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Real-World Outcomes Comparing 3-Monthly with Monthly Goserelin Implant in Premenopausal Women with Breast Cancer

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Background

- In premenopausal patients with estrogen receptor positive breast cancer (BC), tumor growth can be reduced by blocking estrogen production via ovarian ablation or the administration of a gonadotropin-releasing hormone agonist such as goserelin.[1]
- A Phase 3 trial conducted in Asia showed that goserelin 10.8 mg was non-inferior compared with goserelin 3.6 mg for progression-free survival at 24 weeks (61.5% vs. 60.2%; treatment difference 1.3%) in patients with advanced BC.[2]
- The 3-month implant is more convenient to clinicians and patients as it reduces office visits.[3]
- Real-world studies of women in the U.S. with BC comparing goserelin 10.8 mg 3-month implant with goserelin 3.6 mg monthly implant are scarce.

Objective

- The objective of this study was to compare real-world treatment outcomes among BC patients treated with goserelin 3.6 mg and goserelin 10.8 mg.

Methods

Study Design

- Retrospective observational study using structured data and curated progress notes from U.S. electronic medical record (EMR) data.

Data Source

- The ConcertAI Patient360™ Breast Cancer Dataset is a U.S.-based, de-identified, patient-level dataset from the ConcertAI network that contains human abstracted variables from unstructured records in patients' oncology EMR. The dataset is integrated with administrative claims and is refreshed quarterly.

Eligibility

- Women aged 18–55 years without evidence of postmenopausal status at initial BC diagnosis and exposed to goserelin 3.6 mg or 10.8 mg post-BC diagnosis in the ConcertAI Patient360™ dataset were included in the study.
- All patients had at least 360 days of follow-up after the initiation of goserelin or died before 360 days of follow-up.
- Patients with other primary tumors and those enrolled in a clinical trial during goserelin use were excluded.

Study Variables

- The index date was defined as the date of first goserelin exposure. The study period was defined as the interval between initial BC diagnosis and last activity date, data cutoff, or death (whichever occurred first).
- The study cutoff date was January 31, 2024. The earliest index year for both cohorts was 2003.
- Real-world event-free survival (rwEFS) was defined as the time from initiation of goserelin to the first documented date of disease recurrence/disease progression or death from any cause (whichever occurred first). Patients were censored on the date of the last activity date for patients without documented disease recurrence/progression or death.
- Real-world overall survival (rwOS) was defined as the time from initiation of goserelin to the date of death from any cause. For patients not known to be deceased at the time of analysis, rwOS was censored at the last date the patient was known to be alive.
- Real-world time to discontinuation (rwTTD) was defined as the time from initiation of goserelin to the last administration without a 60-day gap or death for the 3.6 mg goserelin cohort, and without a 180-day gap or death for the 10.8 mg goserelin cohort. This time frame allows for 2 cycles of each respective dosage to be missed before being considered as discontinued.

Statistical Methods

- Inverse probability treatment weighting (IPTW) was used to ensure the comparability of baseline demographic and clinical characteristics between the two cohorts.
- The primary outcome was the rwEFS rate at 12 months to assess the non-inferiority of 3-month goserelin 10.8 mg vs. monthly goserelin 3.6 mg. The non-inferiority margin was set at -15% between treatment groups based on published oncology clinical trials. No non-inferiority testing was carried out for other endpoints.
- Weighted Kaplan-Meier analysis was used to characterize rwEFS, rwOS, and rwTTD for patients who received 3-month goserelin 10.8 mg and monthly goserelin 3.6 mg.

Results

Demographics and Clinical Characteristics (Table 1)

- A total of 575 patients received goserelin 3.6 mg, and 123 received goserelin 10.8 mg. After weighting, the sample sizes were 700 in the goserelin 3.6 mg cohort and 670 in the goserelin 10.8 mg cohort.
- After weighting, the 3.6 mg cohort had a median age of 41 years, and 61.0% of patients had early-stage BC at initial goserelin treatment.
- The 10.8 mg cohort had a median age of 42 years, and 61.0% of patients had early-stage BC at initial goserelin treatment.

