Current standards and practice changing studies in metastatic NSCLC with actionable mutations

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Consultant or Advisory Role in the last two years
I have received honoraria as a consultant at advisory boards from Abbvie, AstraZeneca, Boehringer Ingelheim, MSD, Pfizer, Roche and Takeda.

Speaker Honoraria in the last two years
I have received honoraria as a speaker from Astra Zeneca, Boehringer Ingelheim, Lilly, MSD and Roche.

DMC in the last two years
Roche and Takeda

Financial Support of ETOP trials (president and scientific chair)
AstraZeneca, BMS, Boehringer Ingelheim, Genentech, MSD, Roche, and Pfizer.
NSCLC with oncogenic driver mutations: current status

- Activating mutations
- Gene translocations
- Amplifications and/or mutations
Stage IV NSCC: Molecular tests negative (ALK/BRAF/EGFR/ROS1)

PD-L1 expression

PD-L1 ≥ 50%

Any expression of PD-L1

PS 0-1

PS 0-1
Pembrolizumab (≥10 mutations/Mb) [I, A; MCBS b]

High TMB [I, A] MCBS a

Nivolumab/ ipilimumab [I, A]"n

Pembrolizumab/ pemetrexed and platinum-based ChT (4 cycles), followed by pembrolizumab/ pemetrexed [I, A; MCBS a]

Atezolizumab/ pemetrexed and platinum-based ChT (4-6 cycles), followed by atezolizumab/ pemetrexed [I, A]"n

Atezolizumab/ bevacizumab with carboplatin and paclitaxel (4-6 cycles), followed by atezolizumab/ bevacizumab [I, A]"n

4-6 cycles
Platinum-based ChT:
Cisplatin/gemcitabine [I, A]
Cisplatin/docetaxel [I, A]
Cisplatin/paclitaxel [I, A]
Carboplatin/gemcitabine [I, A]
Carboplatin/docetaxel [I, A]
Carboplatin/paclitaxel [I, A]
Carboplatin/vinorelbine [I, A]
Cisplatin/pemetrexed [I, A]
Carboplatin/pemetrexed [I, B]
Carboplatin/nab-P [I, B]
+/− bevacizumab [I, A with carboplatin/ paclitaxel, otherwise III, B]

Partial response or stable disease

Maintenance treatment:
Pemetrexed (continuation) [I, A]
Gemcitabine (continuation) [I, B]
Pemetrexed (switch) [I, B]
+/− bevacizumab (if given before)

< 70 years and PS 2
Selected ≥ 70 years and PS 0-2

PS 3-4

4-6 cycles
Carboplatin-based ChT:
< 70 years and PS 2 [II, A]
≥ 70 years and PS 0-2 [I, A]
Single-agent ChT:
Gemcitabine, vinorelbine, docetaxel [I, B]
or pemetrexed [III, B]

BSC [I, B]
A phase II study of pembrolizumab in EGFR-mutant, PD-L1+, Tyrosine kinase inhibitor naïve patients with advanced NSCLC
Stage IV NSCC: Molecular tests positive (ALK/BRAF/EGFR/ROS1)

**ALK translocation** (refer to Figure 5)
- Crizotinib [I, A; MCBS 4]
- Alectinib [I, A; MCBS 4]
- Ceritinib [I, B; MCBS 4]
- Brigatinib [I, B]a

**BRAF V600 mutation** (refer to Figure 7)
- Dabrafenib/trametinib [III, A; MCBS 2]
- +/- bevacizumab [II, B; MCBS 3]a
- Afatinib [I, A]
- Dacomitinib [I, A]b
- Osimertinib [I, A]e
- Gefitinib/carboplatin/pemetrexed [I, A]e

**EGFR mutation** (refer to Figure 4)
- Gefitinib [I, A]
- Erlotinib [I, A]
- Afatinib [I, A]
- Dacomitinib [I, A]b
- Osimertinib [I, A]e
- Gefitinib/carboplatin/pemetrexed [I, A]e

**ROS1 translocation** (refer to Figure 6)
- Crizotinib [III, A; MCBS 3]
Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib

Thomas J. Lynch, M.D., Daphne W. Bell, Ph.D., Raffaella Sordella, Ph.D., Sarada Gurubhagavatula, M.D., Ross A. Okimoto, B.S., Brian W. Brannigan, B.A., Patricia L. Harris, M.S., Sara M. Haserlat, B.A., Jeffrey G. Supko, Ph.D., Frank G. Haluska, M.D., Ph.D., David N. Louis, M.D., David C. Christiani, M.D., Jeff Settleman, Ph.D., and Daniel A. Haber, M.D., Ph.D.

