Targeted Therapy for NSCLC

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Disclosures

• Relevant financial relationships in the past 12 months.

• Consultant: Abbvie, Celgene, Takeda/Ariad, Biodesix

• The speaker will directly disclose the use of products for which are not labeled.
Evolution of NSCLC Subtyping from Histologic to Molecular-Based

NSCLC as one disease

Histology-based Subtyping

First Targeted Therapies In NSCLC

Adenocarcinoma
- ALK
- EGFR

Squamous Cell Cancer
- EGFR
- PI3KCA
- EGFR
- DDR2
- FGFR1 Amp
- Unknown
## Randomized Studies of First-Line EGFR TKIs in Patients With EGFR Mutations

<table>
<thead>
<tr>
<th>Author</th>
<th>Study</th>
<th>Agent</th>
<th>N (EGFR mut+)</th>
<th>RR</th>
<th>Median PFS (mo)</th>
<th>OS (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mok et al</td>
<td>IPASS</td>
<td>Gefitinib</td>
<td>261</td>
<td>71.2% vs 47.3%</td>
<td>9.8 vs 6.4</td>
<td>21.6 vs 21.9</td>
</tr>
<tr>
<td>Han et al</td>
<td>First-SIGNAL</td>
<td>Gefitinib</td>
<td>42</td>
<td>84.6% vs 37.5%</td>
<td>8.0 vs 6.3</td>
<td>27.2 vs 25.6</td>
</tr>
<tr>
<td>Mitsudomi et al</td>
<td>WJTOG 3405</td>
<td>Gefitinib</td>
<td>172</td>
<td>62.1% vs 32.2%</td>
<td>9.2 vs 6.3</td>
<td>30.9 vs NR</td>
</tr>
<tr>
<td>Maemondo et al</td>
<td>NEJGSG002</td>
<td>Gefitinib</td>
<td>230</td>
<td>73.7% vs 30.7%</td>
<td>10.8 vs 5.4</td>
<td>30.5 vs 23.6</td>
</tr>
<tr>
<td>Zhou et al</td>
<td>OPTIMAL</td>
<td>Erlotinib</td>
<td>154</td>
<td>83% vs 36%</td>
<td>13.7 vs 4.6</td>
<td>22.7 vs 28.9</td>
</tr>
<tr>
<td>Rosell et al</td>
<td>EURTAC</td>
<td>Erlotinib</td>
<td>174</td>
<td>58% vs 15%</td>
<td>9.7 vs 5.2</td>
<td>19.3 vs 19.5</td>
</tr>
<tr>
<td>Wu et al</td>
<td>ENSURE</td>
<td>Erlotinib</td>
<td>217</td>
<td>62.7% vs 33.6%</td>
<td>11.0 vs 5.5</td>
<td>26.3 vs 25.5</td>
</tr>
<tr>
<td>Sequist et al</td>
<td>LUX-Lung 3</td>
<td>Afatinib</td>
<td>345</td>
<td>56% vs 23%</td>
<td>13.6 vs 6.9</td>
<td>30.3 vs 26.2</td>
</tr>
<tr>
<td>Wu et al</td>
<td>LUX-Lung 6</td>
<td>Afatinib</td>
<td>364</td>
<td>67% vs 23%</td>
<td>11.0 vs 5.6</td>
<td>22.1 vs 22.2</td>
</tr>
</tbody>
</table>

EGFR, epidermal growth factor receptor; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival; RR, response rate; TKI, tyrosine kinase inhibitor.

Osimertinib in T790M Acquired Resistance

Mok et al, N Engl J Med, 2017
FLAURA Study Design

Patients with locally advanced or metastatic NSCLC

Key inclusion criteria
- ≥18 years*
- WHO performance status 0 / 1
- Exon 19 deletion / L858R (enrollment by local† or central‡ EGFR testing)
- No prior systemic anti-cancer / EGFR-TKI therapy
- Stable CNS metastases allowed

Stratification by mutation status (Exon 19 deletion / L858R) and race (Asian / non-Asian)

Randomized 1:1

Osimertinib (80 mg p.o. qd) (n=279)

RECIST 1.1 assessment every 6 weeks³ until objective progressive disease

EGFR-TKI SoC#
- Gefitinib (250 mg p.o. qd) or Erlotinib (150 mg p.o. qd) (n=277)

