Capmatinib in *MET*ex14 NSCLC

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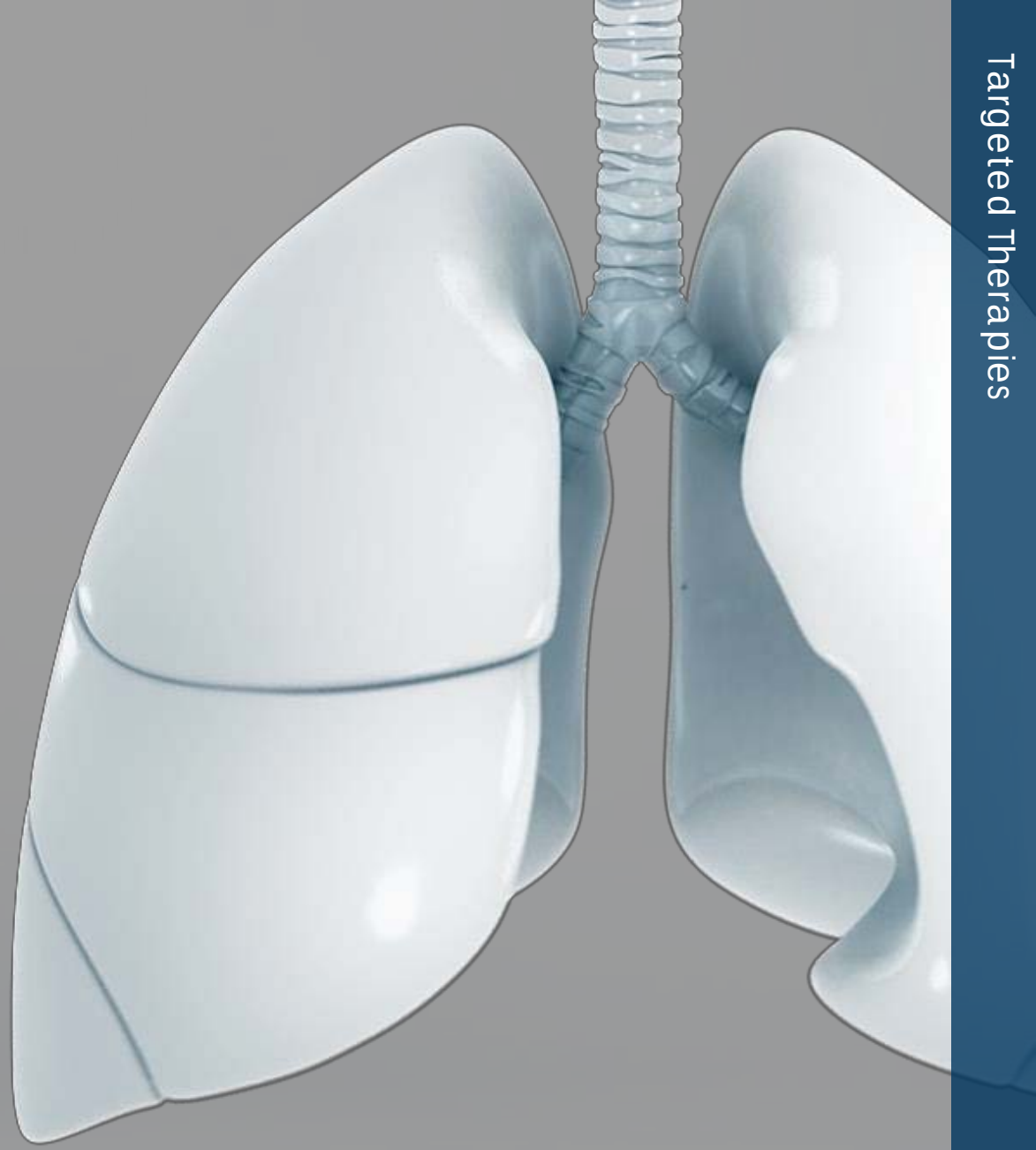

