The goals of treatment for metastatic breast cancer (MBC) are prolonging survival time and improvement of quality of life (QOL). 

S1 is an orally active combination drug, based on biochemical modulation of 5-FU, containing togar, gemiclil and olatin in a molar ratio of 1:0.4:1. It has been widely used as standard regimens in various cancers.

Two Phase II studies of S1 in patients with MBC, including subjects who had received prior chemotherapy as well as those who had not, have been performed in Japan. The response rates were 42.0% and 40.7%, respectively, comparable to the response rates of taxane derivatives.

**CONSORT diagram**

From 258 institutions
Enrollment period: Oct 2006 - Jul 2010
Median follow up time: 31 months
Number of death events: 398

**Effects of treatment**

**HRQOL assessed by EORTC QLC Q-30 (On treatment analysis)**

<table>
<thead>
<tr>
<th>Time from randomization (months)</th>
<th>Pain</th>
<th>Emotional functioning</th>
<th>Social functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
</tr>
<tr>
<td>6-12</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
</tr>
<tr>
<td>12-18</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
</tr>
<tr>
<td>18-24</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
<td>0.06 (p=0.81)</td>
</tr>
</tbody>
</table>

**Survival analysis (n=392)**

(This data was presented at ASCO2014)

**Adverse Events**

(This data was presented at ASCO2014)

**Study design**

**Non-inferiority**

- Patients with HER2-negative MBC (n=162)
- Chemotherapy regimens for MBC
- Stratification factors: Hormone receptor status, histology, age, stage of disease
- Secondary endpoints: Time to Treatment Failure (TTF), Progression-Free Survival (PFS), Adverse Events (AEs), Health-Related Quality of Life (HRQOL), Cost-Effectiveness

**Study objectives**

- To verify the non-inferiority of S1 in efficacy and toxicity to taxanes as first-line chemotherapy for MBC.
- Primary endpoint: Overall Survival (OS)
- Secondary endpoints: Time to Treatment Failure (TTF), Progression-Free Survival (PFS), Adverse Events (AEs), Health-Related Quality of Life (HRQOL), Cost-Effectiveness

**Measures for HRQOL**

- HRQOL was assessed using EORTC QLC Q-30, EQ-5D (EuroQol 5 Dimension).
- Chemotherapy-induced peripheral neuropathy (CIPN) was assessed using the PN2Q (Patient Neuropathy Questionnaire).
- Assessment of these questionnaires were made at pre-treatment, 3, 6, and 12 months after starting the study treatment. Assessment using EQ-5D was continued as far as possible in every six months.

**CIPN assessed by PNQ**

<table>
<thead>
<tr>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extreme and 70% or more pain or tingling (or a hand or feet)</td>
</tr>
<tr>
<td>Grade 1: moderate numbness, pain or tingling</td>
</tr>
<tr>
<td>Grade 2: severe numbness, pain or tingling</td>
</tr>
<tr>
<td>Grade 3: severe numbness, pain or tingling</td>
</tr>
</tbody>
</table>

**HRQOL assessed by EQ-5D (On treatment analysis)**

**Conclusions**

- This study clearly demonstrated that S1 was superior to taxanes in terms of HRQOL, without compromising the prolongation of OS.
- S1 should be considered as a new standard for first-line chemotherapy for non-HER2-mutant MBC.

**Acknowledgement**

- To all of the patients who participated in SELECT BC and their families.
- To the investigators and research coordinators at the 258 institutions and CSPOR.
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