Crossover was allowed for patients in the SoC arm, who could receive open-label osimertinib upon central confirmation of progression and T790M positivity

Endpoints
- Primary endpoint: PFS based on investigator assessment (according to RECIST 1.1)
  - The study had a 90% power to detect a hazard ratio of 0.71 (representing an improvement in median PFS from 10 months to 14.1 months) at a two-sided alpha-level of 5%
- Secondary endpoints: objective response rate, duration of response, disease control rate, depth of response, overall survival, patient reported outcomes, safety

Soria et al, N Engl J Med, 2018
FLAURA: Efficacy

Soria et al, N Engl J Med, 2018
PFS in Patients with Brain Metastasis

Soria et al, N Engl J Med, 2018
Resistance to 1\textsuperscript{st} Line Osimertinib

- Treated with Osimertinib: N=60 Pts
  - Pts with RECIST PD: N=42
    - Pts with post-dose plasma sample: N=38
      - Pts with detectable ctDNA: N=19
      - Pts without detectable ctDNA: N=19

- Resistance mechanisms:
  - EGFR C797S: 2
  - JAK2 V617F: 1
  - PIK3CA E545K: 1
  - HER2 ex20 Ins: 1
  - MEK1 G128V: 1
  - KRAS G12D: 1
  - MET CNV: 1
  - KRAS CNV: 1
  - Other mutations identified post-dose: P53 (N=7); RB1 (N=4).

Mean TTP
- No detectable ctDNA: 19.6m
- Detectable ctDNA: 13.1m

Ramalingam et al, J Clin Oncol, 2017
Mechanisms and clinical activity of an EGFR and HER2 exon 20–selective kinase inhibitor in non-small cell lung cancer

Jacquelyne P. Robichaux¹, Yasir Y. Elamin¹, Zhi Tan², Brett W. Carter³, Shuxing Zhang², Shengwu Liu⁴, Shuai Li⁴, Ting Chen⁴, Alissa Poteete¹, Adriana Estrada-Bernal⁵, Anh T. Le⁶, Anna Truini⁶, Monique B. Nilsson¹, Huiying Sun¹, Emily Roarty¹, Sarah B. Goldberg⁶,⁷, Julie R. Brahmer⁸, Mehmet Altan¹, Charles Lu¹, Vassiliki Papadimitrakopoulou¹, Katerina Politi⁶,⁷,⁹, Robert C. Doebele⁵, Kwok-Kin Wong¹⁰ and John V. Heymach¹⁺

Although most activating mutations of epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancers (NSCLCs) are sensitive to available EGFR tyrosine kinase inhibitors (TKIs), a subset with alterations in exon 20 of EGFR and HER2 are intrinsically resistant and lack an effective therapy. We used in silico, in vitro, and in vivo testing to model structural alterations induced by exon 20 mutations and to identify effective inhibitors. 3D modeling indicated alterations restricted the size of the drug-binding pocket, limiting the binding of large, rigid inhibitors. We found that poziotinib, owing to its small size and flexibility, can circumvent these steric changes and is a potent inhibitor of the most common EGFR and HER2 exon 20 mutants. Poziotinib demonstrated greater activity than approved EGFR TKIs in vitro and in patient-derived xenograft models of EGFR or HER2 exon 20 mutant NSCLC and in genetically engineered mouse models of NSCLC. In a phase 2 trial, the first 11 patients with NSCLC with EGFR exon 20 mutations receiving poziotinib had a confirmed objective response rate of 64%. These data identify poziotinib as a potent, clinically active inhibitor of EGFR and HER2 exon 20 mutations and illuminate the molecular features of TKIs that may circumvent steric changes induced by these mutations.
EGFR Exon 20 Ins NSCLC

Other drugs in development
TAK788
Osimertinib
EGF816
Osimertinib and Necitumumab (PHI-77)
EGFR Exon 20 Insertion PDX (S768_D770dupSVD)/EGFR amplification with Tumor Growth Inhibition to Osimertinib and Cetuximab

**Osimertinib (same below)+Cetuximab (10mg/kg) IV twice per wk***
- Erlotinib (50mg/kg) PO QDx21
- Cisplatin (2mg/kg) IV Q7Dx3
- Osimertinib (25mg/kg) PO QDx21**
- Vehicle (no treatment)

