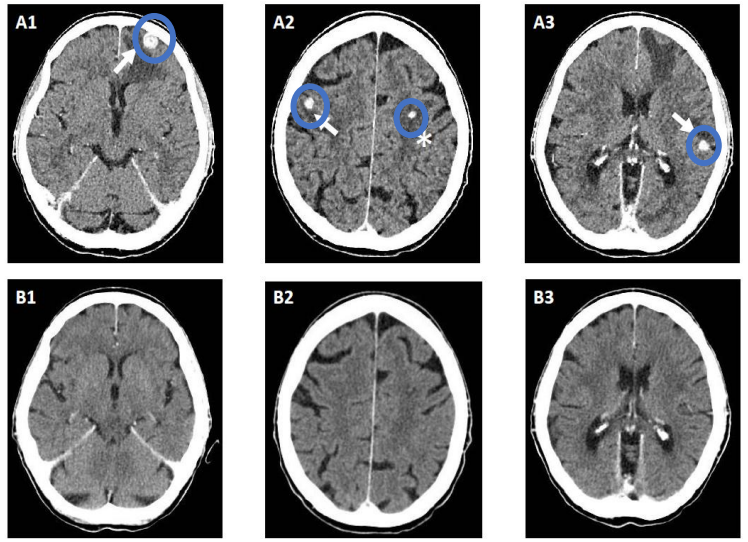
Cohort 5b
***MET*ex14-treatment-naive patients**



Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1 Cohort 4 and Cohort 5b – Confirmed Activity Against Brain Metastases

- 13 evaluable patients with brain metastases at baseline by BIRC (mean 3.3 lesions per patient [range 1–8])[1]
- 54% (N = 7/13) had an intracranial response[1,a]
  - 4 had complete resolution of all brain lesions
  - Of the remaining 3 patients
    - 1 had complete resolution in 3 lesions, stabilization in 4 lesions
    - 1 had complete resolution in 2 lesions, stabilization in 1 lesion
    - 1 had complete resolution in 1 lesion, stabilization in 3 lesions
- Intracranial responses were as fast as responses in extracranial lesions[1]
  - All 7 responders in the brain had an intracranial response at the first evaluation (6 weeks from the start of treatment)
- 12/13 patients had intracranial disease control[1,2]



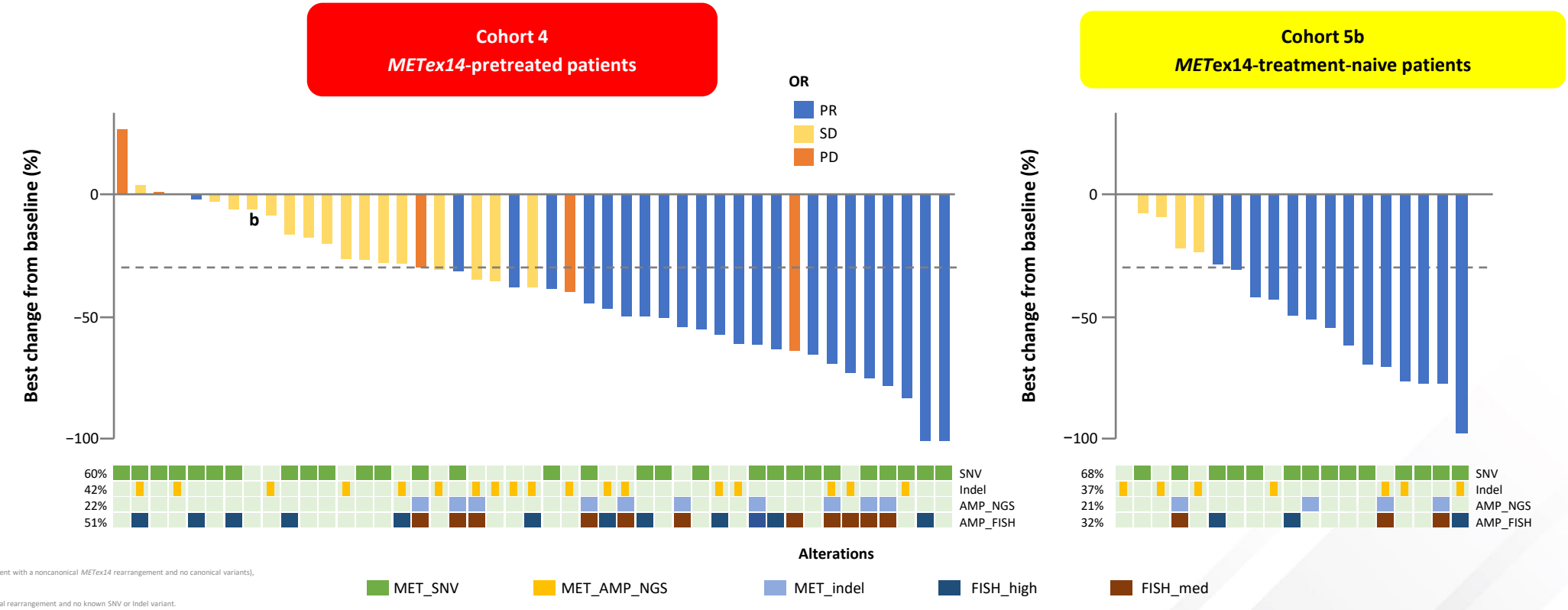
[a] All responses were confirmed at next staging.

