POST-ASCO 2012
Gynecologic Cancers

Dr Nilüfer Güler
23 June 2012, TOD Meeting
İSTANBUL
Post ASCO 2012
Gynecologic Cancers

• **Ovarian Cancer**
  – Primary CT
  – Maintenance therapy
  – Platin refracter disease

• **Cervical Cancer**
  – Stage IVB persistant or recurrent disease
Long-term follow-up of a randomized trial comparing conventional paclitaxel and carboplatin with dose-dense weekly paclitaxel and carboplatin in women with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer: JGOG 3016 trial.

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1Nippon Medical School Musashikosugi Hospital, Kawasaki; 2The jikei University, Tokyo; 3Kitasato University, Tokyo; 4Kousei General Hospital, Tokyo; 5Keio University, Tokyo; 6Social Insurance Sagamino Hospital, Sagamihara; 7Niigata Cancer Center Hospital, Niigata; 8Tokyo Medical University, Tokyo; 9Iwate Medical University, Morioka; Japan

ASCO 2012-5004
JGOG 3016 (NOVEL study)

- Ovarian Epithelial, Primary Peritoneal, or Fallopian Tube cancer
- FIGO Stage II-IV
- Stratified: residual disease, stage, and histology

**Randomize**

**Conventional TC (k-TC)**
- Paclitaxel 180mg/m², day 1
- Carboplatin AUC 6.0, day 1
- every 21 days for 6-9 cycles

**Dose-dense weekly TC (dd-TC)**
- Paclitaxel 80mg/m², days 1,8,15
- Carboplatin AUC 6.0, day 1
- every 21 days for 6-9 cycles

- Primary endpoint: PFS
- Secondary endpoint: OS

Katsumata, Lancet 2009; 374: 1331–38
## JGOG 3016 Study

<table>
<thead>
<tr>
<th></th>
<th>Med FU</th>
<th>Med FU</th>
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<tbody>
<tr>
<td>29 m</td>
<td>6,4 year</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>cTC</th>
<th>ddTC</th>
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<tbody>
<tr>
<td>17.2 m</td>
<td>28 m</td>
<td></td>
</tr>
<tr>
<td>p=0.0015</td>
<td>p=0.0037</td>
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<table>
<thead>
<tr>
<th></th>
<th>Med PFS</th>
<th>Med OS</th>
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<tr>
<td>17.5 m</td>
<td>62.2 m</td>
<td>%65.1</td>
</tr>
<tr>
<td>p=0.0015</td>
<td>p=0.032</td>
<td>%51.1</td>
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<table>
<thead>
<tr>
<th></th>
<th>ddTC</th>
<th>Not reached</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.2 m</td>
<td></td>
<td>%72.1</td>
</tr>
<tr>
<td>p=0.032</td>
<td></td>
<td>%58.7</td>
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<tr>
<td>p=0.039</td>
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### JGOG 3016 Study
Subgroup Analyses - OS

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<tr>
<th></th>
<th>cTC</th>
<th>ddTC</th>
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</thead>
<tbody>
<tr>
<td>&lt;1 cm residue</td>
<td>Not reached</td>
<td>Not reached p=0.234</td>
</tr>
<tr>
<td>&gt;1 cm residue</td>
<td>33.5 m</td>
<td>51.2 m p=0.0267</td>
</tr>
<tr>
<td>Serour-other</td>
<td>61.2 m</td>
<td>Not reached p=0.0252</td>
</tr>
<tr>
<td>Clear cell/münsin</td>
<td>62.2 m</td>
<td>Not reached p=0.776</td>
</tr>
</tbody>
</table>
# First-line IP Therapy-OC

<table>
<thead>
<tr>
<th>Study Patient no</th>
<th>Drugs</th>
<th>Median OS (months)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOG-104 (654)</td>
<td>6 iv cisp+iv cyc/ 6 ip cisp+iv cyc</td>
<td>41</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOG-114 (426)</td>
<td>6 iv cisp+pac / 2 carbo+6 Iv pac+ip cisp</td>
<td>52.5</td>
<td>63.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOG-172 (429)</td>
<td>6 iv pac+cisp/ 6 iv pac+ip cisp ip pacl</td>
<td>49.5</td>
<td>66.9</td>
</tr>
</tbody>
</table>
GOG-158 STUDY