EGFR mutations

<table>
<thead>
<tr>
<th>Gefitinib responders</th>
<th>Non-responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/9</td>
<td>0/7</td>
</tr>
</tbody>
</table>

Lynch, NEJM 2004
T790M mediates gefitinib resistance

EGFR Mutation and Resistance of Non–Small-Cell Lung Cancer to Gefitinib

Susumu Kobayashi, M.D., Ph.D., Titus J. Boggon, Ph.D., Tajhal Dayaram, B.A., Pasi A. Jänne, M.D., Ph.D., Olivier Kocher, M.D., Ph.D., Matthew Meyerson, M.D., Ph.D., Bruce E. Johnson, M.D., Michael J. Eck, M.D., Ph.D., Daniel G. Tenen, M.D., and Balázs Halmos, M.D.

Point mutation leading to threonine-to-methionine amino acid change at position 790 of EGFR

Kobayashi, NEJM 2005
IPASS study on first line EGFR TKI versus chemotherapy

Overall response rate (%)

- Gefitinib: 71.2% (n=132)
- Carboplatin / paclitaxel: 47.3% (n=129)

Mutation positive patients:
- Gefitinib: 23.5% (n=91)
- Carboplatin / paclitaxel: 1.1% (n=85)

EGFR M+ odds ratio (95% CI) = 2.75 (1.65, 4.60), p=0.0001
EGFR M- odds ratio (95% CI) = 0.04 (0.01, 0.27), p=0.0013

Mok, ESMO 2008
Mode of Actions of EGFR TKIs

### 1st-generation TKI
- **Erlotinib**
- **Gefitinib**
  - EGFR inhibition
  - Activity range:
    - Reversible binding to wild-type and mutant EGFR
    - Inactive on T790M mutant

### 2nd-generation TKI
- **Afatinib**
- **Dacomitinib**
  - ErbB Family blockade
  - Activity range:
    - Irreversible covalent binding to EGFR, ErbB2 and ErbB4 to inhibit all ErbB Family signalling
    - Broader activity to overcome EGFR TKI-resistant mutations

### 3rd-generation TKI
- **Osimertinib**
  - EGFR mutant-specific inhibitor
  - Activity range:
    - Specificity for EGFR T790M mutant; EGFR wild-type sparing
    - Irreversible covalent binding to mutant EGFR
Stage IV lung carcinoma with EGFR-activating mutation

PS 0-2 [I, A]
PS 3-4 for all following options [III, A]

Gefitinib [I, A]
Erlotinib [I, A]
+- bevacizumab [II, B; MCBS 3]*
Afatinib [I, A]
Decodontinib [I, A]*
Osimertinib [I, A; MCBS 4]
Gefitinib/carboplatin/pametrexed [I, B]*

Disease progression

Oligoprogression

Local treatment (surgery or RT) and continue targeted systemic treatment [IV, C]

Systemic progression

Exon 20 T790M mutation testing:
Re-biopsy or cfDNA plasma testing, with re-biopsy if plasma test is negative [II, A]

Exon 20 T790M mutation positive

Osimertinib [I, A; MCBS 4]

Systemic progression

Exon 20 T790M mutation negative
Or re-biopsy indicated but not feasible

Platinum-based ChT [I, A] (see Figure 2)
Carboplatin/paclitaxel/bevacizumab/necituzumab [III, A]*
LUX-Lung 7: Comparison of afatinib versus gefitinib in first line treatment of EGFR-mutated NSCLC