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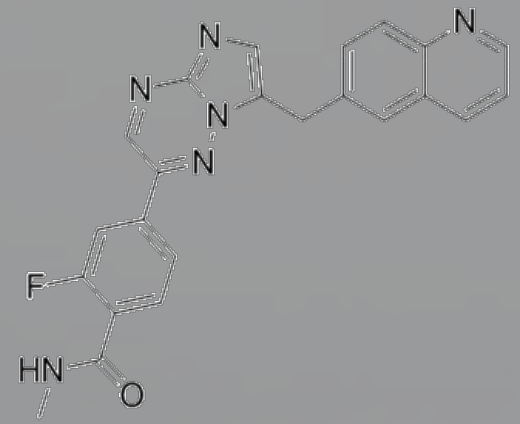
Capmatinib: a selective MET inhibitor

- 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.

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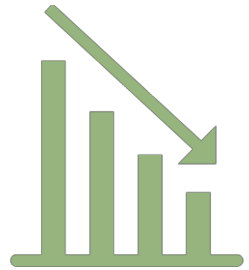
Patients with *MET* Exon 14 Mutations account for 3% of NSCLC and face poor prognosis

Unique Patient Population
Patients with METex14 are older, with a median age of 71 years, and are predominately female. Approximately 40% have never smoked[1]

Aggressive Disease
Patients with METex14 have a high incidence of multi- focal disease and often have brain, bone, and liver metastases[2].

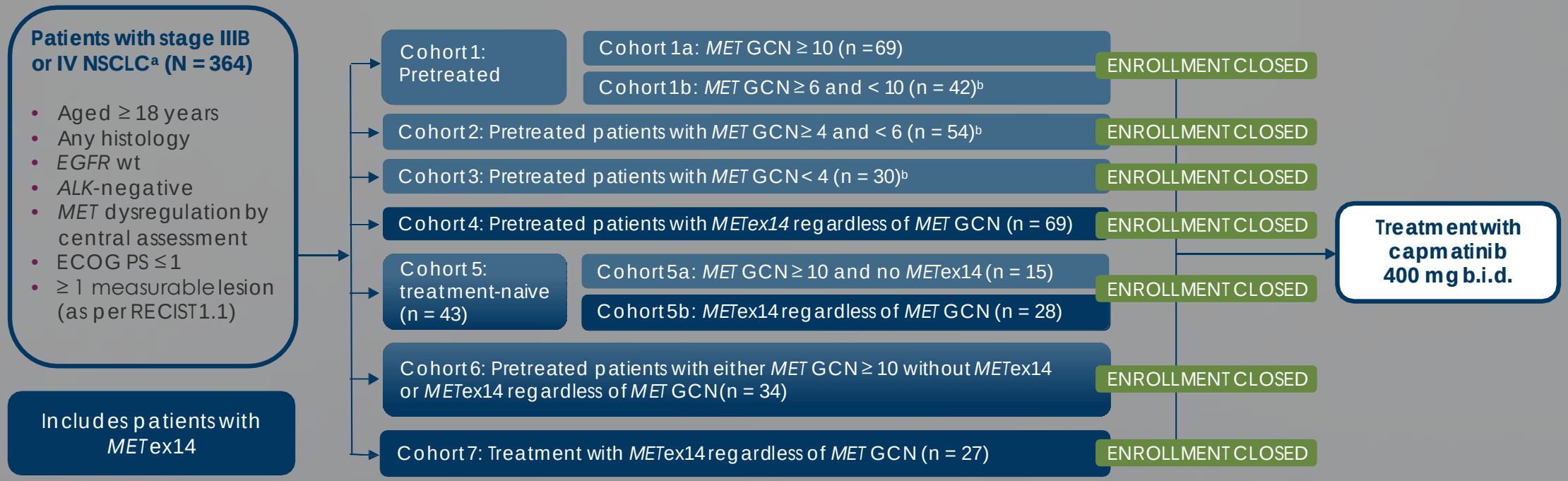


Limited Survival Benefit
METex14 was found to be an independent prognostic factor that predicted worse survival compared with patients without MET alteration. [3, 4, 5]