CT images courtesy Dr Johan Vansteenkiste (University Hospitals KU Leuven, Leuven, Belgium), informed consent by the patient.

1. Garon EB, et al. Oral presentation at the AACR 2020 (virtual meeting); abstract CT082. 2. Wolf J, et al. N Engl J Med. 2020;383:944-57.

GEOMETRY mono-1: Cohort 4 and Cohort 5b – Tumor Shrinkage by *MET* alterations

Deep responses were observed independent of type of *MET* mutation (SNV, Indel), leading to *MET*ex14 or co-occurrence of *MET* amplification[a]



[a] 64 tissue samples; Cohort 4 = 45 (including 1 patient with a noncanonical *METex14* rearrangement and no canonical variants), Cohort 5b = 19.

[b] Patient had noncanonical *METex14* due to internal rearrangement and no known SNV or Indel variant.

AMP_FISH, *MET* FISH copy number; AMP_NGS, amplification detected by FM NGS panel ≥ 6 GCN.

Wolf J, et al. N Engl J Med. 2020;383:944-57.

Capmatinib in MET exon 14-mutated, advanced NSCLC: Updated results from the GEOMETRY mono-1 study

Rahika® (capmatinib) tablets 150 mg · 200 mg

Study design

Key eligibility criteria:

- Stage IIIB/IV
- *MET*ex14 irrespective of *MET* GCN by central RT-PCR
- *EGFR* WT (for L858R and delE19) and *ALK* fusion-negative
- PS 0-1
- ≥ 1 measurable lesions (RECIST 1.1)
- Neurologically stable or asymptomatic brain metastases allowed

Capmatinib 400 mg BID

Pretreated : 1 or 2 prior treatment lines

Cohort 4: *MET*ex14 (any GCN) N = 69

Treatment-naive

Cohort 5b: *MET*ex14 (any GCN) N = 28

Pretreated : 1 prior treatment line

Expansion cohort 6: *MET*ex14 (any GCN) N = 31[a]

Treatment-naive

Expansion Cohort 7: *MET*ex14 (any GCN) N = 32

Primary endpoint

- ORR by BIRC

Key secondary endpoint

- DOR by BIRC

Secondary endpoints

- ORR and DOR (investigator)
- TTR, DCR, PFS (BIRC/investigator)
- OS
- Safety
- Pharmacokinetics

BID, twice daily; BIRC, blinded independent review committee; DCO, data cutoff; DCR, disease control rate; DOR, duration of response; GCN, gene copy number; *MET*ex14, *MET* exon 14 skipping; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors; RT-PCR, reverse transcription polymerase chain reaction; TTR, time to response; WT, wild-type.

