Advances in Breast Cancer – ASCO 2018

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Hartford Healthcare Cancer Institute

Special Thanks to Dawn Holcombe for help with slide preparation
ASCO Highlights

- TAILORx
- HER2 6 vs 12
- Long Term endocrine
- PI3K
- Lung cancer
- Just a few highlights
**Trial Assigning Individualized Options for Treatment (TAILORx):**

Phase III trial of chemoendocrine therapy versus endocrine therapy alone in hormone receptor-positive, HER2-negative, node-negative breast cancer and an intermediate prognosis 21-gene recurrence score.


on behalf of the TAILORx Investigators

Joseph A. Sparano, MD

Used with permission from Dr. J Sparano and ASCO.
Background: Rationale for Design of TAILORx Precision Medicine Trial Biomarker Directed Chemotherapy

Target Population: HR-positive, HER2-negative, Node-negative Breast Cancer

- 50% of all breast cancers in U.S.
- Adjuvant chemotherapy recommended, but benefit small
- Most are overtreated

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Background: Rationale for Design of TAILORx Precision Medicine Trial
Biomarker Directed Chemotherapy

Assay Selected: 21-Gene Assay (Recurrence Score)

• Two prospective validation studies in ER-positive, node-negative breast cancer
  • Prognostic (B-14 study - tamoxifen): low recurrence with ET if RS low
  • Predictive (B-20 study - tam ± CMF): large chemotherapy benefit if RS high

• Uncertain chemotherapy benefit for mid-range RS


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Background: Rationale for Adjusting RS Ranges in TAILORx

NSABP B-20: Relationship Between Continuous RS and Distant Recurrence by Treatment

- RS range adjusted for mid-range
- Preserve prediction in high risk group
- Minimize potential for undertreatment


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### Background: Rationale for Adjusting RS Ranges in TAILORx

**Large Chemotherapy Benefit in NSABP B-20 With Recurrence Score >25 Similar to RS ≥31**

<table>
<thead>
<tr>
<th>RS</th>
<th>Patients</th>
<th>10-year DRFS (%)</th>
<th>Recurrence by Addition of Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>Tam</td>
</tr>
<tr>
<td>0-10</td>
<td>177</td>
<td>27</td>
<td>98</td>
</tr>
<tr>
<td>11-25</td>
<td>279</td>
<td>43</td>
<td>95</td>
</tr>
<tr>
<td>26-100</td>
<td>195</td>
<td>30</td>
<td>63</td>
</tr>
</tbody>
</table>

TAILORx Methods: Treatment Assignment & Randomization
Accrued Between April 2006 - October 2010

Preregister - Oncotype DX RS (N=11,232)

Register (N=10,273)

ARM A: Low RS 0-10
(N=1629 evaluable)
ASSIGN
Endocrine Therapy (ET)

Mid-Range RS 11-25
(N=6711 evaluable)

RANDOMIZE

Stratification Factors: Menopausal Status, Planned Chemotherapy, Planned Radiation, and RS 11-15, 16-20, 21-25

ARM B: Experimental Arm
(N=3399)
ET Alone

ARM C: Standard Arm
(N=3312)
ET + Chemo

ARM D: High RS 26-100
(N=1389 evaluable)
ASSIGN
ET + Chemo
TAILORx Methods: Key Eligibility Criteria
Met NCCN Guidelines for Recommending or Considering Adjuvant Chemotherapy

- Women with invasive breast cancer
- Age 18-75 years
- Node-negative
- ER and/or PR-positive in local lab (before ASCO-CAP guidelines)
- HER2-negative in local lab
- Tumor size – 1.1-5.0 cm (or 0.6-1.0 cm and int-high grade)
- Willing to have chemotherapy treatment assigned or randomized based on RS assay results

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# TAILORx Methods: Endpoints

## Primary endpoints:
- **RS 11-25:** IDFS
- **RS 0-10:** DRFI

<table>
<thead>
<tr>
<th></th>
<th>Distant Recurrence</th>
<th>Local-Regional Recurrence</th>
<th>Contralateral Breast Cancer</th>
<th>Other Second Primary Cancer</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive disease-free survival (IDFS)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Distant recurrence-free interval (DRFI)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse-free interval (RFI)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall survival (OS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>


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TAILORx Methods: Statistical Analysis Plan for RS 11-25

- Non-inferiority design for randomized arms
- Intention-to-treat for primary analysis, as-treated analysis also planned
- Hazard ratio margin 1.322 for IDFS (5 year IDFS rate 90% vs. 87%)
  - Null hypothesis of no difference, type I error rate 10% (1-sided), type II 5%
  - $P$ values shown are stratified log-rank test, and hazard ratios shown are from stratified proportional hazards models
  - Sample size adjusted for non-adherence rate (12%) - Lachin-Foulkes correction
  - Full information - 835 IDFS events

- *Exploratory interaction tests for subgroups that may derive chemo benefit (ITT)*

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Patient characteristics
- Median age 55 years, and 33% were 50 or younger
- 63% had tumor size 1-2 cm and 57% had intermediate grade histology
- Clinical risk criteria: 74% low risk, 26% high risk

Systemic Treatment
- Endocrine therapy
  - Comparable adherence and duration in both arms
  - Postmenopausal - included AI in 90%
  - Premenopausal - included OS in 15%
- Chemotherapy
  - Most common regimens were TC (56%) and anthracycline-containing (36%)

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TAILORx Results: RS Distribution in TAILORx Compared with Concurrent Use in Clinical Practice

TAILORx

Clinical Practice

Genomic Health (data on file)

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## TAILORx Patient Characteristics: Intention-to-Treat Population at Baseline

