Tepotinib plus an EGFR TKI in patients with *EGFR*-mutant NSCLC and resistance to EGFR TKIs due to *MET* amplification

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Disclosure

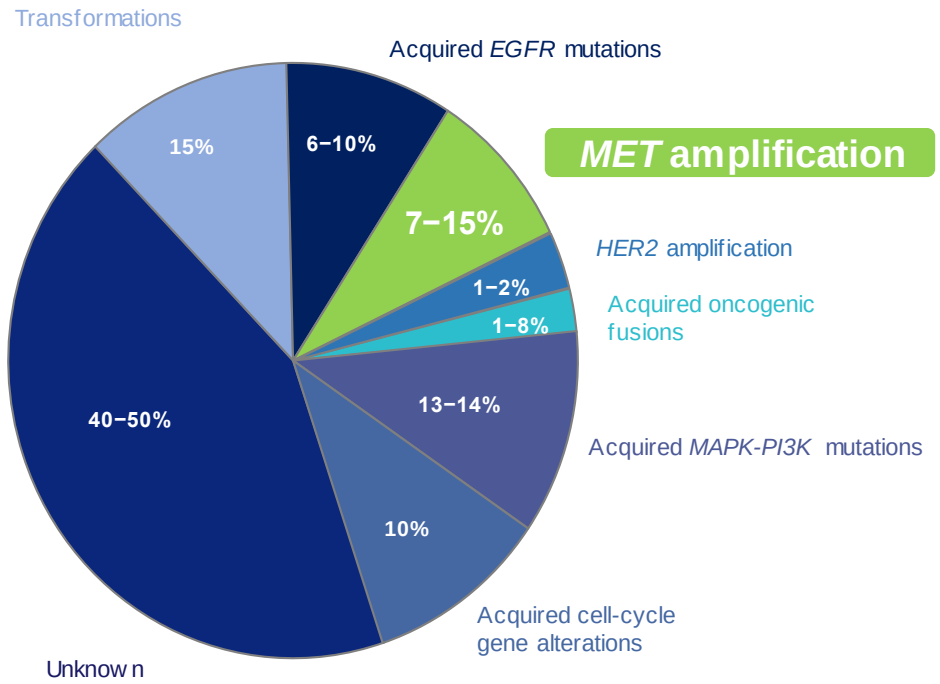
Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**
AstraZeneca, Boehringer Ingelheim	Research grants
AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer and Roche	Honoraria and fees for lectures and advisory board meetings

Content

Introduction

- *MET*amp is a common mechanism of acquired resistance to EGFR TKIs in patients with *EGFR*-mutant NSCLC[1,2]
- These patients have a high unmet need for effective treatments[1]
- Combination therapy with a MET TKI plus an EGFR TKI may overcome *MET*-driven EGFR TKI resistance[3,4]
- Tepotinib, an oral, potent and highly selective MET TKI,[5] induced tumor regression in preclinical models of NSCLC with *MET*-driven EGFR TKI resistance[6]
- In the Phase Ib/II INSIGHT study (NCT01982955), tepotinib + gefitinib demonstrated antitumor activity in patients with *EGFR*-mutant NSCLC, with *MET*amp or MET overexpression and acquired resistance to an EGFR TKI[7]

Mechanisms of resistance to 1L osimertinib[1]



We report further data on the clinical activity of tepotinib plus an EGFR TKI in patients with *EGFR*-mutant NSCLC with *MET*amp from both clinical trials and clinical practice

1L, first-line; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; MAPK, mitogen-activated protein kinase; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NSCLC, non-small cell lung cancer; PI3K, phosphoinositide 3-kinase; TKI, tyrosine kinase inhibitor.

1. Leonetti A, et al. *Br J Cancer*. 2019;121(9):725–737; 2. Wu YL, et al. *Cancer Treat Rev*. 2017;61:70–81; 3. Ahn M, et al. *J Thorac Oncol*. 2017;12(suppl 2):S1768; 4. Sequist LV, et al. *Lancet Oncol*. 2020;21(3):373–386; 5. Falchook GS, et al. *Clin Cancer Res*. 2020;15;26(6):1237–1246; 6. Friese-Hamim M, et al. *Am J Cancer Res*. 2017;7(4):962–972; 7. Wu Y-L, et al. *Lancet Respir Med*. 2020;8(11):1132–1143.

INSIGHT: Trial design

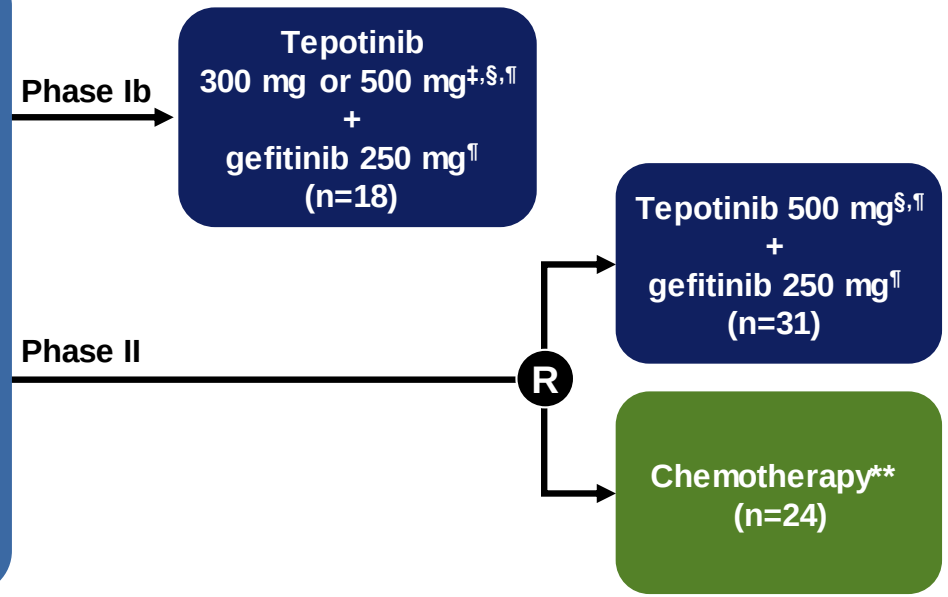
Open-label, Phase Ib/II, randomized, multicenter trial (NCT01982955)[1]