1. Ali A, et al. Curr Oncol. 2013;20(4):e300-306.
2. Subba R. Digumarthy, Dexter P. Mendoza, Eric W. Zhang, Jochen K. Lennerz, and Rebecca S. Heist. Clinicopathologic and Imaging Features of Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations Cancers. 2019 Dec; 11(12): 2033 Tong
3. JH, Yeung SF, Chan AWH, et al. Clin Cancer Res. 2016;22(12):3048-3056
4. Yeung SF, Tong JHM, Law PPW, et al. J Thorac Oncol. 2015;10(9):1292-1300.
5. Katalinic D, Aleric I, Vcev A. MET exon 14 splicing mutation and its correlation with clinicopathological features in subjects with non-small cell lung cancer. Poster presented at: ESMO 2018 Congress; October 20, 2018; Munich, Germany.

GEOMETRY mono-1 (INC280A2201): 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.

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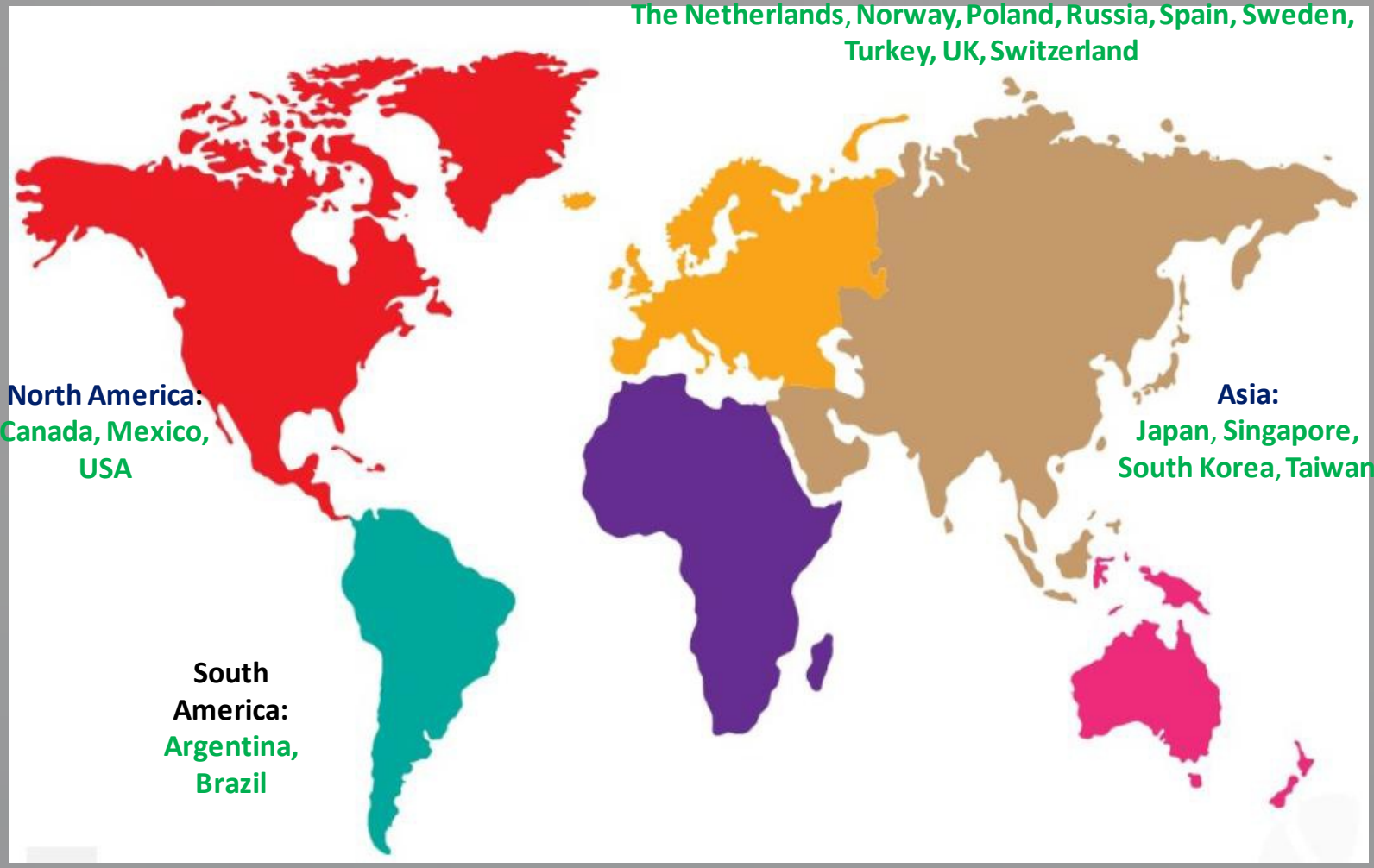
GEOMETRY mono-1 (INC280A2201): Participating Countries