Adjusted Cox analysis
HR 0.86 (99% CI 0.71–1.04)

Carbo-Paclitaxel (3-h)
(n = 392) median 56.7 m

CDDP-Paclitaxel (24-h)
(n = 400) median 48.8 m
## Cox model for OS-JGOG 3016

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
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<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Treatment, c-TC v dd-TC</td>
<td>0.79</td>
<td>0.63-0.99</td>
</tr>
<tr>
<td>Disease, ovary v fallopian tube</td>
<td>0.41</td>
<td>0.21-0.84</td>
</tr>
<tr>
<td></td>
<td>2.17</td>
<td>1.59-2.95</td>
</tr>
<tr>
<td>Stage, II v III</td>
<td>4.91</td>
<td>2.95-8.16</td>
</tr>
<tr>
<td></td>
<td>9.22</td>
<td>5.36-15.86</td>
</tr>
<tr>
<td>Histology, serous v clear/mucinous</td>
<td>0.83</td>
<td>0.61-1.12</td>
</tr>
<tr>
<td>Residual disease, ≤1cm v &gt;1 cm</td>
<td>3.70</td>
<td>2.85-4.78</td>
</tr>
<tr>
<td>Age, &lt; 60 v ≥ 60</td>
<td>1.61</td>
<td>1.29-2.01</td>
</tr>
<tr>
<td>PS, 0-1 v 2-3</td>
<td>2.65</td>
<td>1.94-3.62</td>
</tr>
<tr>
<td>RBC transfusion, no v yes</td>
<td>1.61</td>
<td>1.21-2.13</td>
</tr>
<tr>
<td>Relative dose intensity (Carboplatin) ≥80% v &lt;80%</td>
<td>1.62</td>
<td>1.27-2.06</td>
</tr>
<tr>
<td>Relative dose intensity (Paclitaxel) ≥80% v &lt;80%</td>
<td>1.77</td>
<td>1.40-2.24</td>
</tr>
</tbody>
</table>

JGOG 3016, NOVEL, Japanese Gynecologic Oncology Group
### IP Chemotherapy: GOG 252

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Regimen I: TJ\textsubscript{IV}** | Paclitaxel 80 mg/m\textsuperscript{2} IV wkly x 3  
Carboplatin AUC 6 IV every 3 wks  
Repeated for 6 cycles |
| **Regimen II: TJ\textsubscript{IP}** | Paclitaxel 175 mg/m\textsuperscript{2} IV over 3 hrs on Day 1  
Carboplatin AUC 6 IP on Day 1  
Repeated every 3 wks for 6 cycles |
| **Regimen III: TCT\textsubscript{IP}** | Paclitaxel 135 mg/m\textsuperscript{2} IV over 3 hrs on Day 1  
Cisplatin 75 mg/m\textsuperscript{2} IP on Day 2  
Paclitaxel 60 mg/m\textsuperscript{2} IP on Day 8  
Repeated every 3 wks for 6 cycles |

Each of these regimens are to include bevacizumab 15 mg/kg IV every 3 wks cycles 2-6 and then bevacizumab 15 mg/kg IV cycles 7-22
Ongoing Studies

• **GOG 0262**
  – cTC +/- bevacizumab vs ddTC +/- bevacizumab

• **ICON 8**
  – cTC vs JGOG 3016 vs weekly Carbo AUC=2 and Pac 80 mg/m2

• **Mito 7**

• **IPOCC-dial**
JGOG 3016

• Dd-TC is an effective regimen.
• No benefit for clear cell/musinous carcinoma
• More effective >1 cm residual disease
• It is one of the treatment options in the first-line treatment of EOC in NCCN v3. 2012.
RANDOMISED PHASE III STUDY OF ERLOTINIB VERSUS OBSERVATION IN PATIENTS WITH NO EVIDENCE OF DISEASE PROGRESSION AFTER FIRST LINE, PLATINUM-BASED CHEMOTHERAPY FOR HIGH-RISK STAGE I AND STAGE II-IV EPITHELIAL-OVARIAN, PRIMARY PERITONEAL, OR FALLOPIAN TUBE CANCER