Key eligibility criteria

Both phases:
- Advanced or metastatic NSCLC
- MET overexpression (IHC 2+ or 3+) and/or *MET*amp
- ECOG PS 0 or 1

Phase Ib only:
- Failed on prior gefitinib for reasons other than toxicity or compliance*

Phase II only:
- Activating *EGFR* mutation (other than T790M†)
- Acquired resistance to a first- or second-generation EGFR TKI*



Selected endpoints

Phase Ib:
- Primary: DLTs in Cycle 1, other AEs
- Secondary: ORR by investigator, PK

Phase II:
- Primary: PFS by investigator
- Secondary: ORR and DOR by investigator, OS, and safety

*MET*amp was analyzed centrally in tissue biopsies by FISH (Q^2 Solutions Sponsor-Specific *MET* IQ FISH Kit-111480 Assay; Dako Denmark A/S, Copenhagen, Denmark) and defined as *MET* GCN ≥5 or *MET*:*CEP7* ≥2

*In the Phase Ib part of the study, patients could receive other EGFR TKIs before/after gefitinib; in the Phase II part, only one prior first- or second-generation EGFR TKI (gefitinib, erlotinib, icotinib, or afatinib) was allowed; †In the Phase II part of the study, an exploratory single-arm cohort enrolled a fixed number of patients (n=15) with T790M, all of whom received tepotinib plus gefitinib;[1] ‡3 + 3 dose-escalation design, followed by dose confirmation; §300 mg tepotinib contains 270 mg active moiety and 500 mg tepotinib contains 450 mg active moiety; ¶Administered orally, once daily, until disease progression, intolerable toxicity, or withdrawal of consent; **Consisting of pemetrexed 500 mg/m^2, plus cisplatin 75 mg/m^2 or carboplatin (area under the curve 5–6) by intravenous infusion on Day 1 of each 21-day cycle for up to six 21-day cycles or four cycles plus pemetrexed maintenance.

AE, adverse event; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; GCN, gene copy number; IHC, immunohistochemistry; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; TKI, tyrosine kinase inhibitor.

1. Wu Y-L, et al. *Lancet Respir Med*. 2020;8(11):1132–1143.

INSIGHT: Baseline characteristics of patients with *MET*amp

- Of 49 patients treated with tepotinib + gefitinib, 18 (36.7%) had *MET*amp

		Phase Ib	Phase II[1]	
		Tepotinib + gefitinib (n=6*)	Tepotinib + gefitinib (n=12)	Chemotherapy (n=7)
Male, n (%)		4 (66.7)	3 (25.0)	3 (42.9)
Median age (range), years		67.5 (45–77)	59.3 (42–70)	60.4 (44–74)
Smoker, n (%)		3 (50.0)	3 (25.0)	3 (42.9)
ECOG PS 1, n (%)		5 (83.3)	9 (75.0)	5 (71.4)
Prior EGFR TKI, n (%)	Gefitinib	6 (100.0)	6 (50.0)	5 (71.4)
	Erlotinib	1 (16.7)	2 (16.7)	0
	Icotinib	0	2 (16.7)	0
	Afatinib	1 (16.7)	2 (16.7)	2 (28.6)
	Osimertinib	2 (33.3)	0	0
EGFR mutation, n (%)	Del19	3 (50.0)	7 (58.3)	3 (42.9)
	L858R	3 (50.0)	4 (33.3)	4 (57.1)
	G719X	0	1 (8.3)	0
MET GCN ≥5, n (%)		6 (100.0)	11 (91.7)	7 (100.0)
MET:*CEP7* ≥2, n (%)		2 (33.3)	7 (58.3)	6 (85.7)
MET IHC 3+, n (%)		4 (66.7)	11 (91.7)	6 (85.7)

Data cut-off: Dec 12, 2018. *Among patients with *MET*amp in Phase Ib, two received tepotinib 300 mg and four received tepotinib 500 mg.
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry; GCN, gene copy number; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; TKI, tyrosine kinase inhibitor.
1. Wu Y-L, et al. *Lancet Respir Med*. 2020;8(11):1132–1143.

INSIGHT: Antitumor activity observed with tepotinib + gefitinib in patients with *MET*amp (data cut-off: Dec 12, 2018; Wu Y-L, et al. *Lancet Respir Med.* 2020[1])

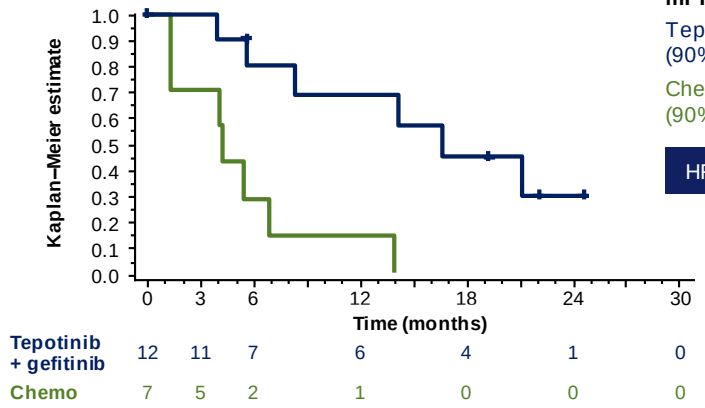
Phase Ib and II: Response (patients with *MET*amp)

- In Phase Ib and II combined, 12/18 patients (66.7%) with *MET*amp had a response