Europe & Middle East:
Austria, Belgium, France, Germany, Italy, Israel, Lebanon, The Netherlands, Norway, Poland, Russia, Spain, Sweden, Turkey, UK, Switzerland

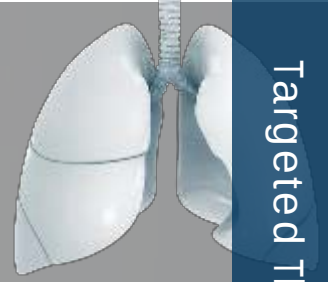


North America:
Canada, Mexico, USA

South America:
Argentina, Brazil

Asia:
Japan, Singapore, South Korea, Taiwan

GEOMETRY mono-1 (INC280A2201): Cohort 4 and Cohort 5b – baseline patient characteristics



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.

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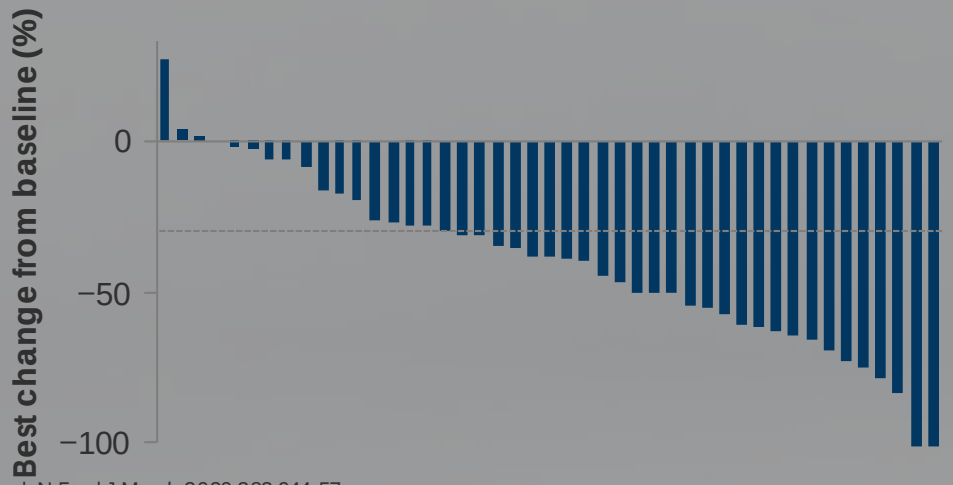
GEOMETRY mono-1 (INC280A2201): Cohort 4 and Cohort 5b - best overall response