Stage IIIIB/IV adenocarcinoma of the lung
EGFR mutation (Del19 and/or L858R) in the tumor tissue
No prior treatment for advanced/metastatic disease
ECOG PS 0/1

Afatinib 40 mg once daily
Gefitinib 250 mg once daily

Stratified by:
- Mutation type (Del19/L858R)
- Brain metastases (present/absent)

Primary endpoints:
- PFS (independent)
- TTP
- OS

Secondary endpoints:
- ORR
- Time to response
- Duration of response
- Duration of disease control
- Tumor shrinkage
- HRQoL
- Safety

Controlled ZNS metastases included

PFS

Controlled ZNS metastases included

<table>
<thead>
<tr>
<th></th>
<th>Afatinib (n=160)</th>
<th>Gefitinib (n=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median, mo</td>
<td>11.0</td>
<td>10.9</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.74 (0.57–0.95)</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.0178*</td>
<td></td>
</tr>
</tbody>
</table>

Pas-Ares, ESMO 2016; Ann Oncol 2017
Dacomitinib versus gefitinib as first-line treatment for patients with EGFR-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial*

* CNS metastases excluded, Asian patients only.
**EGFR-mutated NSCLC: Erlotinib with bevacizumab in first-line**

- **JO25567**: Ph2, randomized, Japanese multicenter, open-label\(^a\)
- **BELIEF**: Ph2, multicenter, single-arm study, stratified by pretreatment T790M status\(^b\)

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Seto, Lancet Oncol 2014; Rosell, Lancet Respir Med. 2017
RELAY: A multinational, double-blind, randomized phase 3 study of erlotinib in combination with ramucirumab or placebo in previously untreated patients with EGFRm metastatic NSCLC

RELAY Primary Endpoint: PFS (Investigator-Assessed)

1 yr PFS rates: 71.9% vs 50.7%

Nakagawa, ASCO 2019
NEJ009: Study Design and Endpoints

# Induction Phase
- Gefitinib (daily)
- Carboplatin + Pemetrexed (4-6 cycles, q21d)

# Maintenance Phase
- Gefitinib (daily)
- Pemetrexed (q21d)
  - Repeat until PD

# Randomized 1:1
- Non-squamous NSCLC
- Previously untreated stage IIIB, IV, recurrence
- 20-75 years old
- PS 0-1
- Positive EGFR mutation

Stratified by sex, stage, type of EGFR mutation, and smoking history

# Recommended by the protocol

**Graphs showing Progression-Free Survival and Overall Survival**

Nakamura, ASCO 2018
Phase III randomized trial comparing gefitinib to gefitinib with pemetrexed-carboplatin chemotherapy in patients with advanced untreated EGFR mutant NSCLC

**Gef vs Gef + C**

**ELIGIBILITY CRITERIA**
- Age ≥ 18 yrs
- Histologic/ cytologic NSCLC
- Stage IIIIB not amenable to radical therapy or Stage IV
- First-line palliative intent
- Activating EGFR mutation (exon 19/21/ 18)
- ECOG PS 0 to 2
- Adequate organ function
- No h/o ILD, radiation pneumonitis that required steroids or IPF

**STRATIFY**
- ECOG PS (0/1 x 2)
- EGFR mutation (exon 19 v. other)

**Randomized 1:1 Open Label**
- Gefitinib 250mg daily
- Pem 500 mg/m² +
- Carbo AUC 5 Q21d x 4 → Pem 500 mg/m² Q21d

**Evaluation:** Clinical- Q 3 wks in Gef + C (pre-chemo), Q 2/mth (gef); Radiologic- Q 2-3 mth

**Duration of Therapy:** until PD, unacceptable toxicity or consent withdrawal

Noronha, ASCO 2019
Phase III randomized trial comparing gefitinib to gefitinib with pemetrexed-carboplatin chemotherapy in patients with advanced untreated EGFR mutant NSCLC

Median PFS
- 16 months
- 8 months

Median OS
- NR
- 21 months

Noronha, ASCO 2019
FLAURA: First or third generation TKI inhibitors as first line therapy for patients with EGFR mutated NSCLC

