2018 ASCO Annual Meeting
Sunday “News of the Day” Press Briefing

**Moderator:**
ASCO Chief Medical Officer Richard L. Schilsky, MD, FACP, FASCO

**Panel Members:**
ASCO Expert Harold Burstein, MD, PhD, FASCO
ASCO Expert Warren Chow, MD
ASCO Expert Sumanta Pal, MD
ASCO Expert John Heymach, MD, PhD

**Presenting Authors:**
Joseph Sparano, MD
Gianni Bisogno, MD, PhD
Arnaud Méjean, MD
Gilberto Lopes, MD, MBA
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
Adjuvant Chemotherapy in Early Breast Cancer:
Rationale for TAILORx Precision Medicine Trial - “Threading the Needle”

• 50% of all BCA are ER+, HER2-neg, node-neg - up to 30% have incurable recurrence by 10 yrs
  • Adjuvant chemo recommended, but benefit small (~3-5%)
  • Most are overtreated - ET alone adequate
  • Some are undertreated - some who did not receive chemo could have benefited

• Gene expression assay - 21-gene assay Recurrence Score (RS)
  • Prognostic - low RS - very low risk (5% or less) with ET alone
  • Predictive - large chemo benefit (25%) when CT added to ET
  • Uncertain chemo benefit for mid-range RS (about 2/3 of those tested)

• Key design elements of TAILORx
  • Assign therapy for low RS (ET alone) or high RS (chemo +ET)
  • Chemo randomization for mid-range RS to determine whether chemo beneficial
  • Mid-range RS adjusted (from 18-30 to 11-25) to account for exclusion of higher risk HER2+
disease and minimize potential for undertreatment
  • Prospective trial - reflects most modern chemo and ET

TAILORx: Study Design, Patient Characteristics, and Treatment

Eligibility criteria
- Women age 18-75 years
- ER+, HER-, Node- BCA
- Met NCCN guidelines for adj.chemo

Statistical plan
- Non-inferiority design
- 5-yr IDFS 90 vs. 87% (HR 1.322)
- Full information - 835 IDFS events

Preregister - Oncotype DX RS (N=11,232)
Register (N=10,273)

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

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)
ET + Chemo

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

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

Patient characteristics
- Age – median 55 yrs
- 33% < 50 yrs
- 63% tumor size 1-2 cm
- 57% with int. grade

Adjuvant chemotherapy
- Standard regimens used

TAILORx: Top-Line Results

- **Primary endpoint – ET non-inferior to ET + Chemo**
  - Hazard ratio 1.08 (95% CI 0.94, 1.24), p=0.26
  - 9 year IDFS rates 83.3% vs. 84.3%

- **Other endpoints in RS 11 – 25 arms - similar outcomes**
  - Distant recurrence rate (5%) and overall survival rates similar at 9 years irrespective of chemo use

- **Other arms: RS 0-10 and RS 26-100**
  - Low RS 0-10: 3% distant recurrence rate with ET alone
  - High RS 26-100: 13% distant recurrence despite chemo

- **Exploratory analysis in RS 11-25 group – determine whether any subgroups derived some chemo benefit**
  - < 50 years & RS 16-25: some chemo benefit – 2% fewer distant recurrences for RS 16-20 & 7% fewer for RS 21-25
TAILORx: Impact on Care

RS Spares Chemo in about 70%
- > 50 yrs with RS 11-25 (45%)
- Any age with RS 0-10 (16%)
- <50 yrs with RS 11-15 (8%)

RS Selects Chemo in about 30%
- All with RS 26-100 (17%)
- < 50 with RS 16-25 (14%)

Dr. Joseph A. Sparano
Maintenance low dose chemotherapy in patients with high risk rhabdomyosarcoma

Gianni Bisogno on behalf of the European paediatric Soft tissue sarcoma Study Group (EpSSG)
Rhabdomyosarcoma

- Rare tumor of mesenchymal origin typical of childhood
- ~350 children diagnosed in US and 320 in EU per year
- Adults may also present with rhabdomyosarcoma
- It is a very aggressive tumor, but with modern intensive treatment 70-80% of children can be cured
• The EpSSG (European paediatric Soft tissue sarcoma Study Group) includes 108 centers in 14 countries

• EpSSG conducted the randomized **RMS2005 Maintenance study** from 20/4/06 to 21/12/16

• **The study enrolled patients with:**
  a) pathologically proven high risk RMS
  b) no evidence of metastasis
  c) age 0-21
  d) previously untreated
  e) written informed consent
The RMS2005 Maintenance study for children with High risk RMS

**STANDARD INTENSIVE THERAPY**
(6-8 months)
- 9 cycles of high dose chemotherapy
- Radiotherapy
- Surgery

**MAINTENANCE TREATMENT**
6 months
(experimental arm)

No radiological evidence of tumor

**STOP TREATMENT**
(standard arm)

186 patients
185 patients

Vinorelbine
25 mg/mq/week i.v.

