

Phase Ib Trial of the Safety and Antitumor Activity of Savolitinib in Advanced Gastric Cancer Patients with Aberrant c-MET

Jiangsu Cancer Hospital Oncology Department

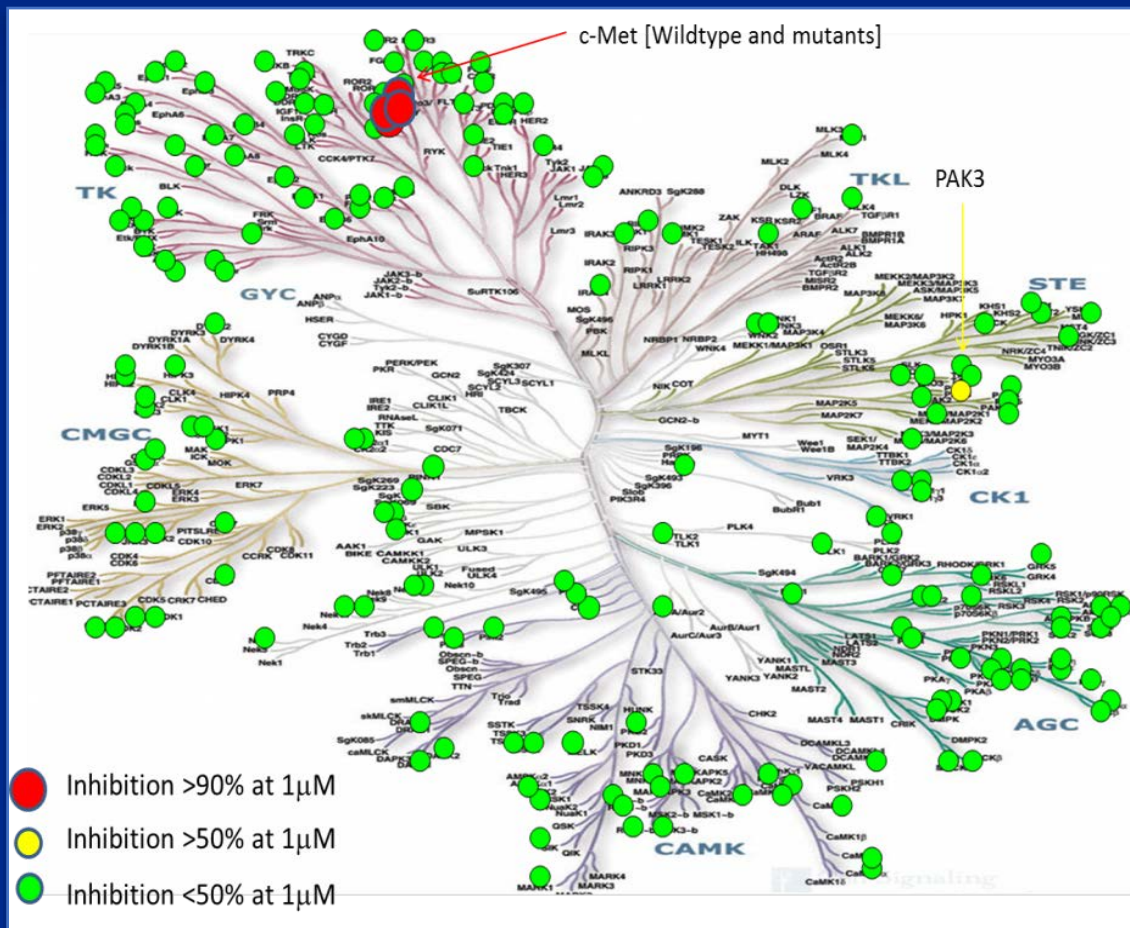
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Savolitinib (AZD6094, HMPL-504)

Highly selective c-MET kinase inhibitor



Kinase	IC ₅₀ (nM) / Inhibition (%) at 1mM
c-MET ^[WT]	4.6 ^a
c-MET ^[M1268T]	5 ^b
c-MET ^[D1246N]	481 ^b
c-MET ^[Y1248C]	596 ^a
c-MET ^[Y1248H]	244 ^b
PAK3	51% ^c
268 other kinases	<50% ^c