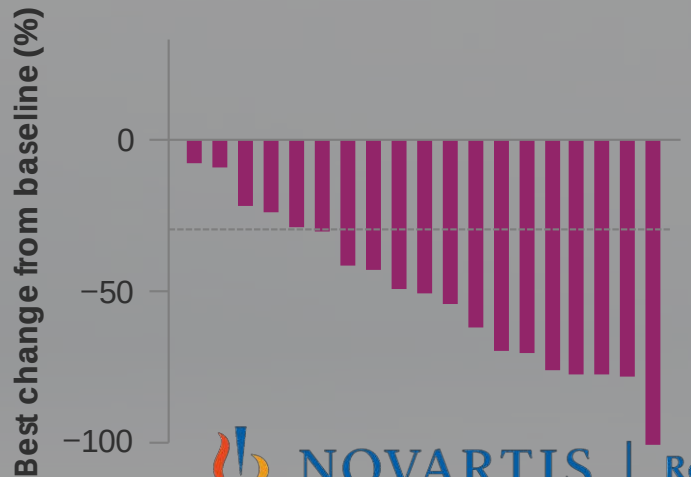
Cohort 4
***MET*ex14-pretreated patients**

	*MET*ex14	
	Pretreated Cohort 4 (N = 69)	
	BIRC	Investigator
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)



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

	*MET*ex14	
	Treatment-naive Cohort 5b (N = 28)	
	BIRC	Investigator
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)



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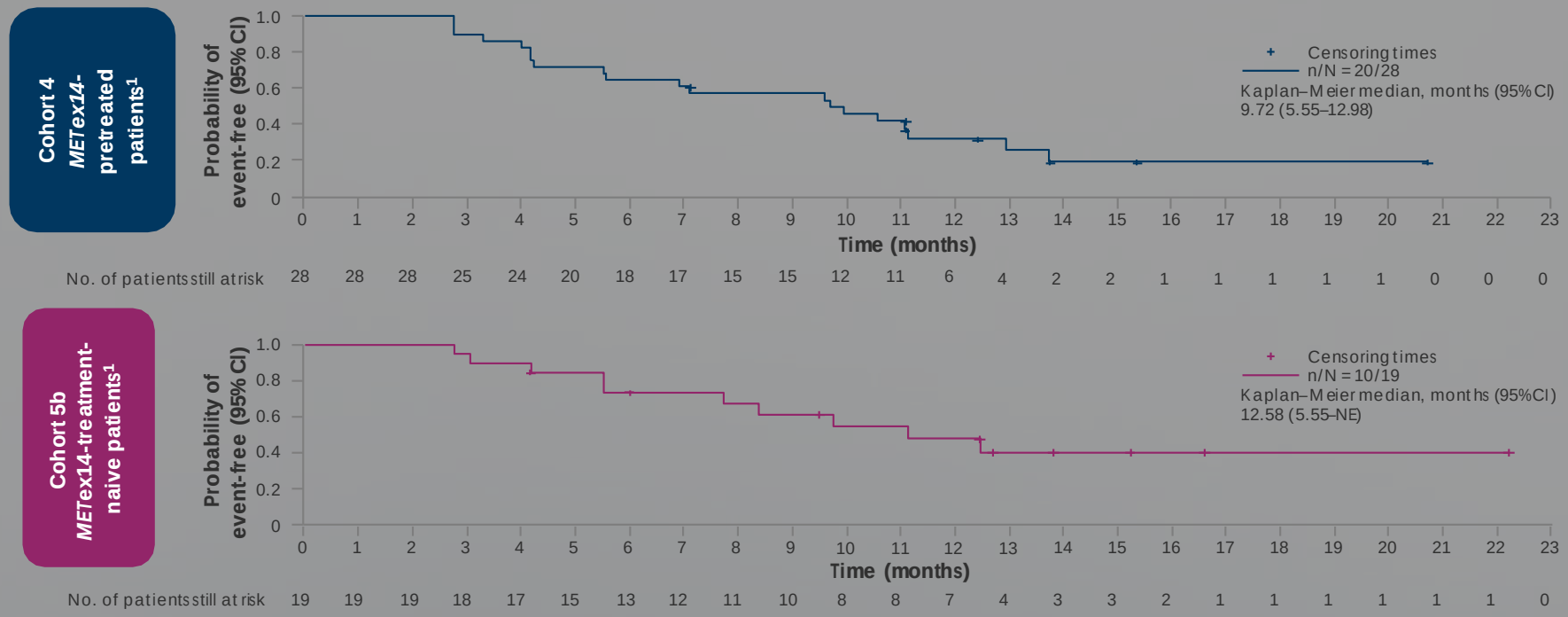
GEOMETRY mono-1 (INC280A2201): Cohort 4 and Cohort 5b – duration of response per BIRC

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



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.