Non-Inferiority Test (Figures 1 and 2)

- The 12-month rwEFS rates for goserelin 3.6 mg and goserelin 10.8 mg, respectively, were as follows:
  - Overall: 76.6% vs. 79.2%
    - Treatment difference: 2.7% (95% CI: -1.8%, 7.0%)
  - Early-stage/locally advanced BC: 93.2% vs. 90.9%
    - Treatment difference: -2.3% (95% CI: -6.0%, 1.4%)
  - Metastatic BC: 50.6% vs. 61.0%
    - Treatment difference: 10.4% (95% CI: 2.0%, 18.9%)
- The treatment difference supports the non-inferiority of goserelin 10.8 mg to goserelin 3.6 mg at the prespecified -15% margin.

Real-World Event-Free Survival

- The rwEFS rates for goserelin 3.6 mg and goserelin 10.8 mg, respectively, were as follows:
  - 1 year: 76.6% vs. 79.2%
  - 3 years: 61.5% vs. 63.4%
  - 5 years: 55.8% vs. 46.9%
- The restricted means for rwEFS for goserelin 3.6 mg and goserelin 10.8 mg, respectively, were as follows:
  - 1 year: 10.3 months vs. 10.6 months
  - 3 years: 26.8 months vs. 27.4 months
  - 5 years: 40.6 months vs. 40.5 months

Real-World Overall Survival (Figure 3)

- The rwOS rates for goserelin 3.6 mg and goserelin 10.8 mg, respectively, were as follows:
  - 1 year: 92.9% vs. 97.4%
  - 3 years: 81.3% vs. 86.2%
  - 5 years: 69.0% vs. 67.4%
- The restricted means for rwOS for goserelin 3.6 mg and goserelin 10.8 mg, respectively, were as follows:
  - 1 year: 11.7 months vs. 12.0 months
  - 3 years: 32.9 months vs. 34.1 months
  - 5 years: 50.7 months vs. 53.0 months

Real-World Time to Discontinuation (Figure 4)

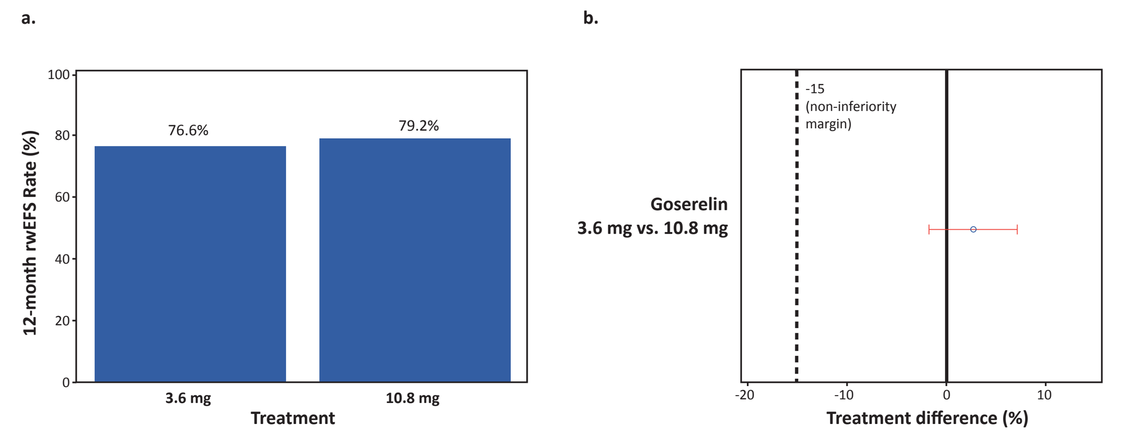
- The rwTTD rates for goserelin 3.6 mg vs. 10.8 mg, respectively, were as follows:
  - 1 year: 39.6% vs. 51.2%
  - 2 years: 23.1% vs. 32.4%

