MONTHLY VERSUS THREE-MONTHLY GOSERELIN TREATMENT IN PREMENOPAUSAL PATIENTS WITH OESTROGEN-RECEPTOR-POSITIVE EARLY BREAST CANCER – UPDATED EFFICACY AND SAFETY

Y. Rai,1 H. Iwata,2 N. Masuda,3 K. Anan,4 T. Takeuchi,5 N. Kohn6, H. Takei,7 Y. Yanagita,8 S. Naguchi9

1Sagara Hospital, Kageyama; 2Aichi Cancer Centre Hospital, Aichi; 3National Hospital Organization Osaka National Hospital, Osaka; 4Kitasoyu Municipal Medical Centre, Kitaoyu; 5Marumochi Hospital, Aichi; 6Tokyo Medical University Hospital, Tokyo; 7Saitama Cancer Centre, Saitama; 8Gunma Cancer Centre, Gunma; 9Osaka University Graduate School of Medicine, Osaka, Japan

INTRODUCTION

- Treatments for endocrine-dependent breast cancer include oestriol deprivation or aromatase by medical or surgical methods.1 In premenopausal breast cancer patients, irreversible ovarian suppression is a traditional treatment option.
- However, valuable treatment alternatives are provided by non-endocrine therapies such as gonadotropin-releasing hormone or luteinising hormone-releasing hormone (LHRH) agonists.1,2
- Gonadotropin- releasing hormone agonists (GnRHa), LHRH agonists, cause potentially irreversible ovarian suppression by preventing pituitary follicle-stimulating hormone (FSH) release and oestradiol synthesis.
- The standard monthly goserelin in 3.6 mg depot is approved for premenopausal breast cancer.1
- Oestradiol and FSH serum concentrations were suppressed in both treatment groups:
  - Baseline and disease characteristics were similar in both treatment groups, with mean patient age of 43.5 years and with the majority of patients (95.3%) having invasive breast cancer.
- Between January 2006 and February 2007, 170 premenopausal patients (84 to goserelin 3.6 mg and 86 to goserelin 10.8 mg) in Japan; 84 to goserelin 3.6 mg and 86 to goserelin 10.8 mg. At data cut-off (August 2007), 79 patients in the goserelin 3.6 mg group and 81 patients in the goserelin 10.8 mg group had completed the study (Figure 1).
- Baseline and disease characteristics were similar in both treatment groups, with mean patient age of 43.5 years and with the majority of patients (95.3%) having invasive breast cancer (Table 1).
- Oestradiol and FSH serum concentrations were similar in both groups to that of the non-menopausal (Table 4).
- In total, six CTC grade 3/4 AEs were observed in four patients from the goserelin 3.6 mg group: - neutropenia and leucopenia.
- There were no grade 3/4 AEs in four patients treated with goserelin 10.8 mg: - hyperpyrexia, (able blood pressure, breast cancer and contralateral breast cancer.
- Serious AEs were observed in three and four patients from the 3.6 mg and 10.8 mg groups, respectively; none of these led to death.
- One patient in the 3.6 mg group discontinued treatment due to a non-related AEs (bone cancer).