Cyclophosphamide
25 mg/mq/day by mouth

weeks
1 2 3 4 5 6 7 8 24

Presented by: Dr. Gianni Bisogno
Maintenance treatment toxicity: a comparison with standard IVA treatment

- Less anemia, neutropenia and thrombocytopenia (less transfusions)

- Less infection episodes

- No cardiac/hepatic/gastrointestinal/renal toxicity

<table>
<thead>
<tr>
<th>Grade 3-4</th>
<th>Standard IVA n=227</th>
<th>Maintenance N= 180</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematological Toxicity</strong></td>
<td></td>
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</tr>
<tr>
<td>Haemoglobin</td>
<td>111 (48.9%)</td>
<td>19 (8.9%)</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>194 (85.5%)</td>
<td>133 (73.9%)</td>
</tr>
<tr>
<td>Neutrophilis</td>
<td>208 (91.6%)</td>
<td>145 (80.6%)</td>
</tr>
<tr>
<td>Platelets</td>
<td>59 (26.0%)</td>
<td>2 (0.6%)</td>
</tr>
<tr>
<td><strong>Non Haematological Toxicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>3 (1.3%)</td>
<td>-</td>
</tr>
<tr>
<td>Hepatobiliary/pancreas</td>
<td>4 (1.8%)</td>
<td>-</td>
</tr>
<tr>
<td>Infection</td>
<td>128 (56.4%)</td>
<td>53 (29.4%)</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>3 (1.3%)</td>
<td>-</td>
</tr>
<tr>
<td>Neurology</td>
<td>18(7.9%)</td>
<td>3 (1.7%)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>33(14.5%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>19(8.4%)</td>
<td>6 (3.3%)</td>
</tr>
<tr>
<td>Allergy</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dermatological</td>
<td>-</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>23 (10.1%)</td>
<td>6 (3.3%)</td>
</tr>
</tbody>
</table>
5-yrs Disease Free Survival

Product-Limit Survival Estimates
With Number of Subjects at Risk

Maintenance: 77.6 (70.6-83.2)
Stop Treatment: 69.8 (62.2-76.2)

HR 0.68 (95%CI 0.45-1.02); p-value: 0.0613

5-yrs Overall Survival

Product-Limit Survival Estimates
With Number of Subjects at Risk

Maintenance: 86.5 (80.2-90.9)
Stop Treatment: 73.7 (65.8-80.1)

HR 0.52 (95%CI 0.32-0.86); p-value: 0.0111

8% increase

13% increase
Conclusions

- Maintenance therapy represents a novel well tolerated effective strategy in patients with high risk rhabdomyosarcoma
- This study establishes the new standard of treatment for patients with high risk rhabdomyosarcoma (at least in EU)
- The same approach is worthwhile to be investigated in other solid tumors of childhood
CARMENA, Cytoreductive nephrectomy followed by sunitinib versus sunitinib alone in metastatic renal cell carcinoma (mRCC) - Results of a phase III non-inferiority trial

Arnaud Méjean


On Behalf of Carmena investigators
Background

• Kidney cancer: 5 % (men) and 3 % (women) of all cancers
• Approximately 20% of patients with kidney cancer present with metastatic renal cell carcinoma (mRCC) at first diagnosis¹
• For the past 20 years, the standard of care for these patients has been surgery (cytoreductive nephrectomy)²,³ and systemic therapy
• In the last 10 years, many targeted therapies (sunitinib) have shown survival benefits in trials and are approved for treating mRCC⁴
• Compared directly with targeted therapy, does upfront nephrectomy still offer a survival benefit?

mRCC, metastatic renal cell carcinoma
Clinical situations in mRCC

1. RCC PS 0
   Small metastatic tumor burden
   - Nephrectomy is useful

2. RCC PS 2
   High metastatic tumor burden
   - Nephrectomy is not useful

3. RCC PS 0-1
   Limited metastatic tumor burden
   - Who knows if nephrectomy is useful?

RCC, Renal cell carcinoma PS, performance status

CARMENA
CARMENA
(CAncer Renal MEtastatique Nephrectomie Antiangiogéniques)

• 450 patients
• 79 centers
• Inclusion over 8 years : 2009 - 2017
• Multidisciplinary approach: urologists and medical oncologists
The CARMENA trial, prospective, randomized, academic, phase 3 non-inferiority study

Patients: N=450
- mRCC diagnosed
- Amenable to nephrectomy
- Eligible for sunitinib

Arm A: N = 226, Standard of Care
- Nephrectomy
- Sunitinib

Arm B: N = 224, Experimental
- Sunitinib

Players stratified by intermediate- and poor-risk prognostic groups

Primary endpoint: Overall survival
Secondary endpoints: Progression-free survival, tumor response, clinical benefit, safety

Arm A, nephrectomy + sunitinib; Arm B, sunitinib alone; mRCC, metastatic renal cell carcinoma; R, randomization
Overall survival