Table 1. Patient Characteristics Post-Weighting by Goserelin Dosage

Variable	Post-Weighting[a] Goserelin 3.6 mg n=700	Post-Weighting[a] Goserelin 10.8 mg[b] n=670	Post-Weighting[a] Standardized Difference
Age at initial BC diagnosis, median (min, max) (years)	41 (24–55)	42 (22–55)	0.0521
Race, n (%)			0.0288
White	492 (70.3)	468 (69.9)	
Black or African American	101 (14.5)	103 (15.3)	
Other or unknown race	106 (15.2)	99 (14.8)	
Stage at initial BC diagnosis, n (%)			0.4676
Stage 0 + Stage I	153 (21.8)	158 (23.5)	
Stage II	246 (35.2)	229 (34.2)	
Stage III	129 (18.5)	114 (17.0)	
Stage IV	106 (15.2)	90 (13.4)	
Unknown	66 (9.4)	79 (11.8)	
Comorbidities at initial BC diagnosis, n (%)			
Chronic obstructive pulmonary disease, unspecified	32 (4.6)	37 (5.5)	
Type 2 diabetes mellitus without complications	31 (4.4)	7 (1.0)	
Autoimmune disease	11 (1.6)	16 (2.4)	
Surgical procedures prior to initial goserelin therapy, n (%)			0.0440
Mastectomy	381 (54.4)	351 (52.3)	
Excision or biopsy	95 (13.6)	98 (14.6)	
Both mastectomy and excision/biopsy	84 (12.0)	80 (12.0)	
No surgery	140 (19.9)	141 (21.1)	
Timing of initial goserelin therapy, n (%)			0.0011
Early-stage/locally advanced BC, prior to metastatic diagnosis (if any)	427 (61.0)	409 (61.0)	
At or after metastatic diagnosis	273 (39.0)	261 (39.0)	
Histology at initial BC diagnosis, n (%)			0.1849
Infiltrating ductal	478 (68.3)	470 (70.2)	
Infiltrating lobular	50 (7.1)	27 (4.1)	
Infiltrating ductal and lobular	36 (5.2)	45 (6.8)	
Carcinoma in situ + other/unknown	136 (19.4)	127 (18.9)	

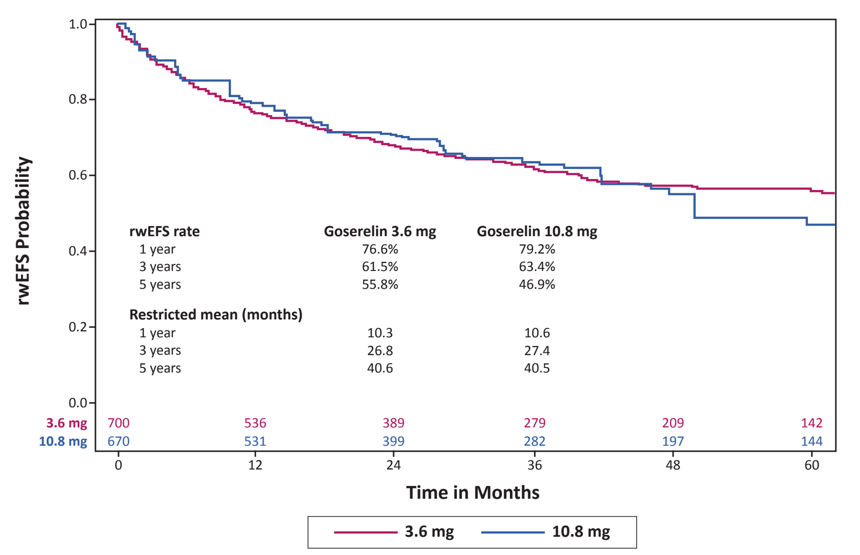
[a] Inverse probability treatment weighting (IPTW) was used to ensure the comparability of baseline demographic and clinical characteristics between the two cohorts.
[b] Patients who received goserelin 10.8 mg and switched to or from 3.6 mg were included in the 10.8 mg category.
BC: breast cancer, Max: maximum, Min: minimum

Figure 1. Weighted Bar Graph (a) and Forest Plot of Differences (b) of 12-Month rwEFS Rate by Dosage of Goserelin