METHODS

- This multicentre, open-label, randomised, parallel group study (NCT00303524) in premenopausal Japanese women with ER+ early breast cancer compared patients receiving subcutaneous depot injection of goserelin 3.6 mg once every 4 weeks with patients receiving goserelin 10.8 mg once every 12 weeks.
- Between January 2006 and February 2007, 170 premenopausal patients with ER+ early breast cancer were recruited from 29 centres in Japan; 84 to goserelin 3.6 mg and 86 to goserelin 10.8 mg. At data cut-off (August 2007), 79 patients in the goserelin 3.6 mg group and 81 patients in the goserelin 10.8 mg group had completed the study (Figure 1).
- The primary endpoint was the area under the concentration curve (AUC) of oestradiol serum concentration for the first 24 weeks of treatment.
- Secondary endpoints included: oestradiol and follicle-stimulating hormone (FSH) serum concentrations, percentage of patients with a mean oestradiol concentration <10 pg/mL, menopausal symptoms, and quality of life (QoL) by means of the Medical Dictionary for Regulatory Activities (MedDRA) and their clinical laboratory test value.
- Analysis of efficacy and pharmacodynamic variables was performed on all patients randomly assigned to study treatment, with data available for any endpoint analysis using intent-to-treat (ITT) analysis. The AUC values were log-transformed prior to analysis and the results were exponentiated. The 95% confidence interval (CI) was constructed around the ratio of the AUCs, with goserelin 3.6 mg being the reference treatment. Menstruation was defined as the first period after the initiation of treatment. Menstruation was defined as the first period after the initiation of treatment. The incidence of AEs was the same (97.6%) in both treatment groups, with no clinically significant differences in the incidence or severity of AEs.
- The less frequently administered, more convenient treatment option of three-monthly goserelin was also not inferior to the monthly goserelin 3.6 mg with respect to disease-free survival, time to progression, and overall survival.
-CONCLUSIONS

- In terms of endocrine suppression, goserelin 10.8 mg three-monthly depot was non-inferior to goserelin 3.6 mg monthly depot in premenopausal patients with ER+ early breast cancer.
- Treatment with both goserelin 10.8 mg three-monthly and 3.6 mg monthly resulted in similar oestradiol and FSH suppression.
- Both treatments effectively suppressed menstruation.
- Both treatments showed similar BDFS.
- Both treatments have similar tolerability profiles.
- The data presented here support the use of the more convenient goserelin 10.8 mg three-monthly depot in place of the monthly dosage regimen.

Study design and patients

- This multicentre, open-label, randomised, parallel group study (NCT00303524) in premenopausal Japanese women with ER+ early breast cancer compared patients receiving subcutaneous depot injection of goserelin 3.6 mg once every 4 weeks with patients receiving goserelin 10.8 mg once every 12 weeks.
- Between January 2006 and February 2007, 170 premenopausal patients with ER+ early breast cancer were recruited from 29 centres in Japan; 84 to goserelin 3.6 mg and 86 to goserelin 10.8 mg. At data cut-off (August 2007), 79 patients in the goserelin 3.6 mg group and 81 patients in the goserelin 10.8 mg group had completed the study (Figure 1).
- Baseline and disease characteristics were similar in both treatment groups, with mean patient age of 43.5 years and with the majority of patients (95.3%) having invasive breast cancer.
- Oestradiol and FSH serum concentrations were similar in both groups to that of the non-menopausal (Table 4).
- In total, six CTC grade 3/4 AEs were observed in four patients from the goserelin 3.6 mg group:
  - neutropenia and leucopenia.
- There were no grade 3/4 AEs in four patients treated with goserelin 10.8 mg:
  - hyperpyrexia, (able blood pressure, breast cancer and contralateral breast cancer.
- Serious AEs were observed in three and four patients from the 3.6 mg and 10.8 mg groups, respectively; none of these led to death.
- One patient in the 3.6 mg group discontinued treatment due to a non-related AEs (bone cancer).

RESULTS

- The data presented here support the use of the more convenient goserelin 10.8 mg three-monthly depot in place of the monthly dosage regimen.

CONCLUSIONS

- In terms of endocrine suppression, goserelin 10.8 mg three-monthly depot was non-inferior to goserelin 3.6 mg monthly depot in premenopausal patients with ER+ early breast cancer.
- Treatment with both goserelin 10.8 mg three-monthly and 3.6 mg monthly resulted in similar oestradiol and FSH suppression.
- Both treatments effectively suppressed menstruation.
- Both treatments showed similar BDFS.
- Both treatments have similar tolerability profiles.
- The data presented here support the use of the more convenient goserelin 10.8 mg three-monthly depot in place of the monthly dosage regimen.

References