	Tepotinib + gefitinib[1]	
	Phase Ib (n=6*)	**Phase II (n=12)**
ORR, n (%)	4 (66.7)	8 (66.7) [90% CI: 39.1, 87.7]
DOR, months	5.5, 5.6, 11.7, 12.5	Median: 19.9 [90% CI: 7.0, NE]

- In Phase II, PFS and OS were greatly improved with tepotinib + gefitinib versus chemotherapy
- Efficacy of tepotinib + gefitinib also compared favorably with previous data for chemotherapy after progression on gefitinib in the IMPRESS trial (median PFS, 5.4 months [95% CI: 4.6, 5.5]; median OS, 19.5 months)[2,3]

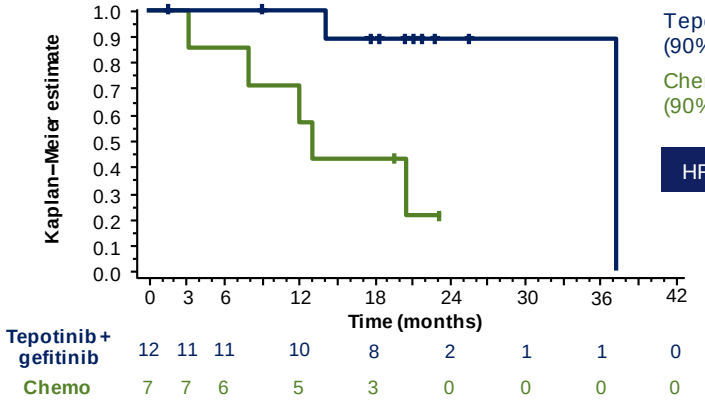
Phase II: PFS (patients with *MET*amp)



mPFS:
Tepotinib + gefitinib: 16.6 months (90% CI: 8.3, NE)
Chemotherapy: 4.2 months (90% CI: 1.4, 7.0)

HR = 0.13; 90% CI: 0.04, 0.43

Phase II: OS (patients with *MET*amp)



mOS:
Tepotinib + gefitinib: 37.3 months (90% CI: NE)
Chemotherapy: 13.1 months (90% CI: 3.25, NE)

HR = 0.08; 90% CI: 0.01, 0.51

Data cut-off: Dec 12, 2018. *Among patients with *MET*amp in Phase Ib, two received tepotinib 300 mg and four received tepotinib 500 mg.
CI, confidence interval; DOR, duration of response; HR, hazard ratio; m; median; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival. 1. Wu Y-L, et al. *Lancet Respir Med*. 2020;8(11):1132–1143; 2. Soria JC, et al. *Lancet Oncol*. 2015;16(8):990–998; 3. Mok TSK, et al. *J Clin Oncol*. 2017;35(36):4027–4034.

INSIGHT: Tepotinib + gefitinib was generally well tolerated in patients with *MET*amp (data cut-off: Dec 12, 2018; Wu Y-L, et al. *Lancet Respir Med.* 2020[1])

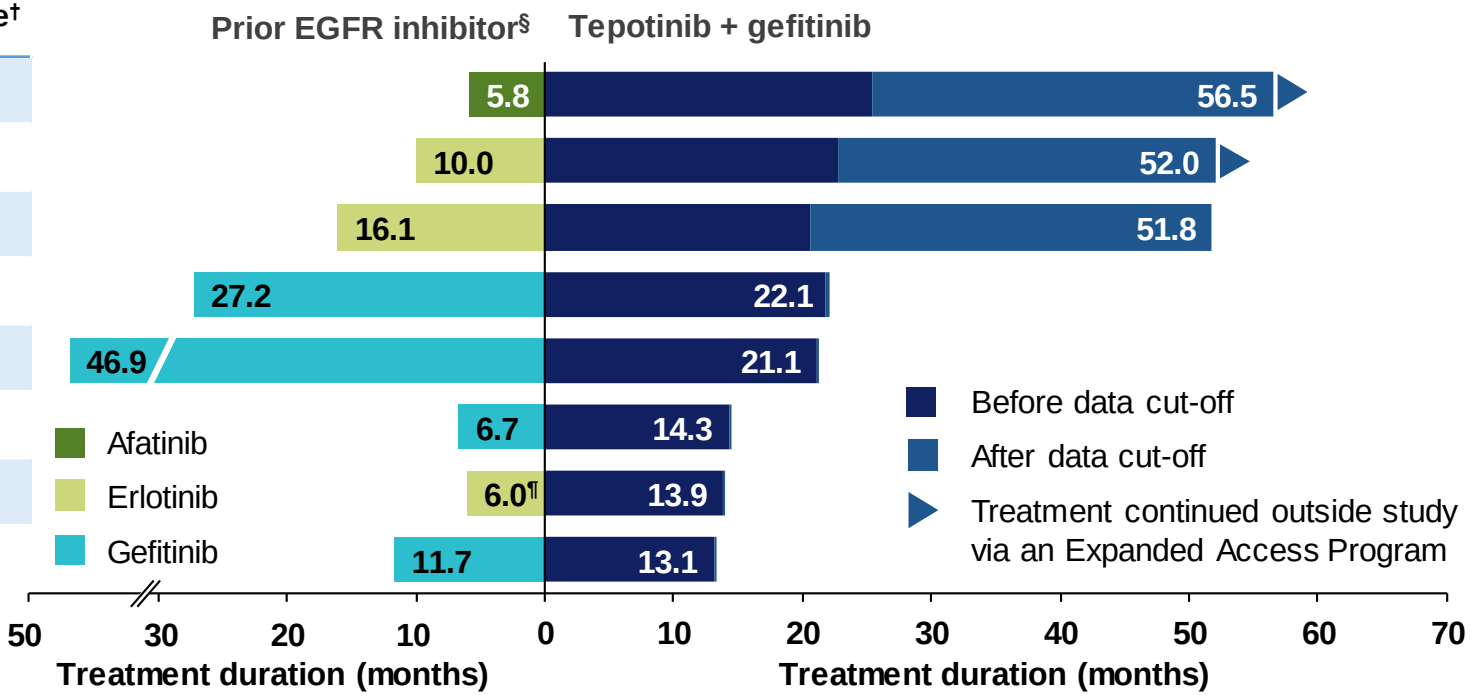
Phase II: TRAEs reported at any grade in ≥20%, n (%)	Tepotinib + gefitinib (n=12)		Chemotherapy (n=7)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TRAE	12 (100)	7 (58.3)	7 (100)	5 (71.4)
Neutrophil count decreased	0	0	4 (57.1)	2 (28.6)
White blood cell count decreased	1 (8.3)	0	4 (57.1)	2 (28.6)
Diarrhea	6 (50.0)	1 (8.3)	1 (14.3)	0
Anemia	0	0	3 (42.9)	2 (28.6)
Nausea	2 (16.7)	0	3 (42.9)	0
Amylase increased	5 (41.7)	4 (33.3)	0	0
Lipase increased	5 (41.7)	4 (33.3)	0	0
Peripheral edema	4 (33.3)	0	1 (14.3)	0
ALT increased	3 (25.0)	0	1 (14.3)	0
AST increased	3 (25.0)	0	1 (14.3)	0
Dry skin	3 (25.0)	0	0	0
Paronychia	3 (25.0)	1 (8.3)	0	0
Pruritus	3 (25.0)	0	0	0
Dizziness	1 (8.3)	0	2 (28.6)	0
Platelet count decreased	1 (8.3)	0	2 (28.6)	0
Vomiting	1 (8.3)	0	2 (28.6)	0