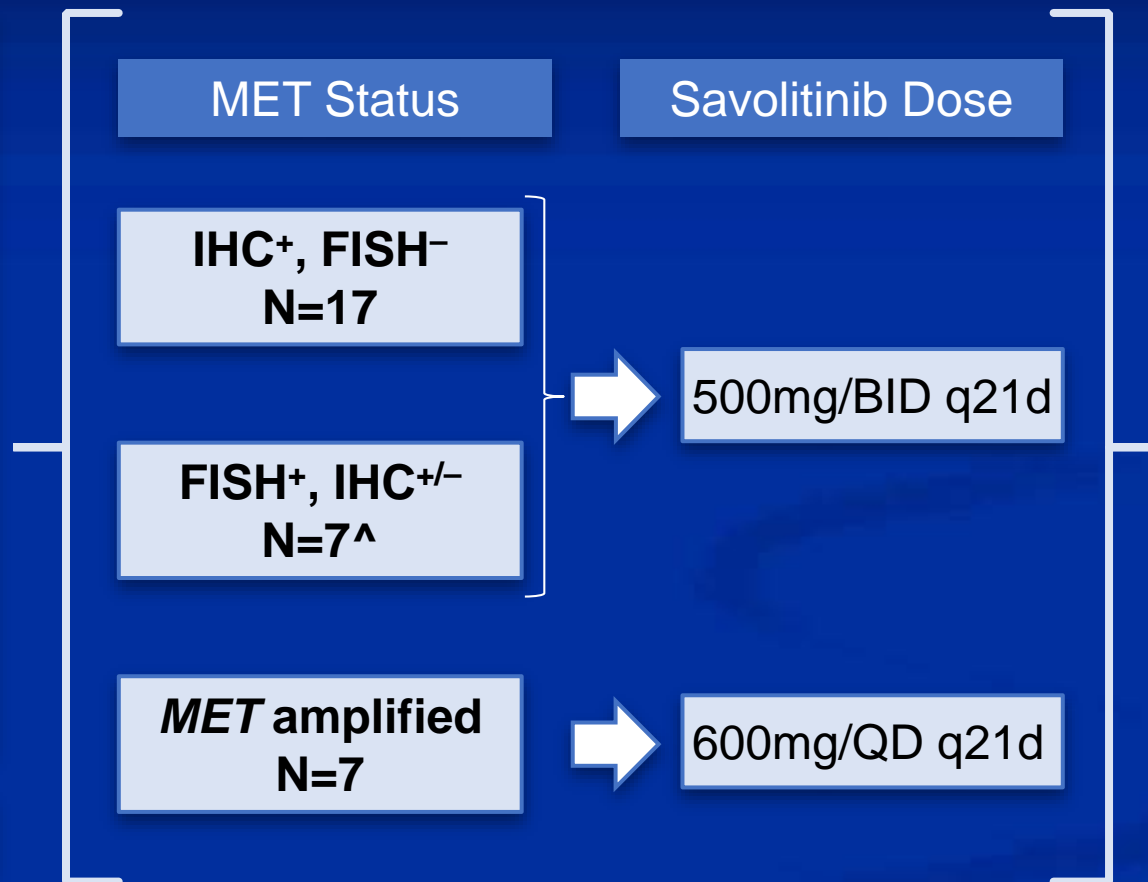
a: the IC₅₀ was determined by Transcreener™ KINASE Assay
 b, c: The data were generated by UBI.

Gastric cancer cohort in Phase Ib study (NCT01985555)

Locally advanced or metastatic gastric cancer patients (including adenocarcinoma of gastroesophageal junction)

- ≥ 2L treatment failed
- Platinum, fluorouracil and taxane combo therapy failed
- Unwilling or not suitable for chemotherapy

N=31



Primary endpoint:

- Safety & tolerability

Secondary endpoints:

- ORR
- DCR
- PFS
- PK

[^] 3 of whom met the *MET* amplification criteria

Baseline information

Baseline info	N=31
Age (y): Median age (range)	54.0 (25-72)
Sex, n (%): Male/Female	24 / 7 (77% / 23%)
TNM Stage, n (%): IV	31 (100%)
Lauren's Criteria, n (%): Diffuse / Intestinal / Mixed	13 (42%) / 17 (55%) / 1 (3%)
Pathological grade, n (%): Poorly differentiated Moderately differentiated Well differentiated	19 (61%) 9 (29%) 3 (10%)
Previous systemic chemotherapy: <2L / ≥2L	4 (13%) / 27 (87%)
Savolitinib dose, n (%): 500mg BID / 600mg QD	24 (77%) / 7 (23%)