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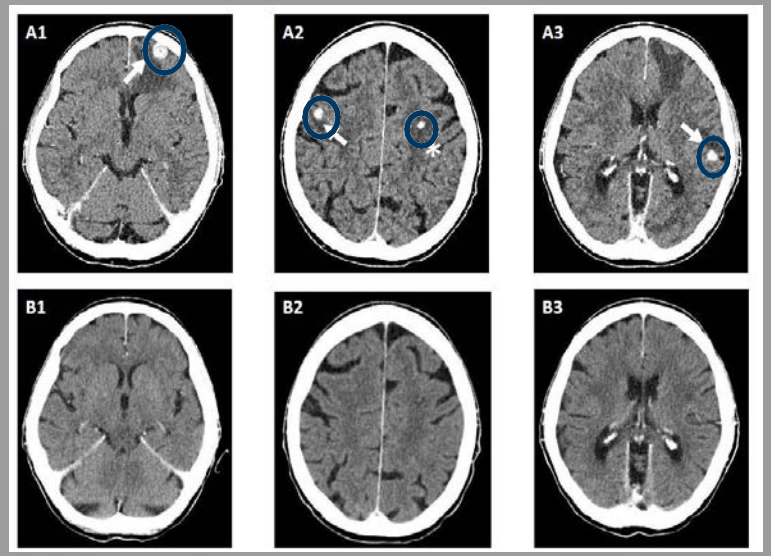
GEOMETRY mono-1 (INC280A2201): Cohort 4 and Cohort 5b – confirmed activity against brain metastases

- 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]
- Intracranial responses were as fast as responses in extracranial lesions[1]
- 12/13 patients had intracranial disease control[1,2]



- 73-year-old female patient with multiple brain metastases treated with WBRT and pembrolizumab (PD-L1 85%)[1,2]
- Progression after 3 cycles, both systemic and intracranial (3 new metastases and progression of pre-existing lesions)
- Feb 2018: start of capmatinib[1,2]
- Brain response since first CT scan; complete resolution of all lesions by second post-baseline CT scan at 12 weeks[1,2]
- Systemic PR; as of October 2020, patient is still ongoing and in response after > 33 months[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.