1. Wolf J, et al. *N Engl J Med*. 2020;38:944-957; 2. Wolf J, et al. *ASCO* 2021. Poster 9020.

NOVARTIS | Reimagining Medicine

Results: 66.7% Response Rate and 98.3% Disease Control in First-Line

- Very high overall response and disease control rates in treatment-naive patients from cohort 5b[1] was confirmed in the expansion cohort 7.[2]
- Consistent responses between BIRC and investigator assessments in treatment-naive patients with *MET*ex14 in cohort 5b[1]

	Cohort 5b; N = 28		Cohort 7; N = 32
Assessment	**BIRC[1,2]**	**Investigator[1]**	**BIRC[2]**
Best overall response, n (%)			
CR	1 (3.6)	0	0
PR	18 (64.3)	17 (60.7)	21 (65.6)
SD	8 (28.6)	10 (35.7)	11 (34.4)
PD	1 (3.6)	1 (3.6)	0
ORR[a], % (95% CI)	67.9 (47.6-84.1)	60.7 (40.6-78.5)	65.6 (46.8-81.4)
DCR[b], % (95% CI)	96.4 (81.7-99.9)	96.4 (81.7-99.9)	100.0 (89.1-100.0)

BIRC, blinded independent review committee; CI, confidence interval; CR, complete response; DCR, disease control rate; *MET*ex14, *MET* exon 14 skipping; NSCLC, non-small cell lung cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

1. Wolf J, et al. *N Engl J Med*. 2020;38:944-957; 2. Wolf J, et al. *ASCO* 2021. Poster 9020.

Results: 51.6% and 40.6% Response Rate for patients in second- and second/third-line, respectively

Rahika® (capmatinib) tablets 150 mg · 200 mg

- High overall response rate and disease control rate in the second-/third-line setting in cohort 4, and in the second-line setting in the expansion cohort 6[1,2]
- 44% ORR in all 100 patients

	Cohort 4 (2/3L) N = 69		Cohort 6 (2L); Group 2, N = 31[a]
Assessment	**BIRC[1,2]**	**Investigator[1]**	**BIRC[2]**
Best overall response, n (%)			
CR	0	1 (1.4)	0
PR	28 (40.6)	28 (40.6)	16 (51.6)
SD	25 (36.2)	22 (31.9)	11 (35.5)
Non-CR/non-PD	1 (1.4)	2 (2.9)	1 (3.2)
PD	6 (8.7)	7 (10.1)	0
Not evaluable[b]	9 (13.0)	9 (13.0)	3 (9.7)
ORR[c], % (95% CI)	40.6 (28.9-53.1)	42.0 (30.2-54.5)	51.6 (33.1-69.8)
DCR[d], % (95% CI)	78.3 (66.7-87.3)	76.8 (65.1-86.1)	90.3 (74.2-98.0)

Cut-off date for analyses: April 15, 2019[1] and September 18, 2020[2]. All responses confirmed per RECIST 1.1.
[a] Cohort 6 also enrolled patients with *MET* amplification GCN ≥ 10 in group 1, n = 3.
[b] Not qualifying for confirmed CR or PR and without SD after > 6 weeks or progression within the first 12 weeks.
[c] ORR = CR + PR.
[d] DCR = CR + PR + SD + (non-CR/non-PD).

BIRC, blinded independent review committee; CI, confidence interval; CR, complete response; DCR, disease control rate; GCN, gene copy number; L, line of therapy; *MET*ex14, *MET* exon 14 skipping; NSCLC, non-small cell lung cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

1. Wolf J, et al. *N Engl J Med*. 2020;38:944-957; 2. Wolf J, et al. *ASCO* 2021. Poster 9020.

Results: The majority of patients experienced a tumor response at first evaluation after initiating capmatinib, with durable responses.

