ANNUAL MEETING
ON WOMEN’S CANCER
2017
NATIONAL HARBOR, MD
MARCH 12 - 15, 2017
Phase III Trial of Maintenance Therapy in Women with Advanced Ovary/Tubal/Peritoneal Cancer after a Complete Response to First-line Therapy – An NRG Oncology (GOG Legacy) Study

VERBAL DISCLOSURE

- Clovis Consulting/Honoraria/Reimbursement
- Advaxis Consulting/Honoraria/Reimbursement
- Janssen Consulting/Honoraria/Reimbursement
- Tesaro DMC/Consulting/Honoraria
- Merck & Co Stockholder/Shareholder
- Lilly Eli & Co Stockholder/Shareholder
- Cardinal Health Stockholder/Shareholder
Maintenance Therapy in Ovarian Cancer

• Advanced stage disease treated with surgery and chemotherapy produces a high percentage of clinical complete response (CCR)

• Following CCR there is a high probability of recurrent progressive disease.

• Maintenance therapy has been proposed to reduce the risk of recurrence and extend survival
Taxane Maintenance Therapy in Ovarian Cancer

- GOG 178/SWOG 9701 – phase III
- CCR – 3 vs 12 cycles paclitaxel
- Defined interim analysis: DMC recommended closure as PFS favored 12 cycles (7 months)
- PFS reported in *JCO* 2003
- OS reported in *Gyn Onc* 2009 – no difference

Markman M et al, Gynecol Oncol 2009;114:195
Maintenance Therapy: GOG 212

EOC, Tubal, Peritoneal
Stage III-IV
Prior chemo 5-8 cycles
CCR
Neuropathy ≤ Gr 1
PS 0-2

N=1100 anticipated
Phase III – Superiority Design
No further treatment until progression

Primary Endpoint: OS
GOG 212 – NRG Oncology Study

- Study activated 03/21/2005
- Closed 01/13/2014
- Primary clinical endpoints:
  - Overall survival (OS)
  - Quality of life (FACT-O)
  - Patient reported neurotoxicity (GOG-NTX4)
- 1157 patients
- Median duration of follow up: 71 months

Report based on data through May 19, 2016
GOG 212: Third Scheduled Interim Analysis

- Analysis of primary end point OS when at least 200 deaths in surveillance arm (May 19, 2016)
- Final analysis when at least 301 deaths in surveillance group
- The logrank statistic for each taxane regimen was below the interval specified in the study design – indicated it is unlikely either of the taxane regimens has superior OS compared to surveillance
# GOG 212 Accrual/Eligibility

<table>
<thead>
<tr>
<th></th>
<th>CT-2103</th>
<th>Paclitaxel</th>
<th>Surveillance</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomized</strong></td>
<td>387</td>
<td>384</td>
<td>386</td>
<td>1157</td>
</tr>
<tr>
<td><strong>Ineligible</strong></td>
<td>7</td>
<td>13</td>
<td>13</td>
<td>33</td>
</tr>
<tr>
<td><strong>Not Treated</strong></td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td><strong>Withdrew Consent</strong></td>
<td>19</td>
<td>12</td>
<td>12</td>
<td>43</td>
</tr>
<tr>
<td><strong>Eligible/treated</strong></td>
<td>353</td>
<td>349</td>
<td>349</td>
<td>1051</td>
</tr>
</tbody>
</table>
## Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CT-2103</th>
<th>Paclitaxel</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: &lt;50</td>
<td>75 (19.4%)</td>
<td>84 (21.9%)</td>
<td>68 (17.6%)</td>
</tr>
<tr>
<td>50 to &lt;60</td>
<td>115 (29.7%)</td>
<td>114 (29.7%)</td>
<td>138 (35.8%)</td>
</tr>
<tr>
<td>60 to &gt;70</td>
<td>137 (35.4%)</td>
<td>132 (34.4%)</td>
<td>126 (32.6%)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>60 (15.5%)</td>
<td>54 (14.1%)</td>
<td>54 (14.0%)</td>
</tr>
<tr>
<td>Race: Asian</td>
<td>7 (1.8%)</td>
<td>11 (2.9%)</td>
<td>9 (2.3%)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>21 (5.4%)</td>
<td>13 (3.4%)</td>
<td>17 (4.4%)</td>
</tr>
<tr>
<td>White</td>
<td>353 (91.2%)</td>
<td>352 (91.7%)</td>
<td>355 (92.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (1.6%)</td>
<td>8 (2.1%)</td>
<td>5 (1.4%)</td>
</tr>
</tbody>
</table>
## Tumor Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CT-2103 (387)</th>
<th>Paclitaxel (384)</th>
<th>Surveillance (386)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site: Ovary</td>
<td>336 (86.8%)</td>
<td>323 (84.1%)</td>
<td>336 (87.0%)</td>
</tr>
<tr>
<td>Tube</td>
<td>9 (2.3%)</td>
<td>16 (4.2%)</td>
<td>6 (1.6%)</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>42 (10.9%)</td>
<td>45 (11.7%)</td>
<td>44 (11.4%)</td>
</tr>
<tr>
<td>Stage: III</td>
<td>330 (85.3%)</td>
<td>328 (85.4%)</td>
<td>329 (85.2%)</td>
</tr>
<tr>
<td>IV</td>
<td>57 (14.7%)</td>
<td>56 (14.6%)</td>
<td>57 (14.8%)</td>
</tr>
<tr>
<td>Histology: Serous</td>
<td>326 (84.2%)</td>
<td>327 (85.1%)</td>
<td>336 (87.0%)</td>
</tr>
<tr>
<td>Endom</td>
<td>17 (4.4%)</td>
<td>10 (2.6%)</td>
<td>15 (3.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>43 (11.1%)</td>
<td>46 (10.4%)</td>
<td>34 (7.7%)</td>
</tr>
<tr>
<td>Grade: Grade 1</td>
<td>22 (5.7%)</td>
<td>11 (2.9%)</td>
<td>13 (3.4%)</td>
</tr>
<tr>
<td>Grade 2/3/?</td>
<td>365 (94.3%)</td>
<td>373 (97.1%)</td>
<td>373 (96.6%)</td>
</tr>
</tbody>
</table>
Overall Survival by Randomized Treatment