Data cut-off: Dec 12, 2018.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; TRAE, treatment-related adverse event.
1. Wu Y-L, et al. *Lancet Respir Med*. 2020;8(11):1132–1143.

INSIGHT: Updated treatment duration (patients with *MET*amp and treatment duration >1 year)

- Of 18 patients with *MET*amp, treatment duration was >1 year in eight patients (44.4%), and >4 years in three patients (16.7%)
- At the end of the study, two patients transitioned to continue tepotinib + gefitinib outside the study via an Expanded Access Program

	Age, years*	Sex	*EGFR* mutation	*MET* GCN	*MET*: *CEP7* ratio	MET IHC score	Best response†
Phase II	42	F	Del19	13.9	4.8	3+	PR
	66	M	L858R	13.3	3.2	3+	PR
	68	F	Del19	6.7	1.8	3+	PR
	52	F	Del19	12.4	5.7	3+	PR
	53	F	Del19	7.7	2.8	3+	PR
	67	M	G719X	5.2	1.5	3+	SD
Phase Ib‡	60	M	Del19	5.4	2.1	3+	PR
	63	M	L858R	7.3	1.3	3+	PR



Data cut-off: 12 Dec 2018. *At start of treatment with tepotinib + gefitinib; †Prior to the data cut-off; ‡Both patients with *MET*amp in Phase Ib with treatment duration >12 months received tepotinib at the 500 mg dose; §Most recent EGFR inhibitor; ¶Prior treatment also included gefitinib and chemotherapy.
EGFR, epidermal growth factor receptor; GCN, gene copy number; IHC, immunohistochemistry; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.

INSIGHT case study 1: Prolonged PR with tepotinib + gefitinib after progression on afatinib in a patient with *MET*amp

Diagnosis
Adenocarcinoma, Stage IV (T4/N3/M1), *EGFR* del19

1L therapy
Best response: PR
Duration of treatment: 5.8 months

Enrolled in INSIGHT Phase II

MET GCN: 13.9
MET:*CEP7:* 4.8
MET IHC 3+
EGFR T790M-negative

Gefitinib regularly interrupted to manage paronychia

Primary analysis data cut-off

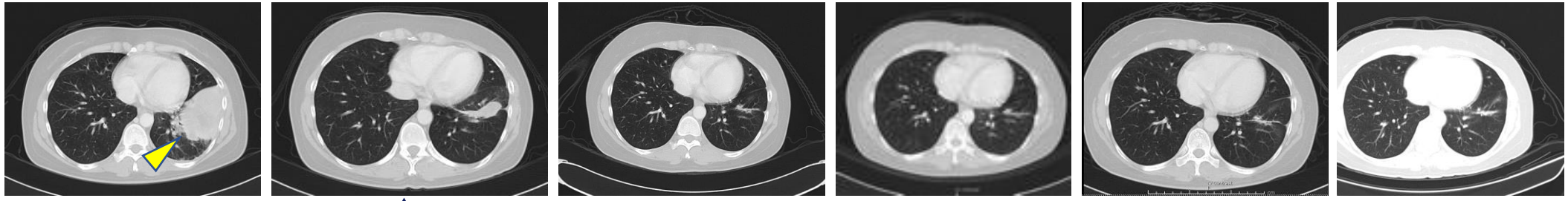
42-year-old Asian female,* never smoker (Malaysia)

01-Mar-16 | 01-Jan-18 | 01-Jan-20 | 31-Jul-21

Afatinib 30 mg → **Tepotinib 500 mg** + **Gefitinib 250 mg**

◆ **Disease progression**

Baseline (24-Oct-16)	08-Dec-16	03-Sep-18	31-Jul-19	21-Sep-20	01-Jun-21



PR at first post-baseline assessment (48% decrease in SOLD)

Response maintained over >4.5 years of treatment

- **Total duration of tepotinib + gefitinib within the study: 56.5 months**
- **After the end of the study, the patient continued treatment via an Expanded Access Program**

Courtesy of Azura Rozila Ahmad (Malaysia). *Age at enrollment into INSIGHT.
1L, first-line; EGFR, epidermal growth factor receptor; GCN, gene copy number; IHC, immunohistochemistry; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; PR, partial response; SOLD, sum of longest diameter.