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n=9719)</th>
<th>Recurrence Score of 0-10</th>
<th>Recurrence Score of 11-25</th>
<th>Recurrence Score of 26-100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Endocrine (n=1619)</td>
<td>Endocrine (n=3399)</td>
<td>Chemoendocrine Therapy (n=3312)</td>
</tr>
<tr>
<td>Median Age (range) - years</td>
<td>56 (25-75)</td>
<td>58 (25-75)</td>
<td>55 (23-75)</td>
<td>55 (25-75)</td>
</tr>
<tr>
<td>Tumor Size - cm Median (IQR)</td>
<td>1.5 (1.2-2.1)</td>
<td>1.5 (1.2-2.0)</td>
<td>1.5 (1.2-2.0)</td>
<td>1.5 (1.2-2.0)</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td>L - 2512 (27%)</td>
<td>L - 34%</td>
<td>L - 29%</td>
<td>L - 29%</td>
</tr>
<tr>
<td></td>
<td>I - 5242 (56%)</td>
<td>I - 59%</td>
<td>I - 57%</td>
<td>I - 57%</td>
</tr>
<tr>
<td></td>
<td>H - 1676 (18%)</td>
<td>H - 7%</td>
<td>H - 13%</td>
<td>H - 14%</td>
</tr>
<tr>
<td>Clinical Risk</td>
<td>L - 6615 (70%)</td>
<td>L - 78%</td>
<td>L - 74%</td>
<td>L - 73%</td>
</tr>
<tr>
<td></td>
<td>H - 2812 (30%)</td>
<td>H - 22%</td>
<td>H - 26%</td>
<td>H - 27%</td>
</tr>
</tbody>
</table>

TAILORx Results - ITT Population: RS 11-25 (Arms B & C)

Primary Endpoint
Invasive Disease-Free Survival

- 836 IDFS events after median of 7.5 years
- 338 of 836 (40.3%) with recurrence as first event
- 199 of 836 (23.8%) were distant recurrence

P = 0.26
Hazard Ratio Arm B vs. Arm C (95% CI)
1.08 (0.94, 1.24)

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TAILORx Results - ITT Population: RS 11-25 (Arms B & C)

Secondary Endpoint
Distant Relapse-Free Interval

- 836 IDFS events after median of 7.5 years
- 338 of 836 (40.3%) with recurrence as first event
- 199 of 836 (23.8%) were distant recurrence

Hazard Ratio Arm B vs. Arm C (95% CI)
1.10 (0.85, 1.41)  

P = 0.48

Number at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>Arm C</th>
<th>CHEMO + ET</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3312</td>
<td>3399</td>
</tr>
<tr>
<td>12</td>
<td>3215</td>
<td>3318</td>
</tr>
<tr>
<td>24</td>
<td>3142</td>
<td>3239</td>
</tr>
<tr>
<td>36</td>
<td>3059</td>
<td>3147</td>
</tr>
<tr>
<td>48</td>
<td>2935</td>
<td>3033</td>
</tr>
<tr>
<td>60</td>
<td>2734</td>
<td>2833</td>
</tr>
<tr>
<td>72</td>
<td>2432</td>
<td>2537</td>
</tr>
<tr>
<td>84</td>
<td>1866</td>
<td>1947</td>
</tr>
<tr>
<td>96</td>
<td>1197</td>
<td>1267</td>
</tr>
<tr>
<td>108</td>
<td>554</td>
<td>581</td>
</tr>
</tbody>
</table>
TAILORx Results - ITT Population: RS 11-25 (Arms B & C)

Other Secondary Endpoints

Relapse-Free Interval

P = 0.33
Hazard Ratio Arm B vs. Arm C (95% CI)
1.11 (0.90, 1.37)

Overall Survival

P = 0.89
Hazard Ratio Arm B vs. Arm C (95% CI)
0.99 (0.79, 1.22)

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**TAILORx Results - ITT Population: All Arms (A,B,C & D)**

**9-Year Event Rates**

- **Arm A**: ET alone (RS 0-10) - 3% Distant recurrence rate
- **Arms B & C**: Randomized (RS 11-25) - 5% Distant recurrence rate overall
- **Arm D**: Chemoendocrine (RS 26-100) - 13% Distant recurrence rate despite chemotherapy + endocrine therapy

**IDFS Decreases as RS Increases**
P<0.001

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## TAILORx Results - ITT Population: RS 11-25 (Arms B & C)

### 9-Year Freedom from Event Rate

<table>
<thead>
<tr>
<th></th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RS 11-25</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDFS</td>
<td>83.3%</td>
<td>84.3%</td>
</tr>
<tr>
<td>DRFI</td>
<td>94.5%</td>
<td>95.0%</td>
</tr>
<tr>
<td>RFI</td>
<td>92.2%</td>
<td>92.9%</td>
</tr>
<tr>
<td>OS</td>
<td>93.9%</td>
<td>93.8%</td>
</tr>
</tbody>
</table>

≤ 1% difference for all endpoints

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TAILORx Results - ITT Population: Exploratory Analysis of Chemotherapy Treatment Interactions in RS 11-25 Arms

**No statistically significant chemotherapy treatment interactions**

- RS
  - 11-15 vs. 16-20 vs. 21-25
  - 11-17 vs. 18-25
- Tumor size (≤2 cm vs. >2 cm)
- Grade (low vs. int. vs. high)
- Menopausal status (pre vs. post)
- Clinical risk category (high vs. low)

