ホルモン抑制剤は乳がん患者の妊孕性を温存する（Abstract: LBA505）

標準的な化学療法にゴセレリンを併用することにより乳がんに対し化学療法を施行される女性の妊孕性が温存される

Adding goserelin to standard chemotherapy helps preserve fertility among women undergoing chemotherapy for breast cancer

ゴセレリン併用ホルモン療法は、ホルモン受容体陰性早期乳がん患者の化学療法による早期卵巣不全（OF）リスクを劇的に減少させるとの第III相研究の結果が、第50回American Society of Clinical OncologyのLate Breaking Clinical Trial sessionで発表された。このスタディにおいて、ホルモン受容体陰性閉経前stage I-IIIA乳がん患者257人が、シクロホスファミドを含む化学療法単独（標準療法群）または化学療法とゴセレリン併用群にランダムに割り付けられた。2年後、OFを来していたのはゴセレリン併用群の8%に対し、標準治療群では22%であった。妊娠を試みたと報告した女性の数は、2群間で同等であった。ゴセレリン併用群の21%（22人）が妊娠したが、化学療法単独群で妊娠したのはわずか11%（12人）であった。ゴセレリンは流産や妊娠中絶のリスクを上昇させることはなかった。ゴセレリンは無病生存期間および全生存期間にも影響したことに研究者らは驚いた。病期で補正後、治療後4年生存率はゴセレリン併用群において標準治療群に比べ50%高かった。

Full Text

New phase III study presented in a Late Breaking Clinical Trial session at the 50th Annual Meeting of the American Society of Clinical Oncology demonstrates that hormone therapy with goserelin dramatically reduces the risk of chemotherapy-associated premature ovarian failure among women with early-stage hormone receptor-negative breast cancer. Women who received the additional therapy were more likely to conceive following cancer treatment, and even had improved survival.

New findings from a federally funded phase III clinical trial, S0230/POEMS, indicate that adding a hormone suppressing drug called goserelin to standard chemotherapy may be an effective method of preserving fertility among women with early-stage hormone receptor-negative breast cancer. In the study, women who received goserelin along with chemotherapy were 64 percent less likely to develop premature ovarian failure compared to women who received chemotherapy alone, and they were more likely to have successful pregnancies. Survival was also improved among women in the goserelin arm: women were 50 percent more likely to be alive four years after starting chemotherapy compared to those in the standard arm.

"Preserving fertility is a common and important concern among younger women diagnosed with cancer, and these findings offer a simple, new option for women with breast cancer, or possibly other cancers," said lead study author Halle Moore, MD, a staff physician at Cleveland Clinic in Cleveland, OH. "Goserelin appears to be not only highly safe but also effective, as it increased the odds of becoming pregnant and delivering a healthy baby following chemotherapy."

Ovarian failure (OF) – defined in this study as cessation of menstrual periods and postmenopausal levels of follicle-stimulating hormone (FSH) – is a common side effect of chemotherapy. OF risk depends on the type and dose of chemotherapy as well as patient age and perhaps ovarian cycling at the time of chemotherapy.

Goserelin and similar luteinizing hormone-releasing hormone (LHRH) analogs temporarily shut down ovarian function, essentially putting the patient into a postmenopausal state. It is speculated that this protects follicles from chemotherapy damage. These medications are widely used to control ovulation timing for infertility procedures, such as *in vitro* fertilization. LHRH drugs are also widely used as hormonal therapies to treat advanced prostate and breast cancer.

In this study, 257 premenopausal women with stage I-IIIA hormone receptor-negative breast cancer were randomized to treatment with cyclophosphamide-containing chemotherapy alone (standard arm) or chemotherapy plus goserelin. Goserelin was given as monthly injections starting one week before the first dose of chemotherapy.

Two years after starting chemotherapy, 8 percent of women in the goserelin arm had OF vs. 22 percent of women in the standard arm. There was not a statistically significant difference in the number of women who reported attempting to conceive in the two arms. Twenty-one percent of women (22 individuals) assigned to goserelin plus chemotherapy became pregnant, and only 11 percent (12 women) among those assigned to chemotherapy alone became pregnant. These pregnancies resulted in 16 patients (15 percent of the group) delivering at least one baby on the goserelin arm compared with eight patients (7 percent) on the control arm. An additional three patients on the goserelin arm and two on the standard arm had not had a documented delivery but were still pregnant at the time of data submission. The study also found goserelin was safe – it was not associated with an increased risk of either miscarriage or pregnancy termination.

Researchers were surprised to find that goserelin also affected disease-free and overall survival. After adjusting for disease stage, women in the goserelin arm were 50 percent more likely to be alive four years after starting treatment compared to those in the standard arm. While these early results are very encouraging, Dr. Moore cautioned that more research is needed to understand any role of goserelin in the treatment of ER-negative breast cancer. On the other hand, the POEMS findings do establish a role for LHRH analogs in preserving ovarian function and fertility prospects for women treated with curative intent chemotherapy for breast cancer.

"Preserving fertility is an important component of quality survivorship care," said Patricia Ganz, MD, ASCO Expert. "This study provides strong evidence for a safe and effective strategy for younger women with breast cancer to preserve ovarian function and the possibility of pregnancy."

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