INSIGHT case study 2: Prolonged duration of tepotinib + gefitinib after progression on erlotinib in a patient with *MET*amp

Diagnosis
Adenocarcinoma, Stage IV (T4/N2/M1b), *EGFR* L858R

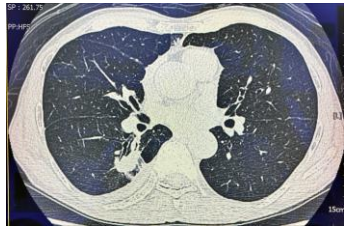
1L therapy
Best response: PR
Duration of treatment: 10.0 months

Enrolled in INSIGHT Phase II

MET GCN: 13.3
MET:*CEP7*: 3.2
MET IHC 3+
EGFR T790M-negative

Tepotinib interruption to manage elevations in lipase and amylase

Primary analysis data cut-off



No PD observed as of May 2021

66-year-old Asian male,* former smoker (Taiwan)

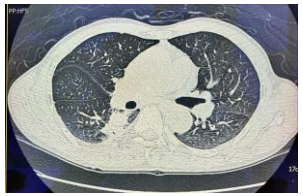
01-Jan-16 | 01-Jan-17 | 01-Jan-18 | 01-Jan-19 | 01-Jan-20 | 01-Jan-21

Erlotinib 150 mg

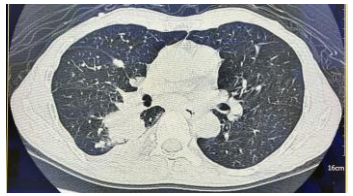
Tepotinib 500 mg

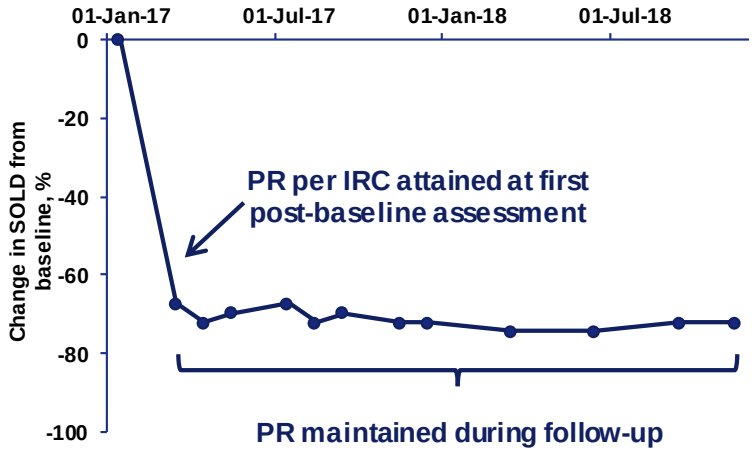
Gefitinib 250 mg

Diagnosis (Feb 2016)

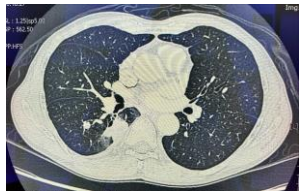


Progression (Dec 2016)

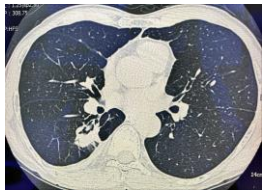




May 2019



May 2020



Disease progression

- **Total duration of tepotinib + gefitinib within the study: 52.0 months**
- **After the end of the study, the patient continued treatment via an Expanded Access Program**

Courtesy of Te-Chun Hsia (Taiwan). *Age at enrollment into INSIGHT. 1L, first-line; EGFR, epidermal growth factor receptor; GCN, gene copy number; IHC, immunohistochemistry; IRC, independent review committee; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; PR, partial response; SOLD, sum of longest diameter.

INSIGHT case study 3: Prolonged duration of tepotinib + gefitinib after progression on erlotinib in a patient with *MET*amp

68-year-old Asian female,* never smoker (Malaysia)

Diagnosis
Adenocarcinoma, Stage IIIA (T2a/N2/M0), *EGFR* del19

Primary treatment
Left lower lobectomy (R0 resection)

Adjuvant therapy
CT†

1L therapy
Best response: PR
DOR: 11.1 months
Duration of treatment: 16.1 months
Erlotinib 150 mg

Enrolled in INSIGHT Phase II
MET GCN: 6.7
MET:*CEP7:* 1.8
MET IHC 3+
EGFR T790M-negative
EGFR del19

Primary analysis data cut-off

SBRT 24 Gy to C2 vertebra

Progression due to increase in a single axillary node (target lesion). Treatment continued beyond progression based on stability of other target and non-target lesions and symptom control

Tepotinib dose reduction due to Grade 3 peripheral edema

Increase in liver lesions. Treatment continued as patient declined chemotherapy or biopsy to evaluate for additional targetable alterations

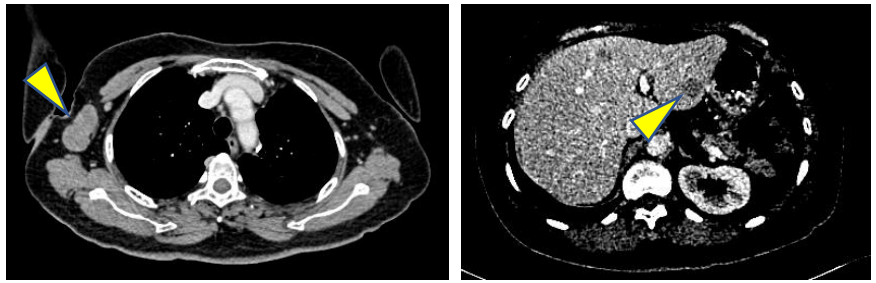
01-May-14 | 01-Jan-16 | 01-Jan-18 | 01-Jan-20 | 31-Jul-21