**Statistically significant chemotherapy treatment interactions**

- Age (≤50, 51-65, >65) and chemotherapy benefit
  - IDFS (p=0.003)
  - RFI (p=0.02)
- Age (or menopause), RS (11-15, 16-20, 21-25), and chemotherapy benefit
  - IDFS - Age-RS (p=0.004)
  - IDFS - Menopause-RS (p=0.02)

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TAILORx Results - ITT Population: Potential Chemotherapy Benefit in Women ≤50 Years (N=2,216) in RS 11-25 Arms

≤50 Years, RS 16-25 - some chemotherapy benefit
  • RS 16-20: 9% fewer IDFS events, including 2% fewer distant recurrences
  • RS 21-25: 6% fewer IDFS events, mainly consisting of fewer distant recurrences

≤50 Years, RS 0-15 - good prognosis with endocrine therapy (ET)
  • RS 0-15: 3% distant recurrence with ET alone
  • RS 11-15: No evidence for chemotherapy benefit

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TAILORx Results - ITT Population: Freedom From Distant Recurrence at 9 Years According to Assigned Treatment in Women ≤50 Years (N=3,054)

*Number of patients per arm displayed under bar chart segments
Subset Analysis: Women ≤ 50 yrs and RS 21-25

Distant events: 17 v 9
Locoregional: 14 v 6

Hazard Ratio Arm B vs. Arm C (95% CI)
1.70 (1.03, 2.80)

P = 0.035

DFS Probability

Number at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
<th>84</th>
<th>96</th>
<th>108</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm C</td>
<td>246</td>
<td>241</td>
<td>235</td>
<td>221</td>
<td>207</td>
<td>190</td>
<td>175</td>
<td>126</td>
<td>76</td>
<td>41</td>
</tr>
<tr>
<td>Arm B</td>
<td>246</td>
<td>234</td>
<td>219</td>
<td>206</td>
<td>192</td>
<td>170</td>
<td>152</td>
<td>113</td>
<td>78</td>
<td>35</td>
</tr>
</tbody>
</table>
Subset Analysis:
Women ≤ 50 yrs and RS 16-20

Hazard Ratio Arm B vs. Arm C (95% CI)
1.90 (1.27, 2.84)

P = 0.0016

Number at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>Arm C</th>
<th>Arm B</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>469</td>
<td>454</td>
</tr>
<tr>
<td>12</td>
<td>453</td>
<td>439</td>
</tr>
<tr>
<td>24</td>
<td>441</td>
<td>423</td>
</tr>
<tr>
<td>36</td>
<td>423</td>
<td>407</td>
</tr>
<tr>
<td>48</td>
<td>404</td>
<td>385</td>
</tr>
<tr>
<td>60</td>
<td>373</td>
<td>356</td>
</tr>
<tr>
<td>72</td>
<td>328</td>
<td>309</td>
</tr>
<tr>
<td>84</td>
<td>259</td>
<td>223</td>
</tr>
<tr>
<td>96</td>
<td>164</td>
<td>153</td>
</tr>
<tr>
<td>108</td>
<td>84</td>
<td>71</td>
</tr>
</tbody>
</table>
TAILORx Results: Association Between Continuous RS 11-25 and 9-Year Distant Recurrence Rate by Treatment Arms Stratified by Age (≤50 vs >50 Years)

≤50 years (N=2216)

>50 years (N=4495)

RS modeled with a natural spline with 2 degrees of freedom, adjusted for tumor size and grade

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TAILORx Results: Summary

• Primary conclusions
  • **RS 11-25:** Endocrine therapy (ET) was non-inferior to chemotherapy + ET (primary endpoint - ITT)
  
  • **RS 0-10:** Distant recurrence rates very low (2-3%) with ET alone at 9 years
  
  • **RS 26-100:** Significantly higher event rates, driven by more recurrences despite adjuvant chemotherapy plus ET

• Other observations
  • Age - RS - Chemotherapy treatment interaction:
    • Some chemotherapy benefit in women 50 or younger with a RS 16-25
    • Greatest impact on distant recurrence with RS 21-25

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Implications for Clinical Practice Based on TAILORx Definitive Results for Primary and Secondary Endpoints

<table>
<thead>
<tr>
<th>Recurrence Score</th>
<th>0-25*</th>
<th>26-100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No CT Benefit</td>
<td>CT Benefit</td>
</tr>
</tbody>
</table>

*Exploratory analysis indicates women ≤50 years with RS 16-20 had ~1.5% benefit in distant recurrence and RS 21-25 had ~7% benefit in distant recurrence from ET + CT (35% of women ≤50 years have RS 16-25).
## TAILORx-Defined Cutoff for Definitively Determining Chemotherapy Benefit with Oncotype DX  
*(Node-negative, HR+, HER2-)*

<table>
<thead>
<tr>
<th>Subgroup Age  &gt;50 years</th>
<th>RS 0-10</th>
<th>RS 11-15</th>
<th>RS 16-20</th>
<th>RS 21-25</th>
<th>RS 26-100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CT Benefit</td>
<td>No CT Benefit</td>
<td>No CT Benefit</td>
<td>No CT Benefit</td>
<td>No CT Benefit</td>
<td>Large CT Benefit$^1$</td>
</tr>
</tbody>
</table>

~15% of patients >50 year old have RS 26-100$^2$

---

$^1$Sparano and Paik, *J Clin Oncol* 2008;  
$^2$Genomic Health (data on file) RS distributions in tested US N-, HR+, HER2- patients in 2017
# TAILORx-Defined Cutoff for Definitively Determining Chemotherapy Benefit with Oncotype DX

(Node-negative, HR+, HER2-)