Treatment Group
- CT-2103
- Paclitaxel
- Surveillance

Events | Total | Median (mos)
---|---|---
194 | 387 | 60.0
206 | 384 | 51.3
200 | 386 | 54.8

Proportion Surviving

CT-2103 387 361 300 213 146 117 82 61
Paclitaxel 384 354 304 204 134 106 66 45
Surveillance 386 366 308 222 155 112 79 52

Months on Study
Overall Survival: Each Treatment Group Compared to Surveillance Group

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>Estimated Hazard Ratio</th>
<th>HR 97.5% Confidence Interval</th>
<th>Logrank (z-scale)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT-2103 v surveillance</td>
<td>0.979</td>
<td>0.781-1.23</td>
<td>0.2266</td>
</tr>
<tr>
<td>Paclitaxel v surveillance</td>
<td>1.104</td>
<td>0.884-1.38</td>
<td>-1.12</td>
</tr>
</tbody>
</table>

A HR less than 1 (logrank value greater than 0) indicates that the experimental regimen is favored.
### Progression-Free Survival by Randomized Treatment

**Treatment Group**
- **CT-2103**
- **Paclitaxel**
- **Surveillance**

<table>
<thead>
<tr>
<th></th>
<th>Events</th>
<th>Total</th>
<th>Median (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT-2103</td>
<td>290</td>
<td>387</td>
<td>16.3</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>281</td>
<td>384</td>
<td>18.9</td>
</tr>
<tr>
<td>Surveillance</td>
<td>304</td>
<td>386</td>
<td>13.4</td>
</tr>
</tbody>
</table>

**Months on Study**

- **CT-2103**: 387 events, 232 total, median 16.3 months
- **Paclitaxel**: 384 events, 259 total, median 18.9 months
- **Surveillance**: 386 events, 203 total, median 13.4 months

**Proportion Surviving Progression-Free**
- **CT-2103**: 13.4%
- **Paclitaxel**: 18.9%
- **Surveillance**: 16.3%

**Graphical Representation**

- The graph shows the survival curves for each treatment group.
- The x-axis represents months on study, ranging from 0 to 84.
- The y-axis represents the proportion surviving progression-free, ranging from 0.0 to 1.0.
- The survival curves for each group are distinct, allowing for easy comparison.

**Additional Notes**

- The data suggests that CT-2103 and Paclitaxel have better survival outcomes compared to Surveillance.
- Median progression-free survival times are provided for each group, aiding in the comparison of treatment effectiveness.

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*Bringing Together the Best in Women’s Cancer Care*
## PFS: Each Treatment Group Compared to Surveillance Group (Not a Primary Endpoint)

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>Estimated Hazard Ratio</th>
<th>HR 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT2103 v surveillance</td>
<td>0.847</td>
<td>0.721-0.995</td>
</tr>
<tr>
<td>Paclitaxel v surveillance</td>
<td>0.783</td>
<td>0.666-0.921</td>
</tr>
</tbody>
</table>
Adverse Events (CTCAE Version 3)

- Adverse events - more common in the taxane treated patients:
  - Allergic reaction/hypersensitivity
  - Fatigue
  - Alopecia
  - Nausea
  - Constipation
  - Sensory neuropathy
# Adverse Events (CTCAE Version 3)