Tepotinib 500 mg → **Tepotinib 300 mg**
Gefitinib 250 mg

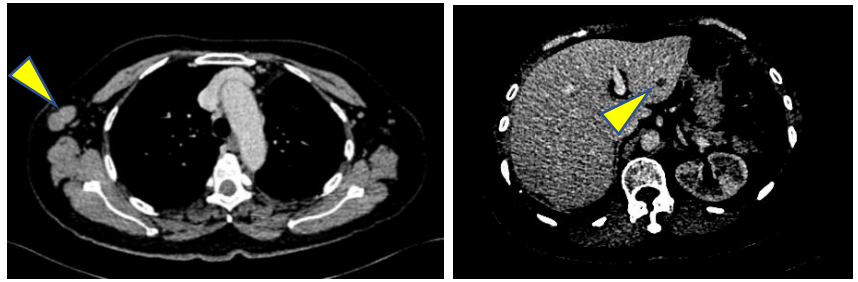
- Disease recurrence
- Disease progression
- Death

- **Total duration of tepotinib + gefitinib: 51.8 months**

Baseline CT (21-Mar-17)



CT (05-May-17)



PR at first post-baseline assessment (Week 6)

Courtesy of Chong Kin Liam (Malaysia). *Age at enrollment into INSIGHT; †Carboplatin + gemcitabine.
1L, first-line; CT, computed tomography; DOR, duration of response; EGFR, epidermal growth factor receptor; GCN, gene copy number; IHC, immunohistochemistry; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; PR, partial response; SBRT, stereotactic body radiotherapy.

Further data on tepotinib plus an EGFR inhibitor in patients with *EGFR*-mutant NSCLC and *MET*amp: INSIGHT 2

- INSIGHT 2 (NCT03940703) is an ongoing Phase II trial evaluating tepotinib + osimertinib in patients with *EGFR*-mutant NSCLC with acquired resistance to 1L osimertinib due to *MET*amp, which opened in September 2019 and had key protocol amendments implemented in April 2020[1]

Original protocol

- Eligible patients must have advanced/metastatic NSCLC harboring activating *EGFR* mutations with acquired resistance to prior **first- to third-generation EGFR TKIs**, with *MET*amp
- *MET*amp determined by **LBx**

Protocol following key amendments

- Eligible patients must have advanced/metastatic NSCLC harboring activating *EGFR* mutations that have relapsed on **first-line osimertinib** due to *MET*amp
- *MET*amp determined by FISH testing with TBx (central or local), or by central LBx, with the primary efficacy analysis set consisting of patients with *MET*amp centrally confirmed by FISH testing with TBx

- A case report of a patient enrolled through the original protocol is shown on the next slide; this patient will not be included in the primary efficacy analysis set of INSIGHT 2[2]

1L, first-line; EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; LBx, liquid biopsy; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

1. Zhu VW, et al. *J Clin Oncol*. 2021;39(suppl 15): Abstract TPS9136; 2. Liam CK. Presentation at the Malaysian Thoracic Society Annual Congress Virtual Meeting, 11–13 December 2020.

INSIGHT 2 case study: Response to tepotinib + osimertinib in a patient with *MET*amp and acquired osimertinib resistance[1]

78-year-old Asian male, never smoker (Malaysia)

Diagnosis
Adenocarcinoma, Stage IVB (cT3/N2/M1c), *EGFR* del19

1L therapy
Best response: PR
Duration of treatment: 15.1 months

*MET*amp by ArcherDX NGS liquid biopsy assay

Enrolled in INSIGHT 2

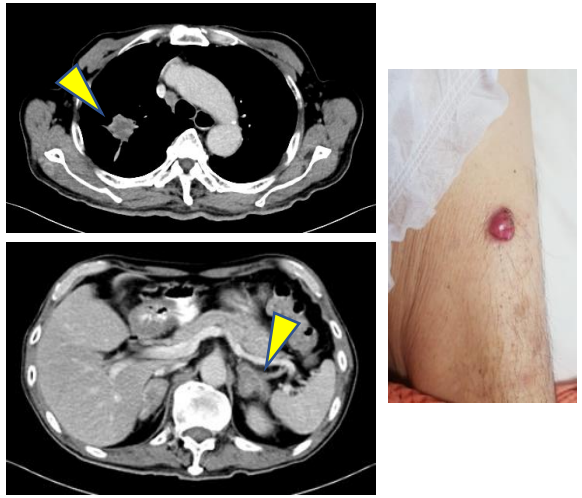
Treatment discontinued due to disease progression

01-Apr-19 | 01-Jan-20 | 01-Jan-21

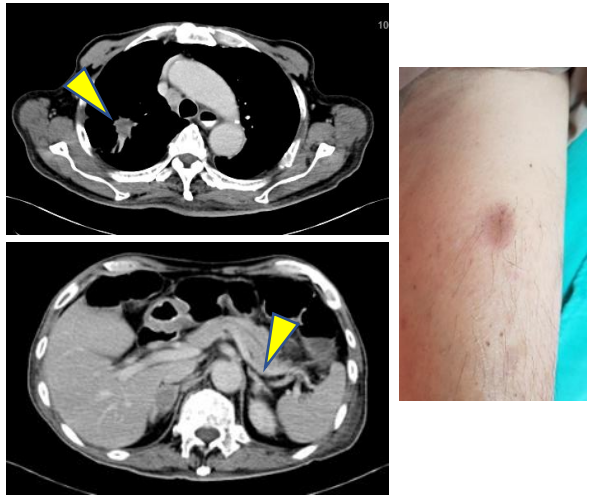
Osimertinib 80 mg

Tepotinib 500 mg
Osimertinib 80 mg

CT (20-May-20): Resistance to 1L osimertinib



CT (18-Aug-20): PR to 2L tepotinib + osimertinib



Duration of tepotinib + osimertinib: 6.4 months

◆ **Disease progression**

Courtesy of Chong Kin Liam (Malaysia).
1L, first-line; 2L, second-line; CT, computed tomography; EGFR, epidermal growth factor receptor; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NGS, next-generation sequencing; PR, partial response.
1. Liam CK. Presentation at the Malaysian Thoracic Society Annual Congress Virtual Meeting, 11-13 December 2020.