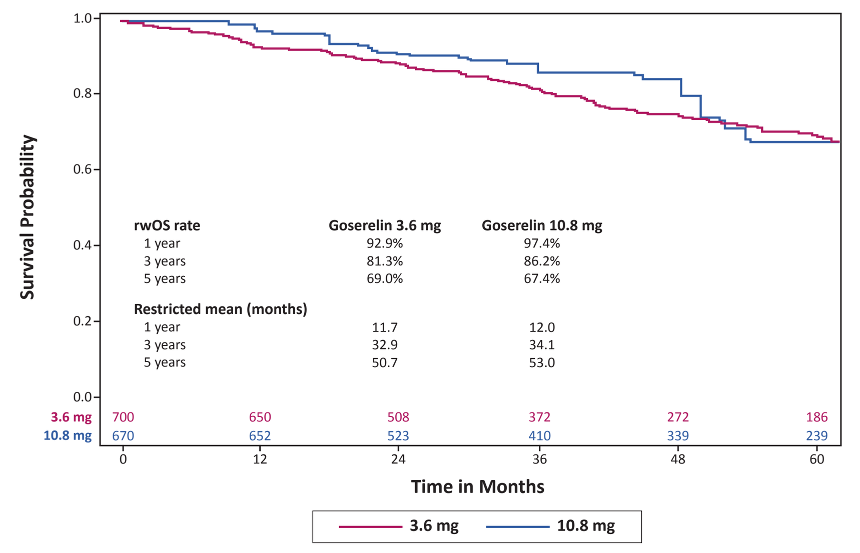
rwEFS: real-world event-free survival

Figure 2. Weighted Kaplan-Meier Analysis of rwEFS by Dosage of Goserelin



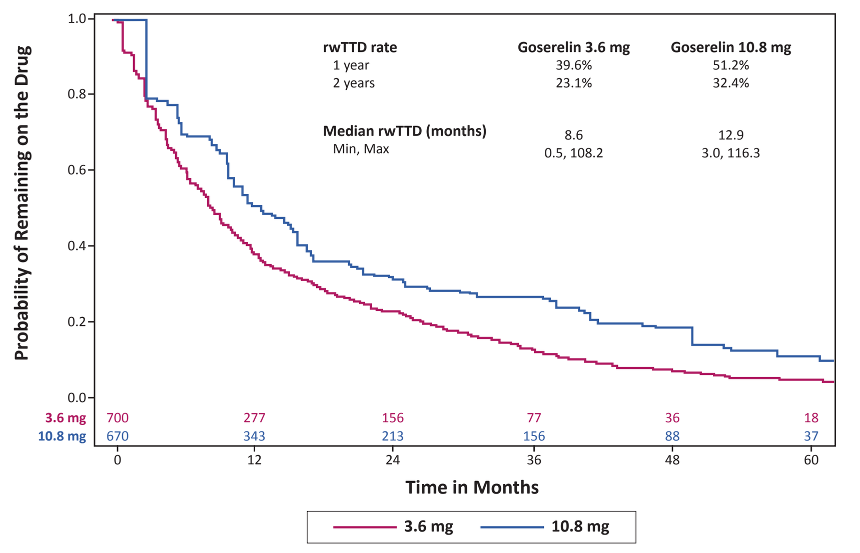
rwEFS: real-world event-free survival

Figure 3. Weighted Kaplan-Meier Analysis of rwOS by Dosage of Goserelin



rwOS: real-world overall survival

Figure 4. Weighted Kaplan-Meier Analysis of rwTTD by Dosage of Goserelin



Max: maximum, Min: minimum, rwTTD: real-world time to discontinuation

Limitations

- As with all retrospective analyses, missing, incomplete, and potentially misclassified data are challenges that limit the interpretation of our findings.
- While IPTW was used to help balance the cohorts, other unmeasurable differences may exist between the two cohorts.
- In order to capture all patients with 10.8 mg exposure, the study included patients in the 10.8 mg cohort who switched to and from 3.6 mg. To reduce the potential confounding by 3.6 mg exposure, the inclusion criteria required the patients to have initiated 10.8 mg within 6 months of their initial goserelin treatment. Of note, only 28.5% of the goserelin 10.8 mg cohort used 3.6 mg.
- The study could not differentiate whether goserelin was prescribed for ovarian function preservation during curative chemotherapy or ovarian function suppression.
- This study reflected treatment practice patterns primarily within community oncology practices in the U.S. that are part of the ConcertAI network and therefore may not accurately reflect the broader patient population.

Conclusions

- This real-world analysis indicates that 3-month goserelin 10.8 mg is non-inferior to monthly 3.6 mg among premenopausal BC women in terms of 12-month rwEFS rate.
- The rwOS rates were similar among both groups at 1, 3, and 5 years.
- At 1 year, almost 40% of patients in the goserelin 3.6 mg cohort remained on goserelin treatment while more than half of patients remained on goserelin in the 10.8 mg cohort.
- This finding may support the use of the 3-month goserelin 10.8 mg implant as an alternative treatment option for this patient population.

References

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