**Mean Tumor Volume (mm³) ± SEM**

(Day 1 = treatment initiation)

** & *** P<0.05; Compared to Vehicle group. One-way ANOVA followed Dunnett's Multiple Comparison test.

**P<0.05; Compared to Vehicle group. One-way ANOVA followed Dunnett's Multiple Comparison test.**
A Phase I Trial of Osimertinib and Necitumumab in EGFR Mutant NSCLC with Previous EGFR-TKI Resistance

Dose Escalation of Osimertinib and Necitumumab in Advanced EGFR Mutant NSCLC with Previous EGFR-TKI Resistance (1\textsuperscript{st}-3\textsuperscript{rd} gen)

Cohort A: T790M negative, PD on afatinib, gefitinib, erlotinib as last treatment

Cohort B: EGFR T790M negative, PD on osimertinib or other 3\textsuperscript{rd} gen EGFR-TKI

Cohort C: EGFR T790M positive, PD on osimertinib or other 3\textsuperscript{rd} gen EGFR-TKI

Cohort D: EGFR Exon 20 Insertion NSCLC with PD on platinum based chemotherapy
Poziotinib is effective in pre-clinical models of both EGFR Exon 20 & HER2 Exon 20 insertion mutations

Robichaux, Heymach et al: NatureMed 2018
Relative Non-Overlap of HER2 Alterations in NSCLC

<table>
<thead>
<tr>
<th>Author</th>
<th>Amplification (FISH)</th>
<th>Mutation</th>
<th>Amp /Mut Overlap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hosokawa (N=1,126)</td>
<td>Asia (Japan)</td>
<td>5.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Mazieres (N=3,800)</td>
<td>Europe</td>
<td>9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Arcila (N=1,478)</td>
<td>USA</td>
<td>2%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Goss (N=245; SQ)</td>
<td>Global</td>
<td>NA</td>
<td>4.9%</td>
</tr>
</tbody>
</table>
# Targeted TKIs for HER2 mutant Cancers

<table>
<thead>
<tr>
<th>Targeted Agent</th>
<th>Author</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neratinib</td>
<td>Gandhi</td>
<td>0/17 (0%)</td>
</tr>
<tr>
<td>Neratinib+Temsirolimus</td>
<td>Gandhi</td>
<td>8/43 (19%)</td>
</tr>
<tr>
<td>Afatinib</td>
<td>Lai</td>
<td>3/22 (14%)</td>
</tr>
<tr>
<td>Dacomitinib</td>
<td>Kris</td>
<td>3/26 (12%)</td>
</tr>
</tbody>
</table>

## What’s New?
Ado-Trastuzumab Emtansine  
Afatinib in SQ-HER2-mutated  
Poziotinib (pre-clinical)

Kris et al. *Ann Oncol* 2015  
Gandhi et al. *WCLC* 2016  
Lai et al. *ASCO* 2017
Ado-Trastuzumab Emtansine in Lung Cancer
HER2 Overexpression vs. *HER2* mutation

Stinchcombe T, et al. ASCO 2017 (abstr 8509)

Li et al. ASCO 2017 & JCO 2018
## ERBB Family Mutation-Positive vs Negative Cancers in LUX-Lung 8