- Median Overall Survival was higher in Arm B than Arm A (18.4 vs 13.9 months)
- Median follow-up: 50.9 months
- The non-inferiority condition was met
  - Hazard Ratio for Arm A vs Arm B = 0.89 (95% CI 0.71-1.10)
  - Predefined non-inferiority margin of ≤1.20 for the upper 95% CI
Conclusions

- **Sunitinib alone is not inferior to nephrectomy followed by sunitinib**
  - Non-inferiority for overall survival was demonstrated in patients with both intermediate-risk and with poor-risk prognostic factors
  - Progression-free-survival and clinical benefit were greater with sunitinib alone compared with nephrectomy followed by sunitinib

- **When medical treatment is required, cytoreductive nephrectomy should no longer be considered the standard of care in metastatic renal cell carcinoma**

mRCC, metastatic renal cell carcinoma; OS, overall survival; PFS, progression-free survival
Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma

Pembrolizumab vs Platinum-Based Chemotherapy as First-Line Therapy for Advanced/Metastatic NSCLC With a PD-L1 TPS ≥1%: Open-Label, Phase 3 KEYNOTE-042 Study

Gilberto Lopes,1 Yi-Long Wu,2 Iveta Kudaba,3 Dariusz M. Kowalski,4 Byoung Chul Cho,5 Gilberto Castro, Jr,6 Vichien Srimuninnimit,7 Igor Bondarenko,8 Karou Kubota,9 Gregory M. Lubiniecki,10 Jin Zhang,10 Debra Kush,10 Tony Mok11

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Background

- Chemotherapy has been the standard approach for patients with non-small cell lung cancer who do not have driver mutations.
- In this study we compared pembrolizumab alone versus standard chemotherapy in patients with non-small cell lung cancer who had PD-L1 expression of 1% or higher and who did not have EGFR mutations or ALK translocation.
Overall Survival: TPS ≥1%

<table>
<thead>
<tr>
<th>Events</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Pembrolizumab</td>
<td>0.81 (0.71-0.93)</td>
<td>0.0018</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>438</td>
<td></td>
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</table>

Median (95% CI)

- Pembrolizumab: 16.7 mo (13.9-19.7)
- Chemotherapy: 12.1 mo (11.3-13.3)

Data cutoff date: Feb 26, 2018.

Dr. Gilberto Lopes
Response Rate and Duration by TPS
(RECIST v1.1, BICR)

CR: 2 patients with TPS ≥20% and 3 patients with TPS ≥1% in the pembrolizumab arm; 1 patient with TPS ≥20% and 3 patients with TPS ≥1% in the chemotherapy arm.

BICR, blinded, independent central review. Data cutoff date: Feb 26, 2018.
Summary of Exposure and Adverse Events: All Treated Patients

<table>
<thead>
<tr>
<th></th>
<th>Pembrolizumab (N = 636)</th>
<th>Chemotherapy (N = 615)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of doses, median (range)</td>
<td>9 (1-36)</td>
<td>6 (1-42)</td>
</tr>
<tr>
<td>Treatment-related AEs</td>
<td>399 (62.7%)</td>
<td>553 (89.9%)</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>113 (17.8%)</td>
<td>252 (41.0%)</td>
</tr>
<tr>
<td>Led to death</td>
<td>13 (2.0%)</td>
<td>14 (2.3%)</td>
</tr>
<tr>
<td>Led to discontinuation</td>
<td>57 (9.0%)</td>
<td>58 (9.4%)</td>
</tr>
<tr>
<td>Immune mediated AEs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>177 (27.8%)</td>
<td>44 (7.2%)</td>
</tr>
<tr>
<td>Grade 3-5</td>
<td>51 (8.0%)</td>
<td>9 (1.5%)</td>
</tr>
<tr>
<td>Led to death</td>
<td>1 (0.2%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
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</table>

<sup>a</sup>Based on a list of terms specified by the sponsor and considered regardless of attribution to treatment or immune relatedness by the investigator.

<sup>b</sup>Pneumonitis.

Data cutoff date: Feb 26, 2018
Summary and Conclusions

• Pembrolizumab significantly improved OS over platinum-based chemotherapy as first-line therapy for advanced/metastatic NSCLC with PD-L1 TPS ≥50%, ≥20%, and ≥1%
  • HR (95% CI) of 0.69 (0.56-0.85), 0.77 (0.64-0.92), and 0.81 (0.71-0.93), respectively
  • Greater magnitude of benefit for pembrolizumab at higher levels of PD-L1 expression is consistent with previous studies of pembrolizumab monotherapy in metastatic NSCLC
  • In an exploratory analysis of TPS 1-49% population, HR (95% CI) was 0.92 (0.77-1.11)

• Given the overall efficacy and safety profile, pembrolizumab monotherapy is a standard-of-care first-line therapy for PD-L1-expressing, locally advanced or metastatic, squamous or nonsquamous NSCLC without sensitizing EGFR mutations or ALK translocation
QUESTION AND ANSWER SESSION