# Ovarian Cancer-Relapse

<table>
<thead>
<tr>
<th>Stage</th>
<th>Recurrence Rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited (low risk)</td>
<td>10</td>
</tr>
<tr>
<td>Limited (high risk)</td>
<td>20</td>
</tr>
<tr>
<td>Advanced stage (small volume)</td>
<td>60-70</td>
</tr>
<tr>
<td>Advanced stage (large volume)</td>
<td>80-85</td>
</tr>
</tbody>
</table>

Overall 62% of the patients will have persistent or recurrent disease.
Studies of Maintenance Therapy

• Several approaches have been evaluated
  – Continuation of frontline therapy: P, PC, PAC
    • SWOG 971-GOG 178: 3 mos vs 12 mos Pac
      – PFS 21 mos vs 28 mos (=0.0035)
      – OS : ND
    • After 6 Protocol 1: Obs vs 6cyc Pac
      – PFS 30 mos vs 34 mos
      – OS: ND
    • GOG Protocol 212:Obs vs Pac vs Pac Poliglumex
      – Abdominopelvic radiation
      – Alternative chemotherapy: topotecan and others
      – Intraperitoneal chemotherapy
      – Biologic agents: tamoxifen, oregovomab
  
• No evidence of benefit from these efforts
Randomised trial on Erlotinib vs observation in first-line ovarian cancer

Ovarian, tubal or peritoneal cancer
FIGO stage high-risk I or II-IV (n = 835)

6 – 9 courses platin-based chemotherapy No progression at the end of chemotherapy

Randomisation

Erlotinib 150mg daily orally 2 years

Observation

Primary Endpoint: Progression-free survival
Secondary endpoints: Overall Survival, Quality of Life, Complications

PRESENTED BY: Ignace Vergote
Randomised trial on Erlotinib vs observation in first-line ovarian cancer: Conclusions

1. Maintenance erlotinib after first line chemotherapy in patients with ovarian, peritoneal or fallopian tube cancer did not increase PFS nor OS.
Figure 3 | Altered pathways in HGS-OvCa. a, b, RB and PI3K/RAS pathways, respectively. c, HR alterations in breast cancer with BRCA1/2 mutations. The diagram illustrates the survival analysis and the percentage of BRCA1 and BRCA2 altered cases. d, FOXM1 signalling pathway. The figure shows the percentage of cases altered in each pathway and the relationship between different genes and pathways.
Integrated genomic analyses of ovarian carcinoma

The Cancer Genome Atlas Research Network

(Nature 474;2011)
AURELIA: A randomized phase III trial evaluating bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer

Eric Pujade-Lauraine¹, Felix Hilpert², Béatrice Weber³, Alexander Reuss⁴, Andres Poveda⁵, Gunnar Kristensen⁶, Roberto Sorio⁷, Ignace Vergote⁸, Petronella Witteveen⁹, Aristotelis Bamias¹⁰, Deolinda Pereira¹¹, Pauline Wimberger¹², Ana Oaknin¹³, Mansoor Raza Mirza¹⁴, Philippe Follana¹⁵, David Bollag¹⁶, Isabelle Ray-Coquard¹⁷, on behalf of the ENGOT–GCIG investigators

¹GINECO and Université Paris Descartes, Paris, France; ²AGO and Klinik für Gynäkologie und Geburtshilfe, Kiel, Germany; ³GINECO and Centre Alexis Vautrin, Vandoeuvre-les-Nancy, France; ⁴AGO and Coordinating Center for Clinical Trials, Marburg, Germany; ⁵GEICO and Instituto Valenciano de Oncologia, Valencia, Spain; ⁶NSGO and Norwegian Radium Hospital, Oslo, Norway; ⁷MITO and Centro di Riferimento Oncologico-IRCCS, Aviano, Italy; ⁸BGOG and University Hospital Leuven, Leuven, Belgium; ⁹DGOG and University Medical Center Utrecht, Utrecht, The Netherlands; ¹⁰HECOG and University of Athens, Athens, Greece; ¹¹GINECO and IPO-Porto, Porto, Portugal; ¹²AGO and Department of Gynecology and Obstetrics, University of Duisburg-Essen, Essen, Germany; ¹³GEICO and Vall d’Hebron University Hospital, Barcelona, Spain; ¹⁴NSGO-Nordic Society of Gynaecological Oncology, Copenhagen, Denmark; ¹⁵GINECO and Department of Medical Oncology, Centre Antoine-Lacassagne, Nice, France; ¹⁶F. Hoffmann-La Roche, Basel, Switzerland; ¹⁷GINECO and Centre Léon Bérard, Lyon, France
Ovarian Cancer-Bevacizumab