MET screening	
Patients screened, n	441
Patients with aberrant <i>MET</i> , n (%)	58 (13.2%)
Patients with <i>MET</i> amp. n (%)	22 (5.0%)
Aberrant <i>MET</i> patients enrolled, n	31
FISH ⁺ , IHC ⁺ or IHC ⁻ , n (%)	7* (22.6%)
IHC ⁺ and FISH ⁻ , n (%)	17 (54.8%)
<i>MET</i> amp, n (%)	10 (32.3%)

* 3 of whom met the criteria of *MET* amplification

Safety summary

Common AEs (occurred in $\geq 10\%$ of patients)

N=31

	n (%)
All	28 (90.3%)
Hepatic function abnormal	12 (38.7%)
Decreased appetite	10 (32.3%)
Anemia	8 (25.8%)
Edema	7 (22.6%)
Vomit	5 (16.1%)
Nausea	5 (16.1%)
Weight decreased	5 (16.1%)
Diarrhea	5 (16.1%)
Bloating	5 (16.1%)
Platelet count decreased	4 (12.9%)
Fatigue	4 (12.9%)
Hypoalbuminemia	4 (12.9%)
Hypoproteinemia	4 (12.9%)

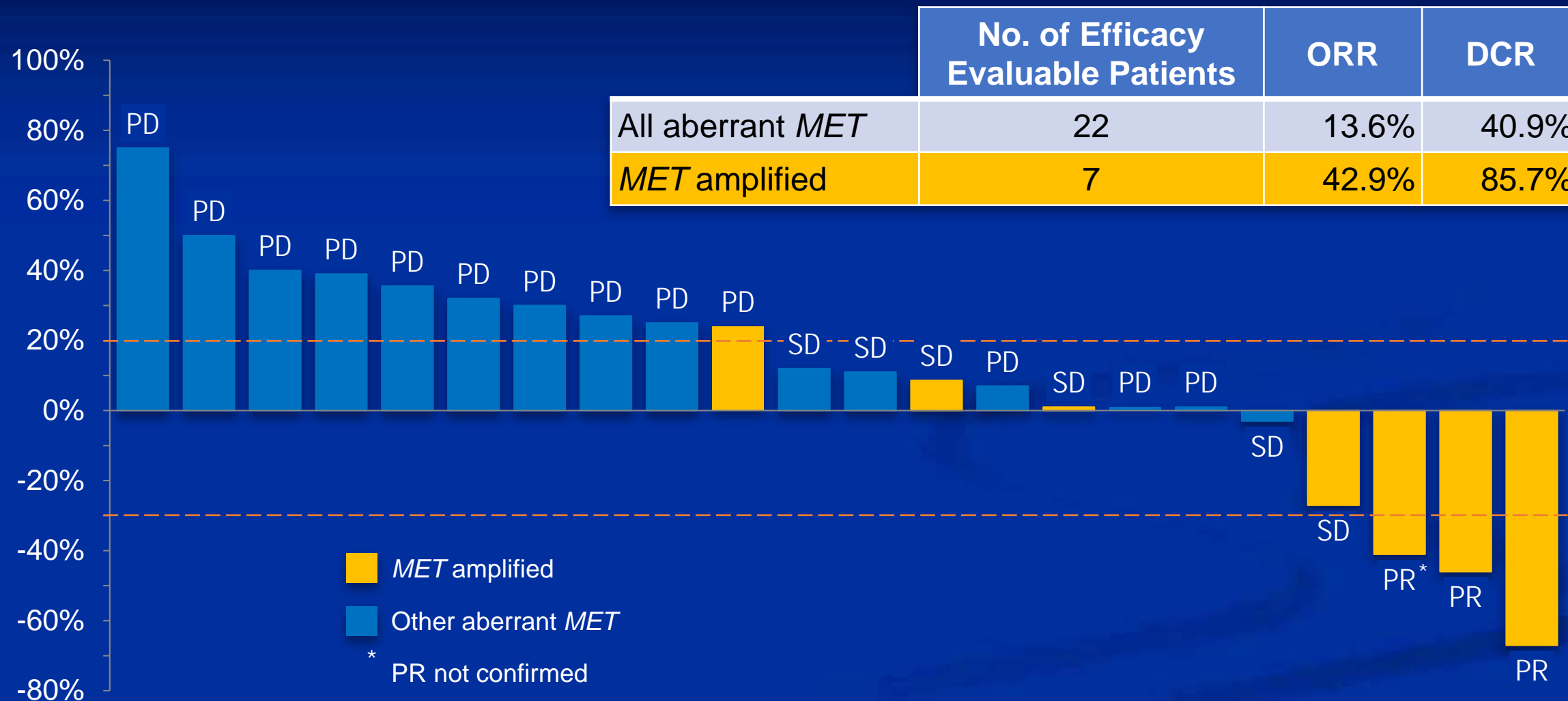
\geq Grade 3 Common AEs (occurred in ≥ 2 patients)