Endpoints
- Primary endpoint: PFS based on investigator assessment (according to RECIST 1.1)
  - The trial had a 90% chance that the hazard ratio of PFS would be 0.71, representing an improvement in median PFS from 10 months to 14.1 months, with a 90% confidence interval of 0.55 to 0.91.
- Secondary endpoints: objective response rate, duration of response, disease control rate, depth of response, overall survival, patient-reported outcomes, safety

FLAURA: First or third generation TKI inhibitors as first line therapy for patients with EGFR mutated NSCLC

Ramalingam, ESMO 2017
Table 3. Adverse Events.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Osimertinib (N = 279)</th>
<th>Standard EGFR-TKI (N = 277)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 1</td>
</tr>
<tr>
<td>Rash or acne †</td>
<td>161 (58)</td>
<td>134 (48)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>161 (58)</td>
<td>120 (43)</td>
</tr>
<tr>
<td>Dry skin †</td>
<td>100 (36)</td>
<td>87 (31)</td>
</tr>
<tr>
<td>Paronychia †</td>
<td>97 (35)</td>
<td>52 (19)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>80 (29)</td>
<td>65 (23)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>56 (20)</td>
<td>27 (10)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>48 (17)</td>
<td>40 (14)</td>
</tr>
</tbody>
</table>
CNS response to osimertinib versus standard EGFR tyrosine Kinase inhibitors in patients with untreated EGFR-mutated advanced NSCLC

CNS progression-free survival

Cumulative incidence of CNS progression

Reungwetawattana, JCO 2018
Mechanisms of acquired resistance to first-line osimertinib: Preliminary data from the phase III FLAURA study: Control group
Mechanisms of acquired resistance to first-line osimertinib: Preliminary data from the phase III FLAURA study: Osimertinib group

No evidence of acquired EGFR T790M
Impower 150: OAS analyses of a randomized phase III study of carboplatin and paclitaxel +/− bevacizumab, with or without atezolizumab in 1L non-squamous metastatic NSCLC: Patients with EGFR-mutated tumors*

Reck, ELCC 2019 and Lancet Oncol 2019
Severe immune related adverse events are common with sequential PD-(L)1 blockade and osimertinib

Schoenfeld, Ann Oncol 2019
TATTON Phase Ib: osimertinib + savolitinib arm in patients who received prior treatment with 3rd generation EGFR TKIs

Safety and preliminary antitumor activity of U3-1402: A HER3-targeted antibody drug conjugate in EGFR TKI-resistant, EGFRm NSCLC

JNJ-61186372 (JNJ-372), an EGFR-cMet bispecific antibody, in EGFR-driven advanced NSCLC

Sequist, AACR 2019

Jänne, ASCO 2019
Systemic therapy for patients with NSCLC with activating EGFR mutations

- There is no clear preference between first and second generation EGFR TKIs. Second generation EGFR TKIs provide a superior PFS, but are associated with higher toxicity.
- Combinations of first generation EGFR TKIs with anti-angiogenic agents provide a longer PFS, combinations with caboplatin-based chemotherapy might also provide a longer OS.
- Osimertinib provides a superior PFS and is associated less side effects and better CNS efficacy as compared to first generation EGFR TKIs. It is approved either as first line treatment or in second line for patients with acquired resistance based on the T790M mutation.
- Currently available data does not yet allow a final judgment on the optimal sequencing of therapies.
Stage IV lung carcinoma with ALK translocation

Disease progression

Oligoprogression
- Local treatment (surgery or RT) and continue targeted systemic treatment

Systemic progression

Systemic progression

Systemic progression

Re-biopsy recommended (not mandatory for decision)

Alectinib [I, A; MCBS 4]
Ceritinib [I, B; MCBS 4]

Systemic progression

Platinum-based ChT (see Figure 2)
In selected cases, alternative new generation ALK TKIs
If available (lorlatinib, brigatinib) [III, B]⁺
Carboplatin/paclitaxel/bevacizumab/atezolizumab [II, B]⁺
Crizotinib versus platin-based chemotherapy in first-line treatment of advanced ALK-positive NSCLC: PRORIPE 1014

