Dacomitinib versus gefitinib for the first-line treatment of advanced EGFR mutation positive non-small cell lung cancer (ARCHER 1050): A randomized, open-label phase III trial.

ASCO Annual Meeting 2017
Dacomitinib versus Gefitinib for the First-Line Treatment of Advanced NSCLC (ARCHER 1050): A Randomized, Open-Label, Phase 3 Trial

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ARCHER 1050: Study Design

- Phase III randomized open-label study to evaluate dacomitinib as an alternative first-line treatment for patients with advanced NSCLC with an EGFR-activating mutation.

Stratification factors:
- Race (inc. Asian vs non-Asian)
- EGFR mutation type (exon 19 vs 21)

Primary endpoint:
PFS by blinded independent review (IR)
- ≥256 PFS events
- PFS HR ≤0.667 (50%)
- 90% power
- 1-sided α = 0.025
- mPFS: 14.3 vs 9.5 months

Secondary endpoints:
PFS (investigator assessed), ORR, DOR, TTF, OS, Safety, PROs

Advanced NSCLC with EGFR-activating mutation(s)
No prior systemic treatment of advanced NSCLC
No CNS metastasis
No prior EGFR TKI or other TKI
ECOG PS 0,1

Dacomitinib
45 mg PO QD
(N=227)

Gefitinib
250 mg PO QD
(N=225)
PFS: Blinded Independent Review (ITT population)

<table>
<thead>
<tr>
<th></th>
<th>Daco (N=227)</th>
<th>Gef (N=225)</th>
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<tbody>
<tr>
<td>Number of Events</td>
<td>136 (59.9%)</td>
<td>179 (79.6%)</td>
</tr>
<tr>
<td>Median PFS</td>
<td>14.7 (11.1, 16.6)</td>
<td>9.2 (9.1, 11.0)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.59 (0.47-0.74)</td>
<td>P&lt;0.0001</td>
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Proportional hazard ratio (HR) 0.59 (95% CI: 0.47-0.74), P<0.0001.
Best Overall Response (Blinded Independent Review; ITT Population)

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<tr>
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<th>Dacomitinib (n=227)</th>
<th>Gefitinib (n=225)</th>
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<tr>
<td><strong>Objective response rate</strong></td>
<td></td>
<td></td>
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<tr>
<td>Percentage of patients</td>
<td>74.9</td>
<td>71.6</td>
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<tr>
<td>95% CI</td>
<td>68.7-80.4</td>
<td>65.2-77.4</td>
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<tr>
<td>P value&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.3883</td>
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<tr>
<td><strong>Duration of response in responders&lt;sup&gt;b&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
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<tr>
<td>Median no. of months</td>
<td>14.8</td>
<td>8.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>12.0-17.4</td>
<td>7.4-9.2</td>
</tr>
<tr>
<td>P value&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
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Overall survival was not mature, with only 36.9% of events at the time of data cutoff

<sup>a</sup>The P-value (2-sided) is from the Cochran-Mantel-Haenszel test stratified by EGFR mutation status at randomization (exon 19 deletion vs. The L858R mutation) and by race (Japanese vs. Chinese and other East Asian vs. Non-Asian).

<sup>b</sup>The duration of response was calculated with the use of the Kaplan-Meier method from the time of the first documented response until the date of progression or the last RECIST assessment for patients who did not have disease progression.
## Dose Modification

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<th>Dacomitinib</th>
<th>Gefitinib</th>
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<tbody>
<tr>
<td></td>
<td>Median time to dose reduction</td>
</tr>
<tr>
<td>(n=227)</td>
<td>2.8 months (range, 0.3 to 20.3)</td>
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<td>3.3 months (1.2 to 25.7)</td>
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</tbody>
</table>

- **Dacomitinib**
  - First dose reduction: 30 mg/day
  - Second reduction: 15 mg/day

- **Gefitinib**
  - 250 mg every two days
**Conclusions**

- **ARCHER 1050** is the first randomized Phase 3 study to compare a second-generation EGFR TKI with a standard first-generation EGFR TKI for first-line treatment of patients with advanced *EGFR*-mutated NSCLC

- Dacomitinib was superior to gefitinib with respect to PFS and DOR
  - Median PFS at 14.7 months is among the highest

- Incidence of diarrhea, skin rash and mucositis is higher with dacomitinib while incidence of hepatic toxicity is higher with gefitinib

- Incidence of AEs reported for dacomitinib was comparable to that reported for other dacomitinib studies; no new safety signals were identified

- Dose modification is more frequent with dacomitinib

- Patients treated with dacomitinib shared similar improvements in patient-reported measures of key disease-associated symptoms as the gefitinib group

- Dacomitinib should be considered as a new treatment option for first-line management of patients with advanced *EGFR*-mutated NSCLC