N=31

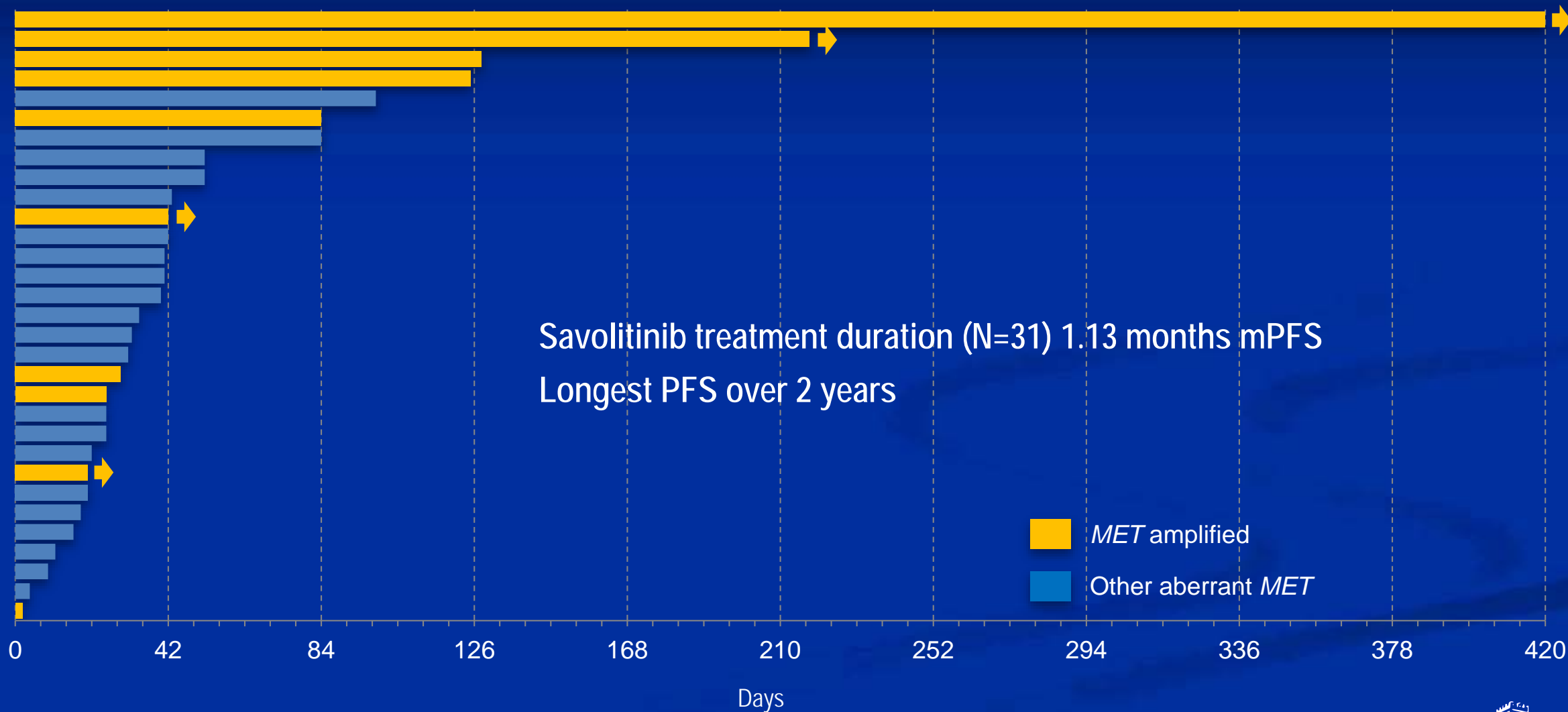
	n (%)
All	16 (51.6%)*
Hepatic function abnormal	4 (12.9%)
Gastrointestinal bleeding	3 (9.7%)
Appetite decreased	3 (9.7%)
Diarrhea	2 (6.4%)
Gastrointestinal perforation	2 (6.4%)