Salomon, NEJM 2014
Final overall survival analysis from a study comparing first-line crizotinib versus chemotherapy in ALK-mutation-positive NSCLC

Overall survival

OS adjusted for cross-over
Case 1: 62-y/o man

- July 2012: Adenocarcinoma of the lung, stage IIIB with bilateral mediastinal and supraclavicular nodal metastases, EGFR WT
- July – September 2012: Treatment with 3 cycles of carboplatin and pemetrexed: Stable disease
- September 2012: Start of Crizotinib
Case 1: 62-y/o man

Continuing crizotinib

- March 2017: Stereotactic radiotherapy of the 4 cerebellar lesions
- November 2018: Stereotactic radiotherapy of lesion at nucleus olivaris
### Alectinib, brigatinib, or ceritinib after crizotinib failure in ALK+ NSCLC patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Alectinib</th>
<th>Brigatinib</th>
<th>Ceritinib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median follow-up, mo</strong></td>
<td>9.9</td>
<td>21</td>
<td>28.3&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>ORR, n/N (%) [95% CI]</strong></td>
<td>35/67 (52) [40–65]</td>
<td>62/122 (51) [42–60]</td>
<td>19/25 (76) [55–91]</td>
</tr>
<tr>
<td><strong>DCR, n/N (%) [95% CI]</strong></td>
<td>55/69 (80) [Not reported]</td>
<td>96/122 (79) [70–86]</td>
<td>22/25 (88) [69–98]</td>
</tr>
<tr>
<td><strong>Dose reduction due to AEs, n/N (%)</strong></td>
<td>Pooled safety population 57/253 (23)&lt;sup&gt;3,8&lt;/sup&gt;</td>
<td>6/32 (19)&lt;sup&gt;h&lt;/sup&gt;</td>
<td>22/110 (20)</td>
</tr>
<tr>
<td><strong>Discontinuation due to AEs, n/N (%)</strong></td>
<td>2/87 (2)</td>
<td>12/138 (9)</td>
<td>4/32 (13)&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

NE = not estimable

First line alectinib versus crizotinib in advanced ALK-positive NSCLC: Progression-free survival

Camidge, ASCO 2018
Brigatinib vs crizotinib in patients with ALK inhibitor–naïve advanced ALK+ NSCLC: First Report of a Phase 3 Trial (ALTA-1L)

### Key Points
- **Stage IIIB/IV ALK+ NSCLC**
  - Randomization based on local ALK testing
  - No prior ALK inhibitor
  - 51-pulse system(s) therapy for locally advanced/metastatic NSCLC

### Randomized 1:1
- **Brigatinib** 190 mg bid with 7-day break at 98 mg
- **Crizotinib** 250 mg bid

### Stratified by:
- **Prior chemotherapy at baseline (yes/no)**
- **Prior metastatic therapy for locally advanced or metastatic disease (yes/no)**

### Disease assessment every 9 weeks, including brain MRI for all patients

### Table: Treatment Summary
<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. (%) of Patients With Events</th>
<th>Median PFS (95% CI)</th>
<th>1-Year PFS, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigatinib</td>
<td>36 (26)</td>
<td>NR</td>
<td>67 (56–79)</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>63 (46)</td>
<td>9.8 months (9.0–12.9)</td>
<td>43 (32–53)</td>
</tr>
</tbody>
</table>

### HR for disease progression or death
- 0.49 (95% CI, 0.33–0.74)
- P = 0.0007 by log-rank test

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Camidge, WCLC 2018
Targeting ALK: Precision medicine takes on drug resistance

Lin, Cancer Discovery 2017
Lorlatinib in patients with ALK-positive NSCLC: Results from a global phase 2 study

A  Treatment naive

B  Treatment post crizotinib

C  Treatment post non-crizo ALK TKI

D  Treatment post 2 or more ALK TKI

Solomon, Lancet Oncol 2018
Systemic therapy for patients with NSCLC with ALK gene rearrangements and other oncogenic driver mutations