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>CT-2103 Gr 1/2</th>
<th>CT-2103 Gr 3/4</th>
<th>Paclitaxel Gr 1/2</th>
<th>Paclitaxel Gr 3/4</th>
<th>Surveill Gr 1/2</th>
<th>Surveill Gr 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>186 (49.1%)</td>
<td>192 (50.7%)</td>
<td>225 (59.9%)</td>
<td>147 (39.3%)</td>
<td>265 (70.9%)</td>
<td>47 (12.5%)</td>
</tr>
<tr>
<td>Neuro</td>
<td>286 (75.4%)</td>
<td>47 (12.4%)</td>
<td>297 (79.4%)</td>
<td>37 (7.2%)</td>
<td>202 (54.0%)</td>
<td>7 (1.9%)</td>
</tr>
<tr>
<td>Alopecia Gr 2</td>
<td>93 (24.5%)</td>
<td>168 (44.9%)</td>
<td></td>
<td></td>
<td>52 (13.9)</td>
<td></td>
</tr>
</tbody>
</table>
PRO/QOL Assessments

PRO/QOL instruments:

• The FACT-O TOI: used to measure Quality of life (QOL)
• The FACT/GOG-NTX4 subscale (short): used to measure Chemotherapy-induced peripheral neuropathy
PRO/QOL Assessments

PRO/QOL Assessment time points:

1. Baseline.
2. Pre-cycle 3 (2 months from date on study for surveillance group)
3. Pre-cycle 5 (4 months from date on study for surveillance group)
4. Pre-cycle 7 (6 months from date on study for surveillance group)
5. Pre-cycle 12 (12 months from date on study for surveillance group)
6. 12 months post treatment (24 months from date on study for surveillance group)
Patient-Reported FACT-O TOI Score

Least Squares Means Differences (99% CIs)

P vs S
-2.9 (4.7~1.0)**
-1.7 (-3.5~0.1)
1.2 (0.6~2.9)

PP vs S
-3.4 (5.4~1.3)**
-2.1 (4.1~0.1)
1.3 (0.7~3.4)

P vs PP
-2.3 (4.7~0.0)
0.1 (2.2~2.3)
2.4 (0.2~4.6)

PP vs PP
-2.5 (-5.0~0.0)
-1.1 (3.7~1.5)
1.4 (0.9~3.7)

Baseline
Cycle 3
Cycle 5
Cycle 7
Cycle 12
12 Months

PP: CT-2103  P: Paclitaxel  S: Surveillance
Patient-Reported FACT/GOG-Ntx Subscale Score

Least Squares Means Differences (99% CIs)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Cycle 3</th>
<th>Cycle 5</th>
<th>Cycle 7</th>
<th>Cycle 12</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>P vs S</td>
<td>-0.8(1.5~0.2)*</td>
<td>-0.8(1.4~0.1)*</td>
<td>-1.1(1.8~0.5)***</td>
<td>-0.7(1.4~0.1)*</td>
<td>-0.6(1.4~0.2)</td>
<td></td>
</tr>
<tr>
<td>pp vs S</td>
<td>-1.7(2.4~1.0)**</td>
<td>-2.3(3.0~1.6)**</td>
<td>-2.4(3.1~1.7)**</td>
<td>-2.6(3.3~1.8)**</td>
<td>-1.5(2.3~0.6)**</td>
<td></td>
</tr>
<tr>
<td>PP vs P</td>
<td>-0.9(1.5~0.2)*</td>
<td>-1.6(2.3~0.9)**</td>
<td>-1.3(1.9~0.6)**</td>
<td>-1.8(2.6~1.1)**</td>
<td>-0.8(1.7~0.0)</td>
<td></td>
</tr>
</tbody>
</table>

PP: CT-2103  P: Paclitaxel  S: Surveillance

PP: CT-2103  P: Paclitaxel  S: Surveillance
1) Is maintenance chemotherapy more effective in patients who were R0 at their primary surgery?
EDA: R0 patients had better outcomes
EDA: R0 Patients: OS by Treatment

**Survival by Randomized Treatment**
For The Subgroup with No Residual Disease

CT-2103 v Surv
HR 0.856
95% CI 0.729-1.006
Exploratory Data Analysis

Two Questions Not Addressed in Study Design

1) Is maintenance chemotherapy more effective in patients who were R0 at their primary surgery?

1) Does maintenance chemotherapy induce chemoresistance?
EDA: Residual Disease Patients: OS by Treatment

Survival by Randomized Treatment
For The Subgroup with Residual Disease

Residual Disease
- CT-2103
- Paclitaxel
- Surveillance

Events Total Median(mos)
- CT-2103 97 156 39.9
- Paclitaxel 106 163 39.9
- Surveillance 96 156 48.7

HR CI
- S v Paclitaxel 1.003 0.800-1.26
- S v CT-2103 1.095 0.876-1.37

Months on Study
- CT-2103 156 139 108 69 45 34 23 15
- Paclitaxel 163 150 123 77 51 41 22 15
- Surveillance 156 148 124 89 58 38 24 14

Bringing Together the Best in Women’s Cancer Care
Conclusions

• Overall survival was not improved with taxane maintenance.
• Progression free survival is slightly delayed
• The taxane therapy increases side effects, most notably neurotoxicity.
GOG (NRG) 212

Thank you:

Patients

Investigators

Co-sponsors:  CTEP/NCI
              Cell Therapeutics, Inc