## Subgroup Age ≤50 years

<table>
<thead>
<tr>
<th>RS 0-10</th>
<th>RS 11-15</th>
<th>RS 16-20</th>
<th>RS 21-25</th>
<th>RS 26-100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CT Benefit</td>
<td>No CT Benefit</td>
<td>~1.5% CT Benefit$^1$</td>
<td>~7% CT Benefit$^1$</td>
<td>Large CT Benefit$^2$</td>
</tr>
</tbody>
</table>

~50% of patients ≤50 year have RS 0-15, 35% RS 16-25, 15% RS 26-100$^3$

---

$^1$CT benefit for distant recurrence from Sparano 2018 ASCO presentation; $^2$Sparano and Paik, *J Clin Oncol* 2008;  
$^3$Genomic Health (data on file) RS distributions in tested US N-, HR+, HER2- patients in 2017
Acknowledgements

- NCI - Sheila Taube, PhD & JoAnne Zujewski, MD
- U.S.P.S Breast Cancer Research Stamp
- Breast Cancer Research Foundation
- Susan G. Komen for the Cure Foundation
- Advocate Community
  - Mary Lou Smith, JD, MBA - ECOG-ACRIN Advocate
  - Research Advocacy Network
  - National Breast Cancer Coalition
- Collaborating groups - NRG, Alliance, SWOG, Canadian Cancer Trials Group, Cancer Trials Ireland, INEN - Peru
- Participating sites - physicians, nurses, physician assistants, research coordinators and assistants
- Genomic Health, Inc. - Steve Shak, MD, Rick Baehner, MD
- Robert L. Comis, MD

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TAILORx

• Practice changing

• Clear data for majority of patients

• Need to find new approaches for Score > 26

• Age < 50: Still a challenge.
  – Individual patient discussions
  – ? Related to ovarian suppression from chemotherapy
PERSEPHONE: 6 versus 12 months of adjuvant trastuzumab in patients with HER2 positive early breast cancer: Randomised phase 3 non-inferiority trial with definitive 4-year disease-free survival results

Helena Earl, Louise Hiller, Anne-Laure Vallier, Shrushma Loi, Donna Howe, Helen Higgins, Karen McAdam, Luke Hughes-Davies, Adrian Harnett, Mei-Lin Ah-See, Richard Simcock, Daniel Rea, Janine Mansi, Jean Abraham, Carlos Caldas, Claire Hulme, David Miles, Andrew Wardley, David Cameron, Janet Dunn, on behalf of the PERSEPHONE Trial Investigators

Presented By Helena Earl at 2018 ASCO Annual Meeting
• **Hypothesis** - Six months adjuvant trastuzumab has similar efficacy to standard twelve months but reduced toxicity and cost

• **PERSEPHONE Trial** - Randomised phase 3 multicentre UK trial of 6 versus 12 months trastuzumab - non-inferiority design (n=4000)

• **Funding acknowledgement**
NIHR HTA programme (project number 06/303/98)

*Department of Health and Social Care disclaimer*
The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.
## Patient Characteristics

### *Stratification variables*

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>12 months (n=2045)</th>
<th>6 months (n=2043)</th>
<th>Overall (n=4088)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ER Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>633 (31)</td>
<td>632 (31)</td>
<td></td>
<td>1265 (31)</td>
</tr>
<tr>
<td>Positive</td>
<td>1412 (69)</td>
<td>1411 (69)</td>
<td></td>
<td>2823 (69)</td>
</tr>
<tr>
<td><strong>Chemotherapy type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anthracycline based</td>
<td>854 (42)</td>
<td>846 (41)</td>
<td></td>
<td>1700 (42)</td>
</tr>
<tr>
<td>Taxane based</td>
<td>200 (10)</td>
<td>203 (10)</td>
<td></td>
<td>403 (10)</td>
</tr>
<tr>
<td>Anthracycline + Taxane based</td>
<td>989 (48)</td>
<td>991 (49)</td>
<td></td>
<td>1980 (48)</td>
</tr>
<tr>
<td>Other (CMF)</td>
<td>2 (&lt;1)</td>
<td>3 (&lt;1)</td>
<td></td>
<td>5 (&lt;1)</td>
</tr>
<tr>
<td><strong>Trastuzumab timing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent</td>
<td>951 (47)</td>
<td>952 (47)</td>
<td></td>
<td>1903 (47)</td>
</tr>
<tr>
<td>Sequential</td>
<td>1094 (53)</td>
<td>1091 (53)</td>
<td></td>
<td>2185 (53)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;=50 years old</td>
<td>657 (32)</td>
<td>677 (33)</td>
<td></td>
<td>1334 (33)</td>
</tr>
<tr>
<td>&gt;50 years old</td>
<td>1388 (68)</td>
<td>1366 (67)</td>
<td></td>
<td>2754 (67)</td>
</tr>
<tr>
<td><strong>Doses received</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0 898 (44)</td>
<td>888 (43)</td>
<td></td>
<td>1786 (44)</td>
</tr>
<tr>
<td>pre-randomisation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 4</td>
<td>780 (38)</td>
<td>755 (37)</td>
<td></td>
<td>1535 (37)</td>
</tr>
<tr>
<td>5 - 9</td>
<td>367 (18)</td>
<td>400 (20)</td>
<td></td>
<td>767 (19)</td>
</tr>
</tbody>
</table>
Disease-free survival

Presented by Helena Earl at 2018 ASCO Annual Meeting

**Graph:**
- **Y-axis:** Disease-Free Survival (%)
- **X-axis:** Years from diagnosis

The graph shows the percentage of patients remaining disease-free over time, with lines representing 12 Months and 6 Months survival rates.