Further data on tepotinib plus an EGFR inhibitor in patients with *EGFR*-mutant NSCLC and *MET*amp: Clinical practice

- Outside clinical trials, several patients have received tepotinib plus an EGFR TKI in clinical practice (including compassionate use)
- A case report based on a patient in the US receiving this combination for >7 months is shown on the next slide

Country	Age*	Sex	Prior treatment	Time on most recent prior EGFR TKI, months	*MET*amp, GCN	EGFR TKI†	Time on treatment,‡ months	Treatment ongoing‡
US	62	Female	Chemo, afatinib, osimertinib, immunotherapy	12.0	N/A (NGS, Archer)	Osimertinib 80 mg	7.8	Yes
Hong Kong	79	Male	Gefitinib, osimertinib	11.5	10 (NGS; Foundation Medicine)	Osimertinib 80 mg	10.4	Yes

*At the beginning of combination treatment; †EGFR TKI given in combination tepotinib 500 mg (450 mg active moiety) treatment; ‡As of August 2021.
EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; GCN, gene copy number; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; N/A, not available; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

Clinical practice case study: Ongoing benefit from tepotinib + osimertinib after progression on afatinib and osimertinib in a patient with *MET*amp

Diagnosis
Adenocarcinoma, Stage IV (T1/N2/M1a), *EGFR* L858R

62-year-old Caucasian female, never smoker (US)

1L therapy

2L therapy
Best response: PR
Duration of treatment: 20.5 months

EGFR T790M

3L therapy
Best response: PR
Duration of treatment: 4.6 months

RT to hilar lymph nodes

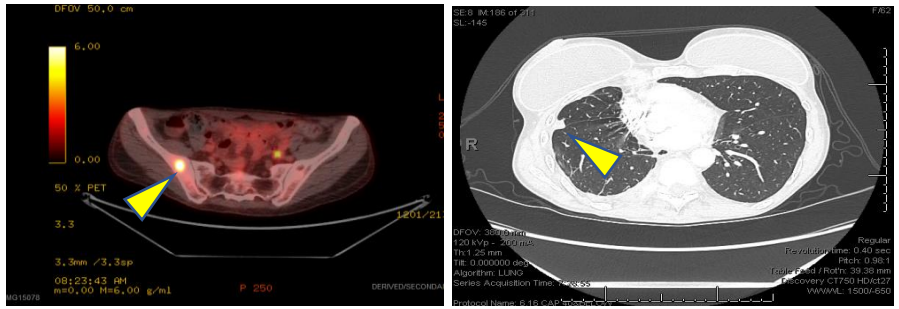
*MET*amp and *EGFR* L858R by ArcherDX NGS liquid biopsy assay

01-Jan-18 | 01-Jan-19 | 01-Jan-20 | T-cell therapy (clinical trial) | 01-Jan-21

CT* | **Afatinib 20–30 mg** | **Osimertinib 80 mg** | **Osimertinib 80 mg†** | **Tepotinib 500 mg** + **Osimertinib 80 mg**

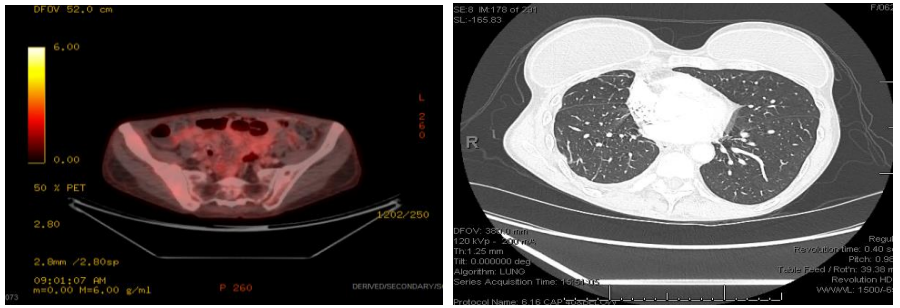
◆ **Disease progression**

Before tepotinib + osimertinib



PET (Dec 2020) **CT (Dec 2020)**

SD with shrinkage of lung tumor and metastatic lymph node



PET (Jan 2021) **CT (Feb 2021)**

Treatment ongoing as of August 2021 (total duration: 7.8 months)

Courtesy of Xiuning Le and John Heymach (US). *Carboplatin + pemetrexed; †Osimertinib was restarted as monotherapy while awaiting approval for compassionate use of tepotinib.
1L, first-line; 2L, second-line; 3L, third-line; CT, computed tomography; EGFR, epidermal growth factor receptor; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NGS, next-generation sequencing; PET, positron emission tomography; PR, partial response; RT, radiotherapy; SD, stable disease.

Clinical practice case study: Ongoing benefit from tepotinib + osimertinib after progression on gefitinib and osimertinib in a patient with *MET*amp

1L therapy
Best response: SD
Duration of treatment: 6 months

2L therapy
Best response: PR
Duration of treatment: 11.5 months

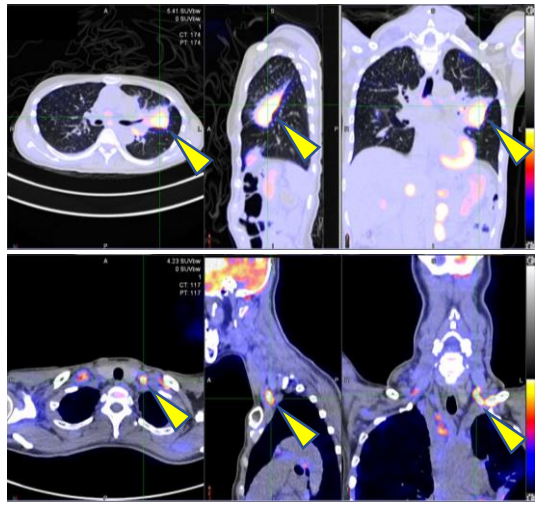
*MET*amp by
Foundation Medicine
NGS tissue biopsy assay
(*MET* GCN: 10)