### OS in patients with and without ERBB mutation-positive tumors

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients</th>
<th>HR (95% CI)</th>
<th>Favors Afatinib Treatment</th>
<th>Favors Erlotinib Treatment</th>
<th>Interaction P Value</th>
<th>Median OS Afatinib</th>
<th>Median OS Erlotinib</th>
<th>HR (95% CI)</th>
<th>P interaction</th>
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<tbody>
<tr>
<td>LL8</td>
<td>795</td>
<td>0.81 (0.69-0.96)</td>
<td></td>
<td></td>
<td></td>
<td>8.1</td>
<td>6.4</td>
<td>0.81 (0.60-1.09)</td>
<td>0.6729</td>
</tr>
<tr>
<td>TGA</td>
<td>245</td>
<td>0.69 (0.51-0.92)</td>
<td></td>
<td></td>
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<tr>
<td>EGFR mutation</td>
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<td></td>
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</tr>
<tr>
<td>Present</td>
<td>16</td>
<td>0.64 (0.17-2.44)</td>
<td></td>
<td></td>
<td>.98</td>
<td></td>
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<tr>
<td>Absent</td>
<td>229</td>
<td>0.67 (0.50-0.91)</td>
<td></td>
<td></td>
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<tr>
<td>HER2 mutation</td>
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<td></td>
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<td></td>
<td>.006</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Present</td>
<td>12</td>
<td>0.06 (0.01-0.59)</td>
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<tr>
<td>Absent</td>
<td>233</td>
<td>0.72 (0.54-0.97)</td>
<td></td>
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<tr>
<td>HER3 mutation</td>
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<td></td>
<td></td>
<td></td>
<td>.69</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Present</td>
<td>15</td>
<td>0.52 (0.16-1.72)</td>
<td></td>
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</tr>
<tr>
<td>Absent</td>
<td>230</td>
<td>0.69 (0.51-0.94)</td>
<td></td>
<td></td>
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<tr>
<td>HER4 mutation</td>
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<td></td>
<td>.91</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Present</td>
<td>14</td>
<td>0.21 (0.02-1.94)</td>
<td></td>
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<tr>
<td>Absent</td>
<td>231</td>
<td>0.67 (0.50-0.91)</td>
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<td>ERBB network mutation</td>
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<td>.72</td>
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</tr>
<tr>
<td>Present</td>
<td>53</td>
<td>0.56 (0.29-1.08)</td>
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<tr>
<td>Absent</td>
<td>192</td>
<td>0.70 (0.50-0.97)</td>
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<tr>
<td>HER2, 3, 4 mutation</td>
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<td></td>
<td>.54</td>
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</tr>
<tr>
<td>Present</td>
<td>38</td>
<td>0.44 (0.19-0.99)</td>
<td></td>
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</tr>
<tr>
<td>Absent</td>
<td>207</td>
<td>0.71 (0.52-0.98)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Goss et al. *JAMA Oncol.* 2018
ALK is a fusion oncogene

- ligand-independent constitutive activation of ALK tyrosine kinase
- detection methods: FISH, IHC, NGS
- 3-7% frequency NSCLC
- See slides from Lung Cancer Case Presentation
• 1-2% of NSCLC-adenocarcinoma.
• ~2500 patients/annually
• ROS1 fusions (Chromosome 6) share sequence homology to ALK
• Transforming in preclinical models
• Detection by FISH and Sequencing methods (RT-PCR, NGS)

ROS1 Inhibition With Crizotinib

ORR = 72%
Median PFS = 19.2 mos.

AT Shaw et al NEJM 2014
On Lorlatinib Majority of ROS1 patients had a Decrease in Target Lesion Size*

*Number of prior TKIs counted by line

Adapted from Solomon et al ASCO 2016
Dabrafenib and Trametinib in BRAF V600E/K NSCLC (~2%)

<table>
<thead>
<tr>
<th>Drug</th>
<th>ORR</th>
<th>PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabrafenib+Trametinib</td>
<td>64%</td>
<td>10.9 months</td>
</tr>
<tr>
<td>Dabrafenib</td>
<td>33%</td>
<td>5.5 months</td>
</tr>
<tr>
<td>Vemurafenib</td>
<td>37%</td>
<td>6.5 months</td>
</tr>
</tbody>
</table>

Larotrectinib development program for NTRK fusion-positive cancers

**Adult phase I**
- Age ≥18 years
- Advanced solid tumors

**SCOUT: pediatric phase I/II**
- Age ≤21 years
- Advanced solid tumors

**NAVIGATE: adult/adolescent phase II ‘basket’ trial**
- Age ≥12 years
- Advanced solid tumors
- TRK fusion positive

- **TRK fusion status** determined by local CLIA (or similarly accredited) laboratories
- **Primary endpoint**
  - Best objective response rate (ORR)
  - RECIST v1.1 per investigator assessment
- **Secondary endpoints**
  - Duration of response (DOR)
  - Progression-free survival (PFS)
  - Safety
- **Dosing**
  - Single-agent larotrectinib, administered predominantly at 100 mg BID continuously
  - Treatment beyond progression permitted if patient continuing to benefit

Data cut-off: April 14, 2017

Drilon et al, N Engl J Med 2017
**NTRK** fusion-positive cancers are sensitive to TRK TKI therapy in a tissue-agnostic manner

*Patient had TRK solvent front resistance mutation (NTRK3 G623R) at baseline due to prior therapy.
†Pathologic CR.
NOTE: One patient not shown here. Patient experienced clinical deterioration and no post-baseline tumor measurements were recorded.