**Table:**

<table>
<thead>
<tr>
<th>Time</th>
<th>#events</th>
<th>HR</th>
<th>90% CI</th>
<th>Non-inferiority p</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>247</td>
<td>1.07</td>
<td>0.93-1.24</td>
<td>0.01</td>
</tr>
<tr>
<td>6 months</td>
<td>265</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Legend:**
- **12 Months**
- **6 Months**

**Non-inferiority Limit:**
- Hazard Ratio: 0.8 to 1.4

**Additional information:**
- [Link](https://warwick.ac.uk/fac/med/research/ctu/trials/cancer/persephone)
Overall survival

Presented By Helena Earl at 2018 ASCO Annual Meeting

<table>
<thead>
<tr>
<th>Years from diagnosis</th>
<th>#events</th>
<th>HR</th>
<th>90% CI</th>
<th>Non-inferiority p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 12 months: 156, HR 1.14, 90% CI 0.95-1.37, p = 0.0006
- 6 months: 179

Hazard Ratio

Non-inferiority limit
Conclusions

- The PERSEPHONE Trial demonstrates that 6m adjuvant trastuzumab is non-inferior to 12m (6m arm 89.4% 4-yr DFS; 12m arm 89.8% 4-yr DFS; HR = 1.07 [90% CI 0.93,1.24] p=0.01)
- 6m compared with 12m treatment reduces cardiac and other toxicities, and costs both to patients and healthcare systems
- Ongoing - QoL, Patient Reported Experiences, and Health Economics
- Future - translational research (blood and tumour samples on these patients)
- These exciting results mark the first steps to the reduction of treatment duration for many women with HER2 positive breast cancer
HER2 Positive Adjuvant

- Unclear impact of new data on standard adjuvant practice

- Dual HER2 blockade - Neo-adjuvant and high risk

- Paclitaxel and trastuzumab for low risk

- Extended HER2 blockade for high risk and hormone positive
Absolute Improvements in Freedom from Distant Recurrence with Adjuvant Endocrine Therapies for Premenopausal Women with HR+ HER2-negative Breast Cancer: Results from TEXT and SOFT

Meredith M. Regan, Prudence A. Francis, Olivia Pagani, Gini F. Fleming, Barbara A. Walley, Giuseppe Viale, Marco Colleoni, István Láng, Henry L. Gómez, Carlo Tondini, Graziella Pinotti, Angelo Di Leo, Alan S. Coates, Aron Goldhirsch, Richard D. Gelber, for the SOFT and TEXT Investigators and International Breast Cancer Study Group
Enrolled: Nov03 - Apr11

SOFT (n=3066)
- Premenopausal HR+
- ≤12 wks after surgery
- No chemo (47%) OR remain premenopausal ≤ 8 mos after chemo (53%)
- Planned OFS
- No planned chemo (40%) OR planned chemo (60%)

TEXT (n=2672)
- Premenopausal HR+
- ≤12 wks after surgery

Randomize

- Tamoxifen+OFS x 5y
- Exemestane+OFS x 5y
- Tamoxifen x 5y
- Tamoxifen+OFS x 5y
- Exemestane+OFS x 5y

Current Follow-up
- Median follow-up 9 years
- Median follow-up 8 years

OFS = ovarian function suppression
Distant Recurrence-free Interval by Cohort (HR+/HER2-)

**TEXT**

**Chemotherapy**

Absolute improvement at 8 yr, \( E+OFS \) vs \( T+OFS \): 5.1%

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>Percent without Distant Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>97.4%</td>
</tr>
<tr>
<td>2</td>
<td>96.5%</td>
</tr>
<tr>
<td>3</td>
<td>95.5%</td>
</tr>
<tr>
<td>4</td>
<td>94.5%</td>
</tr>
<tr>
<td>5</td>
<td>93.5%</td>
</tr>
<tr>
<td>6</td>
<td>92.5%</td>
</tr>
<tr>
<td>7</td>
<td>91.5%</td>
</tr>
<tr>
<td>8</td>
<td>90.0%</td>
</tr>
<tr>
<td>9</td>
<td>88.9%</td>
</tr>
</tbody>
</table>

\( N=1276 \) (159 DRs)

**No Chemotherapy**

Absolute improvement at 8 yr, \( E+OFS \) vs \( T+OFS \): 0.9%

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>Percent without Distant Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>99.3%</td>
</tr>
<tr>
<td>2</td>
<td>98.3%</td>
</tr>
<tr>
<td>3</td>
<td>97.3%</td>
</tr>
<tr>
<td>4</td>
<td>96.3%</td>
</tr>
<tr>
<td>5</td>
<td>95.3%</td>
</tr>
<tr>
<td>6</td>
<td>94.3%</td>
</tr>
<tr>
<td>7</td>
<td>93.3%</td>
</tr>
<tr>
<td>8</td>
<td>92.3%</td>
</tr>
<tr>
<td>9</td>
<td>91.3%</td>
</tr>
</tbody>
</table>

\( N=991 \) (35 DRs)

**SOFT**

**Chemotherapy**

Absolute improvement at 8 yr, \( E+OFS \) vs \( T \): 5.2%

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>Percent without Distant Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>98.2%</td>
</tr>
<tr>
<td>2</td>
<td>96.3%</td>
</tr>
<tr>
<td>3</td>
<td>94.5%</td>
</tr>
<tr>
<td>4</td>
<td>92.7%</td>
</tr>
<tr>
<td>5</td>
<td>90.9%</td>
</tr>
<tr>
<td>6</td>
<td>89.1%</td>
</tr>
<tr>
<td>7</td>
<td>87.3%</td>
</tr>
<tr>
<td>8</td>
<td>85.5%</td>
</tr>
<tr>
<td>9</td>
<td>83.7%</td>
</tr>
</tbody>
</table>

