Innovation all for the patients

CHUGAI

Roche A member of the Roche group

# Anti-Cancer Agent “Xeloda®,” Obtained Approval for Additional Indication of “Postoperative Adjuvant Chemotherapy for Gastric Cancer”

TOKYO, November 20, 2015 - Chugai Pharmaceutical Co., Ltd. (Chugai) (TOKYO: 4519) announced today that it obtained a supplemental approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) on November 20, 2015, for the anti-cancer agent, capecitabine (brand name: Xeloda® Tablets 300) (Xeloda) for the indication of “postoperative adjuvant chemotherapy for gastric cancer”. With this approval, the indication of Xeloda has been changed into “gastric cancer,” covering the current indication of “advanced or recurrent gastric cancer, which is not amenable to curative resection.”

“With the approval of the combination therapy of Xeloda and oxaliplatin showing preventive efficacy for postoperative recurrence, we hope the patients will receive the anti-cancer treatment in a positive frame of mind.” said Chugai’s Director and Executive Vice President, Dr. Yutaka Tanaka. “We are extremely pleased that Xeloda can contribute to the treatment of patients.”

In December 2014, Chugai and Yakult Honsha Co., Ltd. filed an application for approval with the MHLW based on the results of overseas Phase III study (The CLASSIC study) and a Japanese Phase II study.

In The CLASSIC study which was conducted in 1,035 patients with Stage II/III gastric cancer who had received surgical resection, patients were randomized to receive either combination therapy of Xeloda and oxaliplatin (combination group) or surgery alone with follow-up (follow-up group). Disease-free survival (DFS) was evaluated as the primary endpoint. As a result, the three-year DFS rate was 74% in the combination group and 59% in the follow-up group, demonstrating statistically significant prolongation of DFS in the combination group (hazard ratio: 0.56, 95% confidence interval: 0.44 to 0.72, Wald test, $p<0.0001$). Moreover, for overall survival, a secondary endpoint, five-year survival rate was 78% in the combination group and 69% in the follow-up group, showing significant prolongation in the combination group (hazard ratio: 0.66, 95% confidence interval: 0.51 to 0.85, Wald test, $p=0.0015$). The safety profile shown in the combination group was comparable to those which have been reported for the two drugs.

The Japanese Phase II study investigated the combination therapy of Xeloda and oxaliplatin, setting Dose Intensity (cumulative dose of each drug actually administered / cumulative planned dose when eight courses of treatment were completed without treatment interruption or dose reduction) as the primary endpoint. The results showed the average of Dose Intensity is 67.2% in the Xeloda and 73.4% in the oxaliplatin respectively, and the tolerability in the Japanese patients was confirmed as both drugs also exceeded threshold which was defined by the study protocol.

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL: +81-(0)3-3273-0881 E-mail: pr@chugai-pharm.co.jp
Investor Relations Group TEL: +81-(0)3-3273-0554 E-mail: ir@chugai-pharm.co.jp

Gastric cancer is prevalent in Asian countries including Japan, South Korea and China as well as in South America. In Japan, the number of patients newly diagnosed with gastric cancer continues to rise each year and is estimated to become, on annual average, approximately 142,900 during 2015-2019*.

Chugai strongly believes that Xeloda will make a contribution to patients as a treatment option for “postoperative adjuvant chemotherapy for gastric cancer.” Chugai will continue the efforts to contribute to cancer treatment.

* Tomotaka Sobue, et al. “Cancer White Paper 2012 - For data-based cancer control” (Shinoharashinsha Inc.)

**About Xeloda**

Xeloda was developed by Nippon Roche K.K. (currently Chugai) and approved in 1998 for the first time in the US, Switzerland and Canada, in 2001 in the EU and has been approved in more than 100 countries worldwide. In Japan, Xeloda is marketed by Chugai and it received approval for “inoperable or recurrent breast cancer” in June 2003, “the overseas dosage and administration” and “postoperative adjuvant chemotherapy for colon cancer” in December 2007, “advanced or refractory colorectal cancer, which is not amenable to curative resection” in September 2009 and “advanced or recurrent gastric cancer, which is not amenable to curative resection” in February 2011. It has been authorized for the indication of “gastric cancer” in more than 90 countries.

**About oxaliplatin**

Oxaliplatin is a platinum complex, anti-cancer agent of which the development and distribution rights in Japan were obtained by Yakult Honsha Co., Ltd. in 1997 from Debiopharm International SA (Switzerland). Oxaliplatin is marketed by Yakult Honsha Co., Ltd. under the brand name of "Elplat® I.V. Infusion Solution 50mg” (Elplat). Elplat was approved in March 2005 for an indication of “advanced or recurrent colorectal cancer, which is not amenable to curative resection” and started to be marketed in April 2005. It was approved for additional indications of “postoperative adjuvant chemotherapy for colon cancer” in 2009, “pancreatic cancer, which is not amenable to curative resection” in 2013 and “advanced or recurrent gastric cancer, which is not amenable to curative resection” in 2015.

**[Drug Information]**

* The underlined descriptions are newly added and changed.

Brand name: Xeloda® Tablets 300

Generic name: Capecitabine

Indications: Inoperable or recurrent breast cancer
Postoperative adjuvant chemotherapy for colon cancer
Advanced or recurrent colorectal cancer, which is not amenable to curative resection
Gastric cancer

Dosage and administration:

Regimens A or B are available for the treatment of inoperable or recurrent breast cancer. Regimen B should be employed for the postoperative adjuvant chemotherapy for colon cancer, while regimen C should be employed in combination with another anticancer agent for the treatment of advanced or recurrent colorectal cancer, which is not amenable to curative resection. Regimen C should be employed in combination with a platinum agent for the treatment of gastric cancer.

Regimen A:
XELODA is administered orally in the following doses, according to body surface area, twice daily within 30 minutes after morning and evening meals for 21 consecutive days, followed by a 7-day rest period. The administration is repeated with this taken as one course. The dosage should be adjusted according to the patient's condition.

| Body surface area | Each dose |
|---|---|
| $<1.31m^2$ | 900 mg |
| $1.31m^2$ to $<1.64m^2$ | 1,200 mg |
| $\geq 1.64m^2$ | 1,500 mg |

Regimen B:
XELODA is administered orally in the following doses, according to body surface area, twice daily within 30 minutes after morning and evening meals for 14 consecutive days, followed by a 7-day rest period. The administration is repeated with this taken as one course. Dosage should be reduced according to the patient's condition.

| Body surface area | Each dose |
|---|---|
| $<1.33m^2$ | 1,500 mg |
| $1.33m^2$ to $<1.57m^2$ | 1,800 mg |
| $1.57m^2$ to $<1.81m^2$ | 2,100 mg |
| $\geq 1.81m^2$ | 2,400 mg |

Regimen C:

XELODA is administered orally in the following doses, according to body surface area, twice daily within 30 minutes after morning and evening meals for 14 consecutive days, followed by a 7-day rest period. The administration is repeated with this taken as one course. Dosage should be reduced according to the patient's condition.

| Body surface area | Each dose |
|---|---|
| $<1.36m^2$ | 1,200 mg |
| $1.36m^2$ to $< 1.66m^2$ | 1,500 mg |
| $1.66m^2$ to $<1.96m^2$ | 1,800 mg |
| $\geq 1.96m^2$ | 2,100 mg |

Drug price: JPY 360.5/Tablet