Drilon et al, New Engl J Med 2017

**larotrectinib**

ORR 75%, median PFS not reached
RET Fusions in NSCLC

• ~2% NSCLC
• KIF5B most common fusion partner
• Previous RET inhibitors (cabozantinib about 33% ORR)
**MET Exon 14 Alterations**

- **MET** mutations that lead to decreased MET degradation
  - deletions, insertions, or base substitutions
  - many disrupt splice sites flanking **MET** exon 14 → exon 14 skipping
  - increased MET receptor on the tumor cell surface

Crizotinib in METex14-altered lung cancers

Multicenter phase 1 expansion cohort
Crizotinib 250 mg twice daily
Primary endpoint: overall response

Overall response rate (ORR)
44% (95% CI: 22–69), n=8/18

Drilon et al, ASCO Annual Meeting 2016
Crizotinib in *MET*-amplified lung cancers

Multicenter phase 1 expansion cohort
Crizotinib 250 mg twice daily

**Primary endpoint:** overall response

<table>
<thead>
<tr>
<th>MET amplification</th>
<th>Low MET (MET/CEP7 1.8-2.2)</th>
<th>Intermediate MET (MET/CEP7 &gt;2.2-&lt;5.0)</th>
<th>High MET (MET/CEP7 ≥5.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=3</td>
<td>n=14</td>
<td>n=20</td>
</tr>
<tr>
<td>Overall response, n (%)</td>
<td>1 (33%) (95%CI 0.8-90.6)</td>
<td>2 (14.3%) (95%CI 1.8-42.8)</td>
<td>8 (40%) (95%CI 19.1-63.9)</td>
</tr>
<tr>
<td>Medan DoR (mo)</td>
<td>12.1</td>
<td>3.7</td>
<td>5.5</td>
</tr>
<tr>
<td>PFS (mo)</td>
<td>1.8 (0.8, 14.0)</td>
<td>1.9 (1.3, 5.5)</td>
<td>6.7 (3.4, 7.4)</td>
</tr>
</tbody>
</table>

*MET* amplification determined by FISH

Camidge et al, ASCO Annual Meeting 2018; abstract 9062
Osimertinib and Savolitinib in *EGFR*+ NSCLC

*Population: all patients dosed who had a baseline and 6-week RECIST assessment
*Patients ongoing treatment at data cut-off
PD, progressive disease; PR, partial response; PRc, confirmed partial response; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease

32-year-old female with a tumor harboring exon 19 deletion and high MET amplification responds to AZD9291/savolitinib 800 mg.

Oxnard et al J Clin Oncol 2015; abstract 2509
## Multitargeted TKIs

| Multitarget tyrosine kinase inhibitors (small molecules) | PF02341066 (crizotinib) 38 (I), 5 (I/II), 37 (II), 13 (III), 3 (IV) and case reports | Substantial antitumour activity in patients with oesophagogastric, lung and glioblastoma tumours and MET amplification and/or exon 14 deletion<sup>35, 134, 189, 210–213</sup> | *Targets: ALK, ROS1 and MET  
*Approved for the treatment of NSCLC with EML4–ALK in 2011 and NSCLC with CD74–ROS1 in 2016 |
| --- | --- | --- | --- |
| XL184 (cabozantinib) 19 (I), 3 (I/II), 37 (II), 6 (III), 2 (IV) and case reports | Breast cancer, glioblastoma, HCC, kidney cancer, medullary thyroid cancer, melanoma, NSCLC, ovarian cancer and prostate cancer | Complete response was reported for a patient with MET exon 14 deletion<sup>25</sup>. However, the majority of trials failed to show any benefit, likely because patients were not selected for MET alterations | *Targets: MET, RET and others.  
*Approved for treatment of medullary thyroid cancer |
| GSK1363089 (foretinib) 4 (I), 2 (I/II) and 5 (II) | Mixed cancer, breast cancer, gastric cancer, head and neck cancer, liver cancer, NSCLC and papillary renal cancer | Foretinib showed no activity in unselected patients with previously treated metastatic gastric cancer | *Targets: MET, RON, AXL, TIE2 and VEGFR2  
*In 2014, product development was terminated, and no other clinical trials have been started |
| MGCD265 (glesatinib) 5 (I) and 2 (II) | Mixed cancer and NSCLC | Results pending: Phase II trial NCT02544633 is the only one that includes MET genetic alterations as a biomarker | Targets: MET and AXL |
| MP470 (amuvatinib) 2 (I) and 1 (II) | Mixed cancer, gastric cancer, glioblastoma, pancreatic cancer and SCLC | Results pending: patients are not selected for MET alterations | Targets: MET, RET, FLT3 and PDGFRA |
| E7050 (golvatinib) 4 (I) and 4 (I/II) | Mixed cancer, gastric cancer, head and neck cancer and HCC | Results pending: patients are not selected for MET alterations | Targets: MET and VEGFR2 |