\( N=1271 \) (216 DRs)

**No Chemotherapy**

Absolute improvement at 8 yr, \( E+OFS \) vs \( T \): 1.3%

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>Percent without Distant Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>98.0%</td>
</tr>
<tr>
<td>2</td>
<td>96.3%</td>
</tr>
<tr>
<td>3</td>
<td>94.7%</td>
</tr>
<tr>
<td>4</td>
<td>93.0%</td>
</tr>
<tr>
<td>5</td>
<td>91.3%</td>
</tr>
<tr>
<td>6</td>
<td>89.7%</td>
</tr>
<tr>
<td>7</td>
<td>88.0%</td>
</tr>
<tr>
<td>8</td>
<td>86.3%</td>
</tr>
<tr>
<td>9</td>
<td>84.7%</td>
</tr>
</tbody>
</table>

\( N=1353 \) (23 DRs)
STEPP of 8-yr Freedom from Distant Recurrence: TEXT Chemotherapy

In the cohort, 8-yr %:
- 90.0% E+OFS
- 84.9% T+OFS

5.1% E+OFS vs T+OFS, avg. improvement

Improvement increases with increasing composite risk, to 15% at highest composite risks
Endocrine Therapy

• Longer follow up confirms benefit of maximal endocrine therapy in higher risk population

• ? Implications for the higher risk cohort identified in sub-group analysis if TAILORx
Greater selectivity \textit{in vitro} against mutant PI3K\(\alpha\) isoforms and cells than wildtype PI3K\(\alpha\)^{1-4}

<table>
<thead>
<tr>
<th>p110 isoform</th>
<th>Taselisib (k_i)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(K_1 (\alpha))</td>
<td>0.29 nM</td>
</tr>
<tr>
<td>a-H1047R</td>
<td>0.11 nM</td>
</tr>
<tr>
<td>a-E545K</td>
<td>0.14 nM</td>
</tr>
<tr>
<td>(\beta)</td>
<td>9.10 nM</td>
</tr>
<tr>
<td>(\delta)</td>
<td>0.12 nM</td>
</tr>
<tr>
<td>(\gamma)</td>
<td>0.97 nM</td>
</tr>
</tbody>
</table>

Olivero et al, 2014.\(^1\)

**Primary Endpoint:**
- INV-PFS in patients with PI3K\(\alpha\)-mutant tumors (central Roche cobas\(^\circ\) test\(^\circ\))

**Secondary Endpoints:**
- ORR, OS, CBR, DoR, BICR-PFS in patients with PIK3CA-mutant tumors
- Safety

**Exploratory Endpoint:**
- Efficacy in patients without PI3K\(\alpha\)-mutant tumors

**Recurrence or progression during or after AI**

- **Taselisib 4 mg QD + fulvestrant**
  - 2:1 randomization

- **Placebo QD + fulvestrant**
  - 2:1 randomization

Without PIK3CA-mutant tumors: \(n = 120\) (planned)

**Stratification:**
1. Visceral disease
2. Endocrine sensitivity
3. Geographic region

---

Endocrine sensitivity: 1) If no endocrine treatment in advanced or MBC, \(\geq 24\) months of adjuvant endocrine treatment prior to recurrence; 2) Documented clinical benefit (CR, PR, or SD \(\geq 24\) weeks) to most recent endocrine treatment in advanced or MBC.

\(^*\) Roche cobas\(^\circ\) test detects the following PI3K\(\alpha\) mutations: R88Q, N345K, C420R, E542K, E545A/G/K/D, Q546K/R/E/L, M1043I, H1047R/R/Y, and G1049R.

BICR, Blinded Independent Central Radiology; CR, complete response; DoR, duration of response; INV, investigator-assessed; MBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; SD, stable disease; QD, daily.
**SANDPIPER**

**Efficacy Data**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Median PFS, mos</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>INV: Placebo + fulvestrant</td>
<td>176</td>
<td>5.4</td>
<td>3.68, 7.29</td>
</tr>
<tr>
<td>INV: Taselisib + fulvestrant</td>
<td>340</td>
<td>7.4</td>
<td>7.26, 9.07</td>
</tr>
<tr>
<td>BICR: Placebo + fulvestrant</td>
<td>176</td>
<td>5.4</td>
<td>3.68, 9.23</td>
</tr>
<tr>
<td>BICR: Taselisib + fulvestrant</td>
<td>340</td>
<td>9.0</td>
<td>7.39, 9.49</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events</th>
<th>Placebo + fulvestrant</th>
<th>Taselisib + fulvestrant</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INV-PFS</td>
<td>67.6%</td>
<td>57.1%</td>
<td>0.70</td>
<td>0.0037</td>
</tr>
<tr>
<td>BICR-PFS</td>
<td>51.1%</td>
<td>45.9%</td>
<td>0.66</td>
<td>0.0023</td>
</tr>
</tbody>
</table>

**Adverse events:**

50% of patients on taselisib had grade 3 or 4 adverse events

- Diarrhea
- Hyperglycemia
- Rash
- Stomatitis
PI3K/AKT

• One of a few abstracts presented in oral session on PI3K/AKT pathway

• Evidence of some modest activity

• Toxicity a concern. Identifying correct population
Misc Others

• ? Denosumab and breast cancer outcomes

• Neo-adjuvant hormonal and Ki67

• CDK Resistance
Questions and Comments
**KEYNOTE-407 Study Design (NCT02775435)**