- **First-line**
  - **GOG 0218 (1873 pts)**: Stage III incompletely resectable; stage IV
    - Median FU: 17.4 m
    - PFS: +4 months
    - OS: No dif
  - **ICON 7 (1528 pts)**: Stage IIIC,IV; high risk early stage
    - Median FU: 19.4 m
    - PFS: +1.5- + 4 months
    - OS: No dif in all group, Dif in high risk group

- **Platine-sensitive relapse**
  - **OCEANS study (484 pts)**
    - Median PFS: + 4 months
    - OS: NR

J Clin Oncol 2012;
# Recurrent EOC Phase II Bevacizumab Trials

<table>
<thead>
<tr>
<th></th>
<th>Cannistra ASCO (N = 44)</th>
<th>GOG 170-D (N = 63)</th>
<th>NCI 5789 (N = 29)</th>
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<tbody>
<tr>
<td><strong>Study treatment</strong></td>
<td>15 mg/kg q 3 wks</td>
<td>15 mg/kg q 3 wks</td>
<td>10 mg/kg q 2 wks + CTX</td>
</tr>
<tr>
<td><strong>Prior treatment setting</strong></td>
<td>DDP resistant, refractory ≤ 3 CTS</td>
<td>42 % DDP sensitive ≤ 2 CTS</td>
<td>42 % DDP sensitive ≤ 2 CTS</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td>16 %</td>
<td>18 %</td>
<td>28 %</td>
</tr>
<tr>
<td><strong>6-mos PFS</strong></td>
<td>27.4 %</td>
<td>39 %</td>
<td>57 %</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>5 (11%)</td>
<td>2 (3%)</td>
<td>0</td>
</tr>
</tbody>
</table>
Bevacizumab in Platinum-Resistant Patients

- Phase II trial in patients with platinum-resistant epithelial ovarian cancer or peritoneal serous cancer
  - All patients had progressed during or within 3 months of discontinuing topotecan or PLD therapy
- Bevacizumab 15 mg/m² IV given on Day 1 on each 3-week cycles until unacceptable toxicity or radiographic progression
- Objectives
  - Primary: evaluate activity of bevacizumab
  - Secondary: PFS, OS, safety

- Median PFS: 4.4 months
- Median OS: 10.7 months

**AURELIA trial design**

**Platinum-resistant OC**
- ≤2 prior anticancer regimens
- No history of bowel obstruction/abdominal fistula, or clinical/radiological evidence of rectosigmoid involvement

**Stratification factors:**
- Chemotherapy selected
- Prior anti-angiogenic therapy
- Treatment-free interval (<3 vs 3–6 months from previous platinum to subsequent PD)

**Chemotherapy options (investigator’s choice):**
- Paclitaxel 80 mg/m² days 1, 8, 15, & 22 q4w
- Topotecan 4 mg/m² days 1, 8, & 15 q4w (or 1.25 mg/m², days 1–5 q3w)
- PLD 40 mg/m² day 1 q4w

**Chemotherapy**
- Treat to PD/toxicity

**BEV 15 mg/kg q3w**
- + chemotherapy
- Treat to PD/toxicity

**Optional BEV monotherapy**
- Investigator’s choice (without BEV)

**PD = progressive disease**

*a*Epithelial ovarian, primary peritoneal, or fallopian tube cancer;  
*b*Or 10 mg/kg q2w;  
*c*15 mg/kg q3w, permitted on clear evidence of progression
Progression-free survival

Median duration of follow-up: 13.9 months (CT arm) vs 13.0 months (BEV + CT arm)

<table>
<thead>
<tr>
<th></th>
<th>CT (n=182)</th>
<th>BEV + CT (n=179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>166 (91%)</td>
<td>135 (75%)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>3.4 (2.2–3.7)</td>
<td>6.7 (5.7–7.9)</td>
</tr>
<tr>
<td>HR (unadjusted)</td>
<td>0.48 (0.38–0.60)</td>
<td>&lt;0.001</td>
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<tr>
<td>No. at risk:</td>
<td></td>
<td></td>
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<tr>
<td>CT</td>
<td>182</td>
<td>93</td>
</tr>
<tr>
<td>BEV + CT</td>
<td>179</td>
<td>140</td>
</tr>
</tbody>
</table>