- Rapid and durable responses were observed irrespective of line of therapy.[1]
  - In patients with a response to capmatinib, the majority of responses occurred within **2 months of starting treatment**.[1]
- Median DOR to capmatinib
  - 12.6 months in first-line
  - 8.4 months in second-line
  - 9.7 months in second/third-line[1]
- Median PFS
  - 12.3 months in first-line
  - 6.9 months in second-line
  - 5.4 months in second/third-line[1]

Outcome	Cohort 5b (1L), N = 28	Cohort 7 (1L), N = 32	All patients 1L N = 60	Cohort 4 (2/3L), N = 69	Cohort 6 (2L), N = 31
DOR, months, median (95% CI)[a]	12.6 (5.6-NE)	NE (5.5-NE)	12.6 (8.4-NE)	9.7 (5.6-13.0)	8.4 (4.2-NE)
PFS, months, median (95% CI)[a]	12.4 (8.2-23.4)	10.8 (6.9-NE)	12.3 (8.2-21.6)	5.4 (4.2-7.0)	6.9 (4.2-13.3)
TTR ≤ 7 weeks, n/N (%)[b]	13/19 (68.4)	14/21 (66.7)	27/40 (67.5)	23/28 (82.1)	10/16 (62.5)

Data cut-off September 18, 2020.

[a] BIRC assessment.

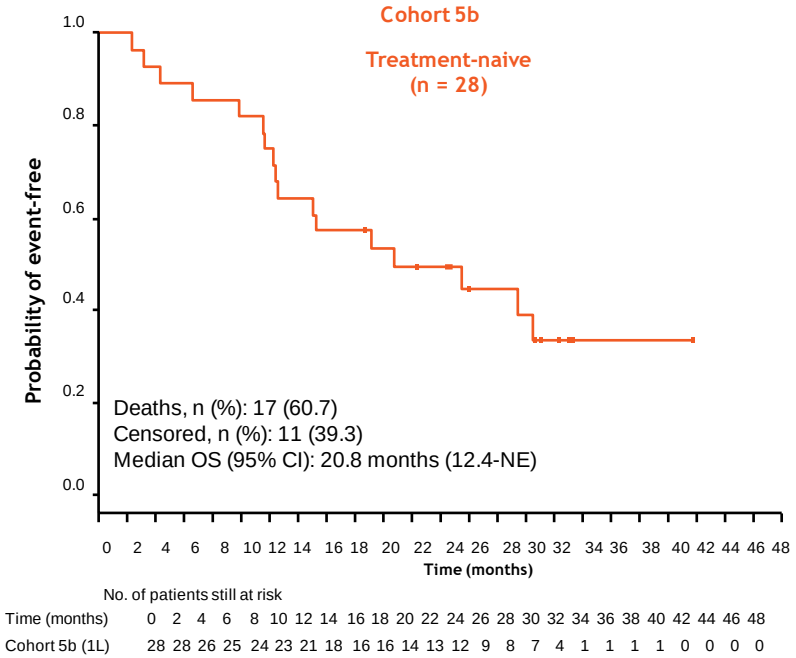
[b] The denominator N refers to the number of patients who had a response.

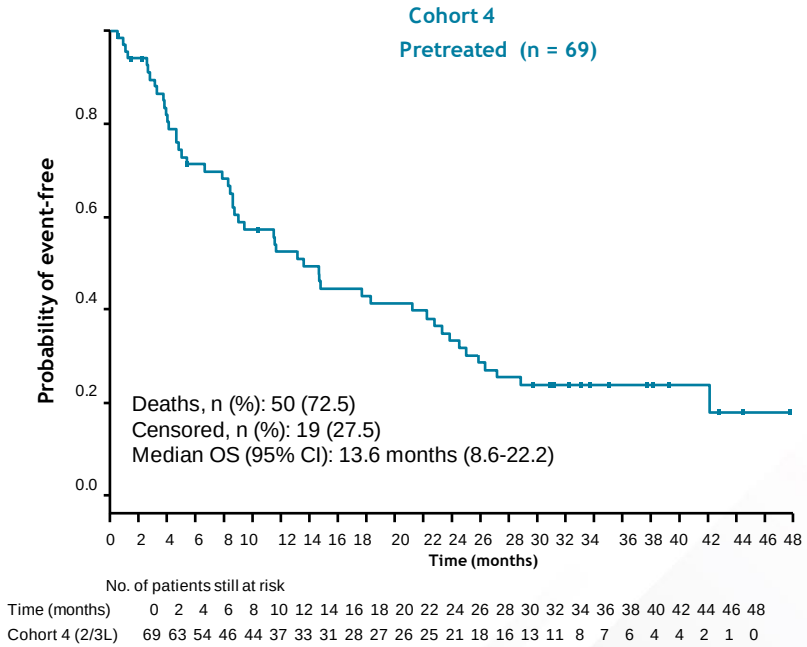
BIRC, blinded independent review committee; CI, confidence interval; DOR, duration of response; L, line of therapy; *MET*ex14, *MET* exon 14 skipping; NE, not estimable; NSCLC, non-small cell lung cancer; PFS, progression-free survival; TTR, time to response.