**Key Eligibility Criteria**
- Untreated stage IV NSCLC with squamous histology
- ECOG PS 0 or 1
- Provision of a sample for PD-L1 assessment
- No symptomatic brain metastases
- No pneumonitis requiring systemic steroids

**Stratification Factors**
- PD-L1 expression (TPS\(^a\) <1% vs ≥1%)
- Choice of taxane (paclitaxel vs nab-paclitaxel)
- Geographic region (east Asia vs rest of world)

**Randomization (R)**
\(1:1\)

**Treatment arms**
- **Pembrolizumab 200 mg Q3W + Carboplatin AUC 6 Q3W + Paclitaxel 200 mg/m\(^2\) Q3W OR nab-Paclitaxel 100 mg/m\(^2\) Q1W for 4 cycles (each 3 wk)**
- **Pembrolizumab 200 mg Q3W for up to 31 cycles**
- **Placebo (normal saline) Q3W + Carboplatin AUC 6 Q3W + Paclitaxel 200 mg/m\(^2\) Q3W OR nab-Paclitaxel 100 mg/m\(^2\) Q1W for 4 cycles (each 3 wk)**
- **Placebo (normal saline) Q3W for up to 31 cycles**

**End points**
- **Primary:** PFS (RECIST v1.1, BICR) and OS
- **Secondary:** ORR and DOR (RECIST v1.1, BICR), safety

**Optional Crossover**
- **Pembrolizumab 200 mg Q3W for up to 35 cycles**

---

*TPS\(^a\) = Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. Patients could crossover during combination therapy or monotherapy. To be eligible for crossover, PD must have been verified by BICR and all safety criteria had to be met.*

Paz-Ares ASCO 2018 Abstract 105

Presented By Gregory Riely at 2018 ASCO Annual Meeting
**Overall Survival at IA2, ITT**

<table>
<thead>
<tr>
<th></th>
<th>Events</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembro + Chemo</td>
<td>30.6%</td>
<td>0.64 (0.49-0.85)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Placebo + Chemo</td>
<td>42.7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Median (95% CI)**
- Pembro + Chemo: 15.9 mo (13.2-NE)
- Placebo + Chemo: 11.3 mo (9.5-14.8)

Data cutoff date: Apr 3, 2018.

Paz-Ares ASCO 2018 Abstract 105
Summary and Conclusions

- Pembrolizumab plus chemotherapy significantly improved OS (HR 0.64) over chemotherapy alone
  - Benefit was observed irrespective of PD-L1 TPS: HR 0.61 for TPS <1%, 0.57 for TPS 1-49%, and 0.64 for TPS ≥50%
- PFS (HR 0.56) and ORR (P = 0.0004) were also improved with pembrolizumab plus chemotherapy and responses were more durable
- AE frequency and severity were mostly similar between arms
  - Observed events consistent with known safety profiles of pembrolizumab and chemotherapy, with no new safety signals identified
  - Rates of discontinuation due to AEs were higher in the pembrolizumab plus chemotherapy arm, but generally low overall
  - Immune-mediated AEs were more frequent in the pembrolizumab arm, with frequency and severity consistent with those observed for pembrolizumab monotherapy
- Data suggest pembrolizumab plus carboplatin and paclitaxel or nab-paclitaxel should become a new standard-of-care for first-line treatment of metastatic squamous NSCLC, irrespective of PD-L1 expression

Paz-Ares ASCO 2018 Abstract 105
IMpower150 Study Design

Stage IV or recurrent metastatic nonsquamous NSCLC Chemotherapy-naive
Tumor tissue available for biomarker testing Any PD-L1 IHC status
Stratification factors:
- Sex
- PD-L1 IHC expression
- Liver metastases

N = 1202

Arm A
Atezolizumab\textsuperscript{b} + Carboplatin\textsuperscript{c} + Paclitaxel\textsuperscript{d}
4 or 6 cycles

Arm B
Atezolizumab\textsuperscript{b} + Carboplatin\textsuperscript{c} + Paclitaxel\textsuperscript{d}
+ Bevacizumab\textsuperscript{e}
4 or 6 cycles

Arm C (control)
Carboplatin\textsuperscript{c} + Paclitaxel\textsuperscript{d}
+ Bevacizumab\textsuperscript{e}
4 or 6 cycles

Maintenance therapy (no crossover permitted)

Treated with atezolizumab until PD by RECIST v1.1 or loss of clinical benefit
AND/OR
Treated with bevacizumab until PD by RECIST v1.1

\textsuperscript{a} Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. \textsuperscript{b} Atezolizumab: 1200 mg IV q3w. \textsuperscript{c} Carboplatin: AUC 6 IV q3w. \textsuperscript{d} Paclitaxel: 200 mg/m\textsuperscript{2} IV q3w. \textsuperscript{e} Bevacizumab: 15 mg/kg IV q3w. \textsuperscript{f} WT refers to patients without EGFR or ALK genetic alterations. \textsuperscript{g} The T-effector (Teff) gene signature is defined by expression of PD-L1, CXCL9 and IFN\gamma and is a surrogate of both PD-L1 IHC expression and pre-existing immunity (Kowanetz M, et al. WCLC 2017).
Updated PFS Analysis in the ITT-WT (Arm B vs Arm C)

- Statistically significant and clinically meaningful PFS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was previously observed\(^1\) and continued to improve with additional follow-up.