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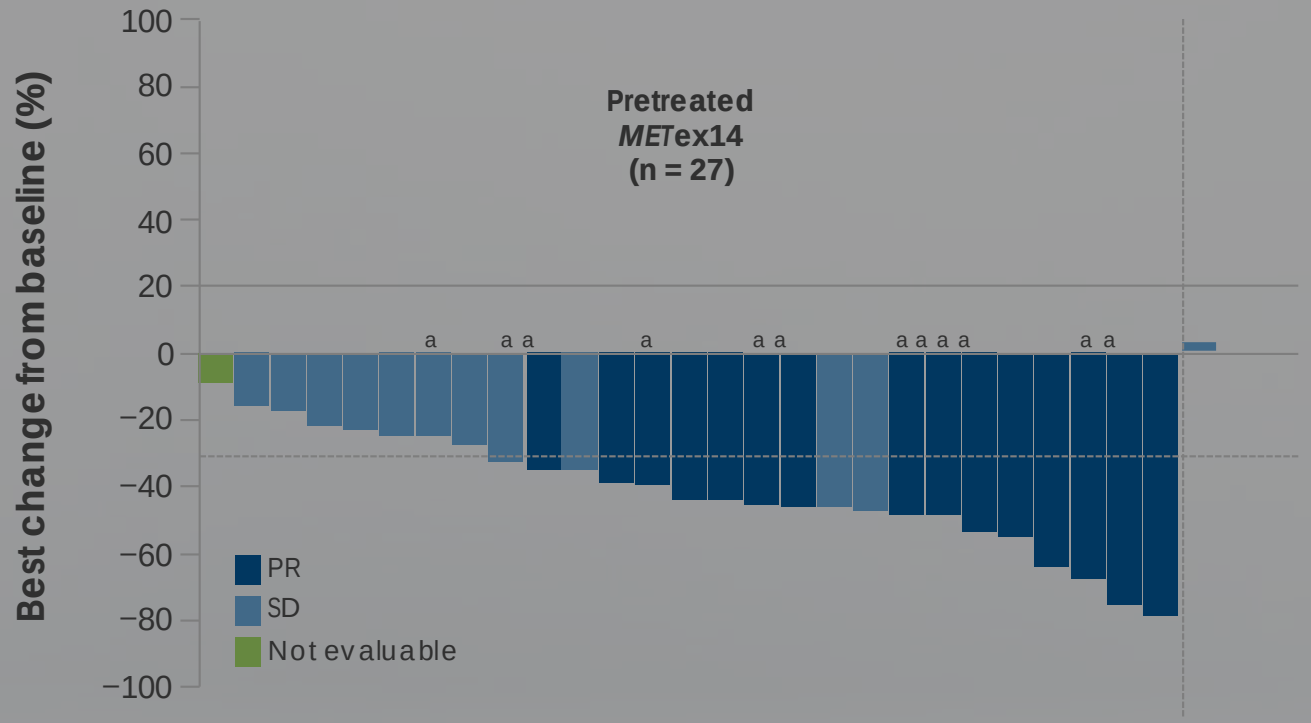
GEOMETRY mono-1 (INC280A2201): efficacy in Cohort 6

- Cohort 6 further confirms the efficacy of capmatinib in 2L pretreated patients with *MET*ex14 NSCLC (without fasting restrictions)
  - BIRC-assessed ORR 48.4% (95% CI 30.2–66.9)



[a] Patients still on treatment.

Groen HJM, et al. Oral presentation at ASCO 2020; abstract 9520.

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GEOMETRY mono-1: safety

- Safety was assessed in all patients treated across study cohorts (N = 364)
  - The majority of AEs were grade 1 or 2
  - Most AEs were predictable and manageable with appropriate dose adjustments
  - Peripheral edema, gastrointestinal symptoms, and increased blood creatinine were the most frequently reported treatment-related AEs
- Safety profile under both fasting and non-fasting conditions was consistently manageable
  - There was a trend towards fewer gastrointestinal AEs of any grade when capmatinib was taken without fasting restrictions

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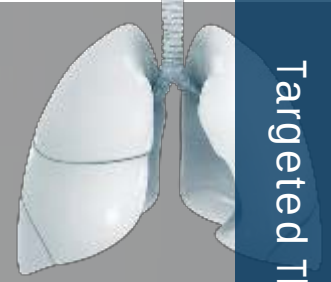
GEOMETRY mono-1 (INC280A2201): treatment-related adverse events across different cohorts