1. Wolf J, et al. ASCO 2021. Poster 9020.

Results: A clinically meaningful median Overall Survival of 20.8 months in first-line (cohort 5b) and 13.6 months in second/third-line (cohort 4) was observed.

- Mature OS data reported for cohorts 5b and 4
- Data still immature for expansion cohorts 6 and 7[1]





CI, confidence interval; L, line of therapy; *MET*ex14, *MET* exon 14 skipping; NE, not estimable; NSCLC, non-small cell lung cancer; OS, overall survival.

1. Wolf J, et al. *ASCO* 2021. Poster 9020.

Results: Peripheral edema, gastrointestinal symptoms, and increased blood creatinine were the most frequent adverse events.

Rahika® (capmatinib) tablets 150 mg · 200 mg

- Out of 373 patients across all cohorts, including patients with *MET*ex14 and *MET* amplification, 367 (98.4%) experienced an AE of any grade irrespective of study-drug relationship.
- Peripheral edema (54%), nausea (45%), vomiting (28%), and increased blood creatinine (27%) reported in the GEOMETRY mono-1 trial[1]
- SAEs of any grade and irrespective of study-drug relationship were reported in 190 (50.9%) patients.

AEs regardless of causality (≥ 20% all grades)	All patients (N = 373)	
	All grades, n (%)	Grade 3/4, n (%)
Any	367 (98.4)	256 (68.6)
Peripheral edema	202 (54.2)	36 (9.7)
Nausea	168 (45.0)	9 (2.4)
Vomiting	105 (28.2)	9 (2.4)
Increased blood creatinine[a]	99 (26.5)	0
Dyspnea	87 (23.3)	25 (6.7)
Fatigue	83 (22.3)	16 (4.3)
Decreased appetite	79 (21.2)	4 (1.1)

The safety set includes patients with *MET*ex14 or *MET* amplification.
Data cut-off September 18, 2020.

AE, adverse event; *MET*ex14, *MET* exon 14 skipping; NSCLC, non-small cell lung cancer; SAE, serious adverse event.

1. Wolf J, et al. *ASCO* 2021. Poster 9020.

Conclusions

- The preliminary efficacy results of expansion cohort 7 (65.6% ORR) are comparable to those previously reported for cohort 5b (67.9% ORR), both in treatment-naive patients with *MET*ex14 NSCLC.
- In pretreated patients, the ORR was 51.6% in 2L (cohort 6) and 40.6% in 2/3L (cohort 4).
- Clinically meaningful median OS of 20.8 months and 13.6 months were observed in treatment-naive (cohort 5b) and pretreated patients (cohort 4), respectively, demonstrating a long-term survival benefit of capmatinib in these patient populations.
- The manageable safety profile of capmatinib remains unchanged based on the updated safety results from the GEOMETRY mono-1 study.
- The updated results further confirm *MET*ex14 as a targetable oncogenic driver in NSCLC and strengthen the evidence for capmatinib as a valuable targeted treatment option for patients with *MET*ex14 NSCLC.

L, line of therapy; *MET*ex14, *MET* exon 14 skipping; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival

Basic Succinct Statement

RAHIKA®

Important note: Before prescribing, consult full prescribing information.

Presentation: Film-coated tablets containing 150 mg or 200 mg capmatinib (free base), corresponding to 176.55 mg or 235.40 mg capmatinib hydrochloride (anhydrous basis).

Indications: Rahika® is a kinase inhibitor indicated for the treatment of adult patient with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal epithelial transition (MET) exon 14 skipping.