\(^a\) Stratiﬁed HR. \(^b\) For descriptive purposes only. Data cutoff: January 22, 2018

\(^1\) Reck M, et al. ESMO IO 2017 [abstract LBA1_PR].
OS in the ITT-WT (Arm B vs Arm C)

<table>
<thead>
<tr>
<th>Landmark OS, %</th>
<th>Arm B: atezo + bev + CP</th>
<th>Arm C: bev + CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-month</td>
<td>67%</td>
<td>61%</td>
</tr>
<tr>
<td>18-month</td>
<td>53%</td>
<td>41%</td>
</tr>
<tr>
<td>24-month</td>
<td>43%</td>
<td>34%</td>
</tr>
</tbody>
</table>

HR\textsuperscript{a}, 0.780
(95% CI: 0.636, 0.956)
P = 0.0164
Median follow-up: ~20 mo

- Statistically significant and clinically meaningful OS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was observed

\textsuperscript{a} Stratified HR.
Data cutoff: January 22, 2018

Presented By Gregory Riely at 2018 ASCO Annual Meeting
Summary

- IMpower150 met its co-primary PFS and OS endpoints and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy in 1L nonsquamous NSCLC, across all PD-L1 subgroups

- Clinical benefit was observed in the key subgroups of patients with EGFR/ALK genomic alterations and liver metastases at baseline, with the addition of bevacizumab to atezolizumab + chemotherapy

- The efficacy boundary has not yet been crossed for atezolizumab + chemotherapy vs bevacizumab + chemotherapy and will be tested again at the time of the final analysis

- These data demonstrate that atezolizumab + bevacizumab + chemotherapy provide a new standard of care, particularly for key patient populations studied in this trial
CheckMate 227 Part 1 Study Design

Key eligibility criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No known sensitizing EGFR/ALK alterations
- ECOG PS 0–1

Stratified by SQ vs NSQ

- Co-primary endpoints: OS in PD-L1–selected populations and PFS in TMB-selected populations treated with nivolumab + ipilimumab vs chemotherapy

Secondary endpoint: Nivolumab + chemotherapy vs chemotherapy
- PFS in patients with <1% tumor PD-L1 expression

Database lock: January 24, 2018; minimum follow-up: 11.2 months

\(^{a}\)NSQ: pemetrexed + cisplatin or carboplatin, Q3W for ≤4 cycles, with optional pemetrexed maintenance following chemotherapy or nivolumab + pemetrexed maintenance following nivolumab + chemotherapy; SQ: gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤4 cycles; \(^{b}\)One patient was randomized with <1% tumor PD-L1 expression in IVRS, but was subsequently found to have ≥1% tumor PD-L1 expression; \(^{c}\)Per BICR
PFS: Nivolumab + Chemotherapy vs Chemotherapy in Patients With <1% Tumor PD-L1 Expression

All Randomized Patients (Squamous and Non-squamous)

<table>
<thead>
<tr>
<th></th>
<th>Nivo + chemo (n = 177)</th>
<th>Chemo (n = 186)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, a,b mo</td>
<td>5.6</td>
<td>4.7</td>
</tr>
<tr>
<td>HR</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(0.58, 0.94)</td>
<td></td>
</tr>
</tbody>
</table>

95% CI: nivo + chemo (4.6, 6.7 mo), chemo (4.3, 5.6 mo); a,b In the nivo + ipi arm (n = 187), median (95% CI) PFS was 4.4 (3.1, 6.0), 1-y PFS was 29%, and HR vs chemo was 0.79 (0.62, 1.01)
PFS: Nivolumab + Chemotherapy and Nivolumab + Ipilimumab in Patients With TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression

<table>
<thead>
<tr>
<th></th>
<th>Nivo + chemo (n = 43)</th>
<th>Nivo + ipi (n = 38)</th>
<th>Chemo (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, mo</td>
<td>6.2</td>
<td>7.7</td>
<td>5.3</td>
</tr>
<tr>
<td>HR (vs chemo)</td>
<td>0.56</td>
<td>0.48 (0.35, 0.91)</td>
<td>(0.27, 0.85)</td>
</tr>
</tbody>
</table>

Exploratory analysis:
*95% CI: nivo + chemo (4.3, 9.1 mo), nivo + ipi (2.7, NR mo), chemo (4.0, 6.8 mo)
Summary: Nivolumab + Ipilimumab and Nivolumab + Chemotherapy in 1L NSCLC With <1% Tumor PD-L1 Expression

- Nivolumab + chemo vs chemo PFS HR was 0.74 (95% CI: 0.58, 0.94)\(^a\) in patients with <1% PD-L1 expression,\(^b\) consistent with other PD-(L)1 + chemo studies

- TMB testing may be clinically relevant to select patients for IO + chemo in addition to IO + IO
  - In patients with <1% PD-L1 expression, PFS benefit from nivolumab + chemo vs chemo was enhanced with high TMB (≥10 mut/Mb)
  - Patients with low TMB (<10 mut/Mb) and <1% PD-L1 did not appear to have PFS benefit from nivolumab in combination with either chemo or ipilimumab

- Responses were more durable and 1-year PFS rates were higher with nivolumab + ipilimumab vs nivolumab + chemo in patients with high TMB (≥10 mut/Mb) and <1% PD-L1 expression

- There were fewer grade 3–4 TRAEs with nivolumab + ipilimumab than nivolumab + chemo

\(^a\)NSQ PFS HR = 0.68 (95% CI: 0.51, 0.90); \(^b\)NSQ and SQ
Front Line NSCLC

• Multiple chemotherapy and immunotherapy combinations have been demonstrated to improve PFS and OS

• Important to test for PDL1 expression and TMB to help identify non chemotherapy related strategies

• No head to head data
How do we describe lung cancer in 2018?

- Histology
- Molecular Analysis
- PD-L1 Status
- Tumor Mutational Burden