79-year-old male (Hong Kong)

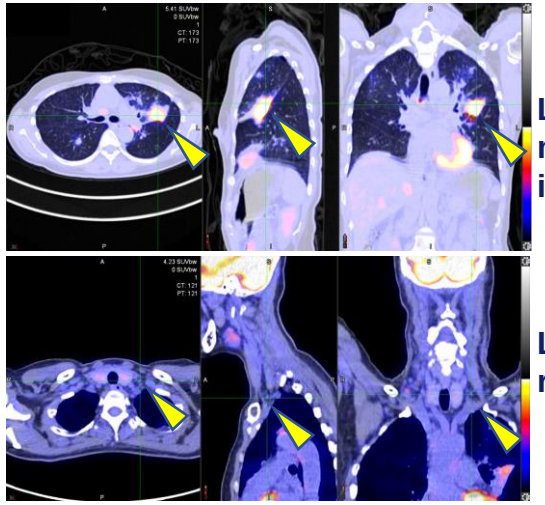
14-Mar-19 — 09-Sep-19 — 19-Sep-20

Gefitinib | **Osimertinib** | **Tepotinib 500 mg + Osimertinib 80 mg**

August 2020



February 2021



LUL lung metastasis improved

Left SCF LN resolved

Treatment ongoing as of August 2021 (best response: PR; total duration: 10.4 months)

Courtesy of Jacky Yu-Chung Li (Hong Kong).
1L, first-line; 2L, second-line; GCN, gene copy number; LN, lymph nodes; LUL, left upper lobe; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NGS, next generation sequencing; PR, partial response; RT, radiotherapy; SCF, supraclavicular fossa; SD, stable disease.

Conclusions

- The combination of tepotinib with an EGFR TKI, including osimertinib, shows clinical activity in the treatment of patients with EGFR TKI-resistant NSCLC due to *MET*amp; the relevance of MET IHC 3+ in this setting warrants further investigation
- In INSIGHT, three patients with *MET*amp received tepotinib + gefitinib for >4 years, of whom two continued treatment after study end via an Expanded Access Program
- Tepotinib + osimertinib is currently being investigated in patients with *MET*amp *EGFR*-mutant NSCLC with acquired resistance to 1L osimertinib in the INSIGHT 2 study[1]
  (see Abstract 167)
- Currently, 108 sites are active in 17 countries; encouraging preliminary activity has been observed

Global, open-label, two-arm, Phase II INSIGHT 2 trial (NCT03940703)[1]

Key eligibility criteria (N≈120)

- Locally advanced/metastatic NSCLC with activating *EGFR* mutation
- *MET*amp on tissue biopsy (FISH) or liquid biopsy
- Acquired resistance to 1L osimertinib

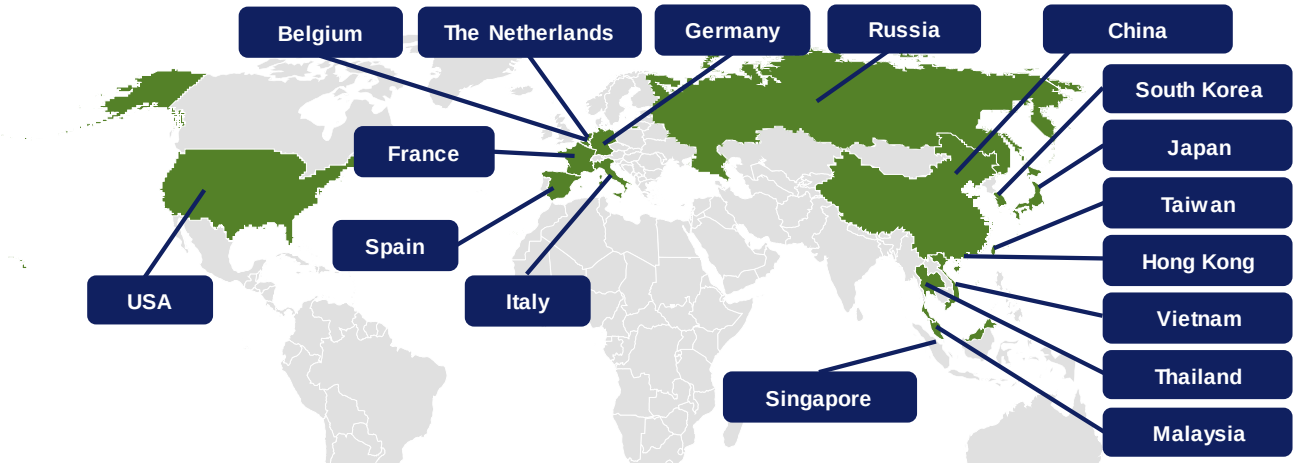
Tepotinib 500 mg*

+

Osimertinib 80 mg*

21-day cycles until PD†

INSIGHT 2 POSTER



*Initially, eligible patients who are positive for *MET* amplification will be randomly assigned in a ratio of 2:1 to either the combination of tepotinib + osimertinib or tepotinib alone, until 12 are enrolled in the monotherapy arm. After this, all patients will be assigned to the combination. Patients who are randomized to tepotinib monotherapy will have the opportunity to switch over to the combination at the time of disease progression; †Treatment continues until disease progression, death, an adverse event leading to discontinuation, study withdrawal, or consent withdrawal.

1L, first-line; EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; NSCLC, non-small cell lung cancer; PD, disease progression; TKI, tyrosine kinase inhibitor.

1. Zhu VW, et al. *J Clin Oncol*. 2021;39(suppl 15): Abstract TPS9136.

INSIGHT 2 resources

VIEW INSIGHT 2 POSTER

GET INSIGHT 2 TRIAL CARD

GET INSIGHT 2 TRIAL ANIMATION

GET INSIGHT 2 PATIENT BROCHURE

GET INSIGHT 2 PHYSICIAN BROCHURE

Acknowledgements

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