Treatment-related AE, n (%)	*MET*ex14				*MET* amplification				All cohorts[a] (N = 364)	
	Pretreated Cohort 4 (N = 69)		Treatment-naive Cohort 5b (N = 28)		Pretreated Cohort 1a GCN ≥ 10 (N = 69)		Treatment-naive Cohort 5a GCN ≥ 10 (N = 15)			
Grade	**Any**	**3/4**	**Any**	**3/4**	**Any**	**3/4**	**Any**	**3/4**	**Any**	**3/4**
At least one event	60 (87.0)	35 (50.7)	27 (96.4)	16 (57.1)	60 (87.0)	27 (39.1)	14 (93.3)	8 (53.3)	312 (85.7)	137 (37.6)
Reported in ≥ 10% of patients (any cohort)										
Peripheral edema	31 (44.9)	10 (14.5)	19 (67.9)	2 (7.1)	26 (37.7)	5 (7.2)	11 (73.3)	3 (20.0)	156 (42.9)	30 (8.2)
Nausea	26 (37.7)	0	12 (42.9)	0	25 (36.2)	3 (4.3)	6 (40.0)	0	125 (34.3)	6 (1.6)
Vomiting	14 (20.3)	0	5 (17.9)	0	16 (23.2)	4 (5.8)	2 (13.3)	0	68 (18.7)	7 (1.9)
Blood creatinine ↑	18 (26.1)	0	7 (25.0)	0	14 (20.3)	0	3 (20.0)	0	67 (18.4)	0
Fatigue	10 (14.5)	4 (5.8)	2 (7.1)	1 (3.6)	8 (11.6)	0	2 (13.3)	1 (6.7)	50 (13.7)	10 (2.7)
Appetite ↓	10 (14.5)	1 (1.4)	5 (17.9)	0	8 (11.6)	1 (1.4)	2 (13.3)	0	45 (12.4)	3 (0.8)
Diarrhea	9 (13.0)	0	3 (10.7)	0	14 (20.3)	1 (1.4)	0	0	40 (11.0)	1 (0.3)
ALT ↑	6 (8.7)	5 (7.2)	4 (14.3)	2 (7.1)	9 (13.0)	5 (7.2)	3 (20.0)	2 (13.3)	33 (9.1)	20 (5.5)
Amylase ↑	6 (8.7)	3 (4.3)	2 (7.1)	2 (7.1)	9 (13.0)	2 (2.9)	3 (20.0)	1 (6.7)	29 (8.0)	11 (3.0)
Lipase ↑	7 (10.1)	6 (8.7)	4 (14.3)	2 (7.1)	5 (7.2)	3 (4.3)	1 (6.7)	0	27 (7.4)	19 (5.2)
Pruritus	6 (8.7)	0	1 (3.6)	0	5 (7.2)	0	2 (13.3)	0	24 (6.6)	0
AST ↑	5 (7.2)	2 (2.9)	2 (7.1)	1 (3.6)	6 (8.7)	2 (2.9)	3 (20.0)	1 (6.7)	23 (6.3)	9 (2.5)
Constipation	5 (7.2)	1 (1.4)	3 (10.7)	0	3 (4.3)	0	1 (6.7)	0	20 (5.5)	2 (0.5)
Serious AEs	13 (18.8)	9 (13.0)	4 (14.3)	4 (14.3)	10 (14.5)	8 (11.6)	4 (26.7)	2 (13.3)	48 (13.2)	34 (9.3)
AEs leading to discontinuation	11 (15.9)	6 (8.7)	4 (14.3)	3 (10.7)	7 (10.1)	5 (7.2)	2 (13.3)	2 (13.3)	39 (10.7)	22 (6.0)

[a] All patients from Cohorts 1–7 who received ≥ 1 dose of capmatinib.

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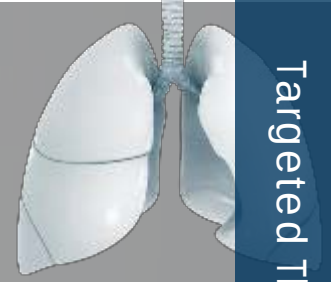

GEOMETRY mono-1 (INC280A2201): conclusions

- Patients with advanced NSCLC harboring *MET*ex14 are older compared to other molecularly unselected NSCLC patients, with a median age of 71 years
  - This was not expected at the beginning of the study and the usual site selection footprint was applied with no further adjustments for identifying METex14 NSCLC pts
- >68% of patients with lung cancer in the US are >65 years at diagnosis therefore oncologist treating NSCLC are experienced in managing such patients and did not require special training or procedures during the conduct of the study
- Capmatinib demonstrated clinically meaningful efficacy in patients with advanced NSCLC harboring METex14, and efficacy was also documented in patients with brain metastases
- Capmatinib was well tolerated with a manageable safety profile with no deterioration in the more elderly MET ex14 cohorts

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