Dosage and administration:

Adults: Recommended dose is 400 mg orally twice daily with or without food. Dose modification based on individual safety and tolerability. Discontinue in patients unable to tolerate 200 mg twice daily.

Children (below 18 years): Safety and efficacy of Rahika® have not been established.

Special populations: ♦Renal impairment: Caution in patients with severe renal impairment. No dose adjustment in patients with mild to moderate renal impairment. **♦Hepatic impairment:** No dose adjustment in patients with mild, moderate, or severe hepatic impairment. **♦Geriatric patients (65 years of age or above):** No dose adjustment.

Contraindications: None.

Warnings and precautions:

Interstitial lung disease (ILD)/pneumonitis: ILD/pneumonitis, which can be fatal, occurred in patients treated with Rahika®. Promptly investigate in any patient with worsening of pulmonary symptoms indicative of ILD/pneumonitis. Withhold immediately in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified. **♦Hepatic effects:** Transaminase elevations occurred in patients treated with Rahika®. Monitor liver function tests prior to start of treatment, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop transaminase or bilirubin elevations. Based on the severity of the adverse drug reaction, temporarily withhold, dose reduce, or permanently discontinue Rahika®. **♦Embryo-fetal toxicity:** Rahika® can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Sexually-active females of reproductive potential should use effective contraception during treatment with Rahika® and for at least 7 days after the last dose. Male patients with sexual partners who are pregnant, possibly pregnant, or who could become pregnant should use condoms during treatment with Rahika® and for at least 7 days after the last dose. **♦Photosensitivity:** Based on findings from animal studies, there is a potential risk of photosensitivity reactions. Advise patients to minimize exposure to sunlight and artificial ultraviolet (UV) light.

Pregnancy, lactation, females and males of reproductive potential:

Pregnancy: Rahika® can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus if Rahika® is used during pregnancy or if the patient becomes pregnant while taking Rahika®.

Lactation: Breastfeeding not recommended during treatment with Rahika® and for at least 7 days after the last dose.

Females and males of reproductive potential: Verify pregnancy status of females of reproductive potential prior to starting treatment. Sexually-active females of reproductive potential should use effective contraception during treatment with Rahika® and for at least 7 days after the last dose. Male patients with sexual partners who are pregnant, possibly pregnant, or who could become pregnant should use condoms during treatment with Rahika® and for at least 7 days after the last dose.

Infertility: No data on the effect of Rahika® on human fertility.

Adverse drug reactions:

Very common (≥10%): decreased appetite, dyspnea, cough, nausea, vomiting, diarrhea, constipation, alanine aminotransferase increased, hypoalbuminemia, blood creatinine increased, peripheral oedema, fatigue, non-cardiac chest pain, pyrexia, back pain, and weight decreased.

Common (≥1 to <10%): cellulitis, hypophosphatasemia, hyponatremia, ILD/pneumonitis, amylase increased, lipase increased, aspartate aminotransferase increased, blood bilirubin increased, pruritus, urticaria, and acute kidney injury.

Uncommon (≥0.1 to <1%): acute pancreatitis.

Interactions: ♦Avoid strong CYP3A inducers. Consider alternative medication with no or minimal potential to induce CYP3A. ♦Exercise caution with moderate CYP3A inducers, strong CYP3A inhibitors, CYP1A2 substrates with a narrow therapeutic index, P-gp and BCRP substrates, proton pump inhibitors. Take Rahika® at least 3 hours before or 6 hours after an H_2-receptor antagonist. Take Rahika® at least 2 hours before or 2 hours after an antacid.

Before prescribing, please consult full prescribing information available from Novartis Healthcare Private Limited, Inspire BKC, Part of 601 & 701, Bandra Kurla Complex, Bandra (East), Mumbai – 400 051, Maharashtra, India, Tel: 022 5024 3336.

For the use of only Oncologist.

India BSS dated 27 May 2021 based on International BSS dated 29 May 2020 effective dated 06 Jul 2021.

Rahika® (capmatinib) tablets 150 mg · 200 mg

THANK YOU