* \geq Grade 3 AEs all occurred in 500mg BID dosage group, except one AE (appetite decreased) in 600mg QD dosage group

Efficacy summary

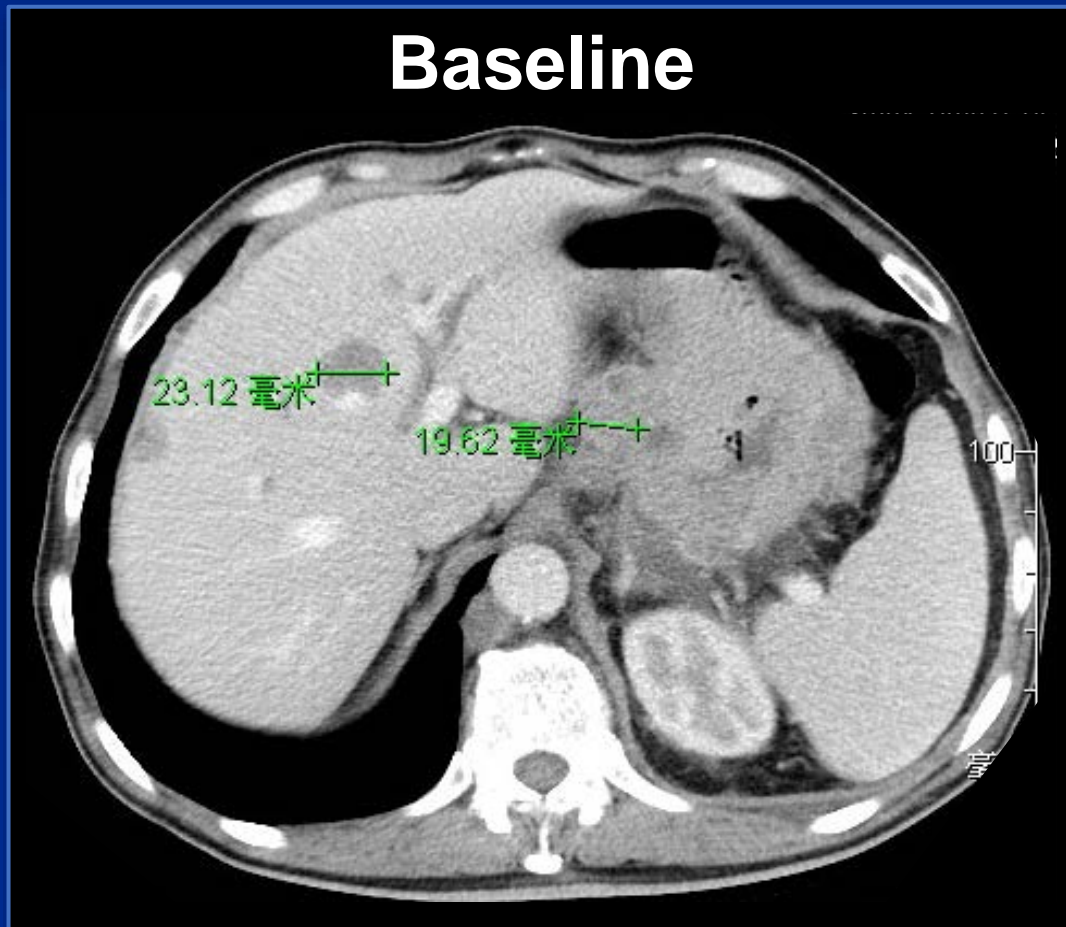


Efficacy summary



Case Report

55y Male, mixed adenocarcinoma, previous 3L chemotherapy, liver and lymph nodes multiple metastases



Discussion and Conclusion

- Savolitinib monotherapy demonstrated promising anti-tumor efficacy in GC patients with *MET* gene amplification, suggesting that patients with *MET* gene amplification may potentially benefit from *MET* inhibitors – warrants further exploration
- Savolitinib monotherapy is well tolerated in patients with advanced gastric cancer
- Incidence of *MET* gene amplification is low in patients with advanced gastric cancer

Acknowledgements

- Patients and their families
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