Estimated probability

Time (months)

Median duration of follow-up: 13.9 months (CT arm) vs 13.0 months (BEV + CT arm)
## Subgroup analysis of PFS

**Median PFS, months**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of patients</th>
<th>CT</th>
<th>BEV + CT</th>
<th>HR(^a) better</th>
<th>CT better</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>361</td>
<td>3.4</td>
<td>6.7</td>
<td>0.48</td>
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<tr>
<td>Age, years</td>
<td></td>
<td></td>
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<tr>
<td>&lt;65</td>
<td>228</td>
<td>3.4</td>
<td>6.0</td>
<td>0.49</td>
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<tr>
<td>≥65</td>
<td>133</td>
<td>3.5</td>
<td>7.8</td>
<td>0.47</td>
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<td>PFI, months(^b)</td>
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<td>&lt;3</td>
<td>96</td>
<td>2.1</td>
<td>5.4</td>
<td>0.53</td>
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<td>3–6</td>
<td>257</td>
<td>3.6</td>
<td>7.8</td>
<td>0.46</td>
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<td>Measurable disease, cm</td>
<td></td>
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<tr>
<td>No (&lt;1)</td>
<td>74</td>
<td>3.7</td>
<td>7.5</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Yes (1–&lt;5)</td>
<td>126</td>
<td>3.3</td>
<td>7.5</td>
<td>0.50</td>
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<tr>
<td>Yes (≥5)</td>
<td>161</td>
<td>3.3</td>
<td>6.0</td>
<td>0.47</td>
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<tr>
<td>Ascites</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>113</td>
<td>2.5</td>
<td>5.6</td>
<td>0.40</td>
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<tr>
<td>No</td>
<td>248</td>
<td>3.5</td>
<td>7.6</td>
<td>0.48</td>
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<td>Chemotherapy</td>
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<td></td>
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<tr>
<td>Paclitaxel</td>
<td>115</td>
<td>3.9</td>
<td>10.4</td>
<td>0.46</td>
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<tr>
<td>PLD</td>
<td>126</td>
<td>3.5</td>
<td>5.4</td>
<td>0.57</td>
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<tr>
<td>Topotecan</td>
<td>120</td>
<td>2.1</td>
<td>5.8</td>
<td>0.32</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Unadjusted. \(^b\) Missing n=8.
Summary

• The primary objective was met
  – PFS HR 0.48 (p<0.001) in favor of BEV combination therapy vs single-agent CT
  – Median PFS: 6.7 vs 3.4 months, respectively

• Significant improvement in ORR
  – 30.9% vs 12.6%, respectively (p=0.001) by RECIST and/or CA-125

• BEV safety profile consistent with previous experience
  – Patients at high risk of GI perforation were excluded from the study

• Overall survival data expected in 2013
Conclusions

• AURELIA is the first randomized phase III trial in platinum-resistant OC to demonstrate:
  – Benefit with biologic therapy
  – Benefit with a combination regimen versus monotherapy

• Comparison with only bevacizumab vs CT+ bevacizumab?
Acknowledgments

The 361 patients and their families, and
JCOG 0505 trial

A randomized, phase III trial of paclitaxel plus carboplatin (TC) versus paclitaxel plus cisplatin (TP) in stage IVB, persistent or recurrent cervical cancer

Ryo Kitagawa, Noriyuki Katsumata,
Taro Shibata, Toru Nakanishi,
Sadako Nishimura, Kimio Ushijima,
Masashi Takano, Toyomi Satoh,
Hiroyuki Yoshikawa, Toshiharu Kamura (PI)
## Cervical Cancer-GOG Studies

Two drugs combinations vs Cisplatin (Stage 4B, persistent or recurrent)