- Crizotinib, certitinib and alectinib are approved by EMA for the first line treatment of patients with ALK translocated NSCLC.
- Ceritinib, alectinib and brigatinib are approved for patients progressing under crizotinib.
- Lorlatinib will likely be approved for third line therapy.
- Currently, based on its activity and approval, alectinib is the preferred agent in first line.
- Crizotinib is approved for ROS1 translocated tumors, other active agents include ceritinib, lorlatininb and entrectininb.
ROS1 rearrangement in NSCLC: Activity of crizotinib

- ROS1 fusion with the transmembrane solute carrier protein SLC34A2 resulting in a constitutive kinase activity in a NSCLC cell line
  Rikova, Cell 2007

Response rate 72%

Median PFS 19.2 months

Shaw, NEJM 2014
Systemic therapy for patients with NSCLC with ALK gene rearrangements and other oncogenic driver mutations

- Dabrafenib and trametinib combination is approved for NSCLC with V600E BRAF mutation.
- Encouraging developments are seen for NSCLC with MET exon 14 mutations (tepotinib, capmatinib), RET (LOXO-292, BLU-667) and NTRK (larotrectinib, entrectinib) fusions.
Dabrafenib plus trametinib in patients with previously untreated \( \text{BRAF}^{\text{V600E}} \)-mutant metastatic NSCLC: an open-label, phase 2 trial

Response rate 64%

Median PFS 10.4 months

Median OS 24.6 months

Planchard, Lancet Oncol 2017
Capmatinib (INC280) in METΔex14-mutated advanced NSCLC: Efficacy data from the phase II GEOMETRY mono-1 study

- Stage IIIb/IV NSCLC
- METΔex14 irrespective of MET G/CN by central RT-PCR
- EGFR wt (for L858R and delE19) and ALK-negative
- PS 0-1
- ≥1 measurable lesion (RECIST 1.1)
- Neurologically stable or asymptomatic brain metastases allowed

Cohort 4
- Pretreated, 2/3L
- N=60
- Enrollment Closed

Cohort 5b
- Treatment-naïve
- N=28
- Enrollment Closed

Primary endpoint
- ORR by blinded independent central review (BIRC)

Secondary endpoints
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival (OS)
- Safety

Progression-free survival per BIRC

Median PFS was 5.42 months in Cohort 4 (2/3L) and 9.69 months in Cohort 5b (1L)

- RR 40%
- Kaplan-Meier median [95% CI] (months): 5.42 [2.56, 9.69]
- Event-free rate at 12 months [95% CI]: 25.8% (11.9, 39.9)

- RR 61%
- Kaplan-Meier median [95% CI] (months): 9.69 [3.5, 13.86]
- Event-free rate at 12 months [95% CI]: 49.7% (29.3, 67.1)

Wolf, ASCO 2019
A phase 1 study of LOXO-292, a potent and highly selective RET inhibitor, in patients with RET-altered cancers

Clinical activity and tolerability of BLU-667, a highly potent and selective RET inhibitor, in patients (pts) with advanced RET-fusion+ NSCLC

Drilon, ASCO 2018

Gainor, ASCO 2019
New agents for NTRK fusions

Efficacy and safety of entrectinib in patients with NTRK fusion-positive tumours: pooled analysis of STARTRK-2, STARTRK-1 and ALKA-372-001

Efficacy of larotrectinib in TRK fusion–positive cancers in adults and children

Drilon, NEJM 2018

Demetri, ESMO 2018
Novel NSCLC agents targeting exon 20 insertions in the EGFR and HER2 genes (standard TKIs are ineffective)

Antitumor activity of TAK-788 in NSCLC with EGFR exon 20 insertions
- Response 43%
- PFS 7.3 months
- Grade 3 toxicities 40%

Antitumor activity of paziotinib in HER2 exon 20 insertions

Tumour responses to paziotinib in HER2 exon 20 mutations

Best response HER2 (evaluable patients n=12)

ORR: 50%

Heymach, WCLC 2018

Jänni, ASCO 2019
Trastuzumab emtansine (T-DM1) in patients with previously treated HER2-overexpressing metastatic NSCLC: Efficacy, safety, and biomarkers

Peters, CCR 2018
Thomas Hart Benton: "America Today"