Comoglio, Trusolino & Boccaccio Nat Rev Cancer 2018; 341-358
## MET-specific TKIs

**Specific MET tyrosine kinase inhibitors (small molecules)**

<table>
<thead>
<tr>
<th>Inhibitor</th>
<th>Phase</th>
<th>Disease</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARQ197 (tivantinib)</td>
<td>21 (I), 4 (II/II), 17 (II) and 4 (III)</td>
<td>Mixed cancer, colorectal cancer, HCC, liver cancer, mesothelioma, NSCLC, stomach cancer and SCLC</td>
<td>Phase II and III trials failed despite reported weak overall survival benefit in patients with high MET expression. One phase III trial recruiting patients with MET+ HCC (NCT02029157), has remained open since 2013. Tivantinib is a questionable MET inhibitor; the effects observed are likely explained by the taxane-like cytotoxic activity.</td>
</tr>
<tr>
<td>INCB28060 (also known as INC280 and capmatinib)</td>
<td>9 (I), 5 (II/II), 11 (II) and 1 (IV)</td>
<td>Mixed cancer, colorectal cancer, glioblastoma, head and neck cancer, HCC, NSCLC and papillary renal cancer</td>
<td>In phase I and II trials, significant responses were reported in patients with high MET amplification and MET exon 14 deletion. One phase IV rollover trial (NCT03040973) to assess long-term follow-up of MET-dependent tumours started in May 2017.</td>
</tr>
<tr>
<td>AZD6094 (also known as HMPL-504, HMP-504, savolitinib or volitinib)</td>
<td>6 (I), 2 (II/II), 3 (II) and 1 (III)</td>
<td>Mixed cancer, colorectal cancer, gastric cancer, kidney cancer, NSCLC and papillary renal cancer</td>
<td>Results pending.</td>
</tr>
<tr>
<td>AMG337</td>
<td>1 (I), 2 (II/II) and 2 (II)</td>
<td>Mixed cancer, renal clear cell cancer, oesophageal cancer and stomach cancer</td>
<td>Results pending: one phase II trial (NCT03147971) selecting patients with tumours overexpressing MET has been started. The phase II trial NCT02016534 including MET-amplified tumours was terminated owing to safety concerns.</td>
</tr>
<tr>
<td>MSC2156119J (tepotinib)</td>
<td>2 (I) and 2 (II/II)</td>
<td>Mixed cancer, lung cancer and NSCLC</td>
<td>Results pending: latest phase II trial (NCT02864992) will study tumours with MET exon 14 deletion that did not respond to chemotherapy.</td>
</tr>
<tr>
<td>OMO-1 (also known as JNJ-38877618)</td>
<td>1(I)</td>
<td>Mixed cancer, lung cancer and NSCLC</td>
<td>Results pending. Placebo-like adverse event profile observed up to the highest dose tested; favourable pharmacokinetic profile after oral dosing.</td>
</tr>
</tbody>
</table>

Comoglio, Trusolino & Boccaccio Nat Rev Cancer 2018; 341-358
Summary

• Active, approved therapies for EGFR-mut, ALK, ROS1 rearranged NSCLC, BRAF V600E/K NSCLC
• Promising activity for RET fusion, NTRK fusion, MET fusion, HER2 mutation, EGFR Exon 20 ins.
• More pieces of the pie!!!