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>RR</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin-Bleomycin</td>
<td>+</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Cisplatin-Fluorouracil</td>
<td>+</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Cisplatin-Paclitaxel</td>
<td>+</td>
<td>+</td>
<td>--- (4,8 -2,8 mo)</td>
</tr>
<tr>
<td>Cisplatin-Vinorelbin</td>
<td>+</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Cisplatin-Gemcitabine</td>
<td>+</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Cisplatin-Topotecan</td>
<td>+</td>
<td>+</td>
<td>+ (9,4-6,5 mo)</td>
</tr>
<tr>
<td>Cisplatin-Ifosfamide</td>
<td>+</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>
GOG 204 – Phase III Study (513 pts)

Regimen 1:
Paclitaxel 135 mg/m² over 24 h and
CDDP 50 mg/m² repeated q 3 weeks for 6 cycles

Regimen 2:
Vinorelbine 30 mg/m² i.v. bolus days 1 and 8 and
CDDP 50 mg/m² i.v. day 1 repeated q 3 weeks for 6 cycles

Regimen 3:
Gemcitabine 1000 mg/m² i.v. days 1 and 8 and
CDDP 50 mg/m² i.v. day 1 repeated q 3 weeks for 6 cycles

Regimen 4:
Topotecan 0.75 mg/m² days 1, 2 and 3
CDDP 50 mg/m² i.v. day 1, q 3 weeks for 6 cycles

Primary end point: OS
Other end points: PFS, QoL, toxicity

Figure 4. Schema: Gynecologic Oncology Group 204, a Phase III trial of platinum-based doublets in patients with primary stage IVB, recurrent or persistent carcinoma of the cervix.
CDDP: Chemotherapy with low-dose cisplatin; OS: Overall survival; PFS: Progression-free survival; QoL: Quality of life.
GOG 204 Study ; PFS

PC kolu YO:%30
PFS 5,82 ay
GOG 204 Study ; OS

PC kolu
OS:12,87 ay
Trial Design
Multicenter (30 specialized institutions), Randomized Phase III Trial

Stage IVB, persistent or recurrent cervical cancer; not amenable to curative surgery / radiotherapy

* Balancing factors:
  • Tumors outside of the prior irradiation field (yes or no)
  • PS 0-1 or 2
  • SCC or non-SCC
  • Institution

**Standard arm: TP**
Paclitaxel 135 mg/m² 24h d1
Cisplatin 50 mg/m² 2h d2

every 21 days for 6 cycles

**Experimental arm: TC**
Paclitaxel 175 mg/m² 3h d1
Carboplatin AUC 5 1h d1
Overall Survival

<table>
<thead>
<tr>
<th>Arm</th>
<th>N</th>
<th>Events</th>
<th>Median (m) [95% CI]</th>
<th>1-yr OS</th>
<th>2-yr OS</th>
<th>3-yr OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP</td>
<td>123</td>
<td>106</td>
<td>18.3 m [16.1-22.9]</td>
<td>72.4%</td>
<td>38.8%</td>
<td>18.3%</td>
</tr>
<tr>
<td>TC</td>
<td>121</td>
<td>98</td>
<td>17.5 m [14.2-20.3]</td>
<td>67.6%</td>
<td>31.5%</td>
<td>21.3%</td>
</tr>
</tbody>
</table>

HR: 0.994 [90% CI: 0.789-1.253 (<1.29)]
non-inferiority one-sided p = 0.032

#stratified Cox regression with “tumors outside prior irradiation field[yes/no]” as strata
Effects on OS of Prior Platinum

Without prior platinum (n=117)

- Median (months): TP 23.2, TC 13.0
- HR 1.57 (95% CI: 1.06-2.32)
- Non-inferiority one sided p=0.838

With prior platinum (n=127)

- Median (months): TP 16.3, TC 19.0
- HR 0.69 (95% CI: 0.47-1.02)
- Non-inferiority one sided p=0.0008

(www.jcog.jp/en/)
Summary

- Both TP and TC were well tolerated.
- **TP**
  - febrile neutropenia,
  - creatinine elevation,
  - nausea/vomiting.
  - More hospitalizations
- **TC**
  - arthralgia,
  - myalgia,
  - neuropathy,
- One of these regimens can be recommended after discussion with the patients.
Stage IVB, rekurrent or persistent cervical cancer
First-line Combination Chemotherapy Options

- Cisplatin/paclitaxel  2A
- Carboplatin/paclitaxel  2A
- Cisplatin/topotecan  2A
- Cisplatin/gemcitabine  2B