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Tailored Chemotherapy Trial for Women at Advanced Age with Endocrine-Nonresponsive Breast Cancer: The CASA Trial

Silvia Dellapasqua, Diana Crivellari, Anne Hamilton, Richard D. Gelber, Monica Castiglione-Gertsch, Karen N. Price, and Aron Goldhirsch for the International Breast Cancer Study Group (IBCSG) and Breast International Group (BIG)

Rationale

Therapeutic dilemma: How to treat older women with an endocrine-nonresponsive early breast cancer?

- Relapses may occur earlier compared with hormone receptor-expressing tumors, justifying some chemotherapy even when life expectancy is short
- Such a dilemma does not exist for patients who are biologically and functionally young, and may be offered a “standard” chemotherapy regimen
- Physicians may not offer a relatively frail patient any treatment for fear of toxic effects of chemotherapy

Typically, older patients are treated heterogeneously with arbitrary modifications of standard treatments

Why CASA?

- This trial is designed to test a reasonably tolerated cytotoxic regimen tailored for older patients
- The endocrine-nonresponsive population selection is advantageous because the magnitude of the chemotherapy effect for this postmenopausal cohort is likely to be quite large
- Avoiding dilution with patients having endocrine-responsive tumors maximizes the chance to observe a benefit in the shortest time with the fewest number of patients

IBCSG Trial 32-05/BIG 1-05

Chemotherapy Adjunct Studies for Women at Advanced Age (CASA)

Objective

- Evaluate the role of CAELYX® (pegylated liposomal doxorubicin) as adjuvant chemotherapy for older postmenopausal women (66 years old and above) with endocrine-nonresponsive breast cancer who are NOT suitable for being offered a “standard chemotherapy regimen”

The CASA trial provides two randomization options to accommodate patient and physician preference:

Option 1: CAELYX - nil

For patients who, according to the treating physician and/or to the patient’s preferences, are candidates to receive no adjuvant therapy

CAELYX 20 mg/m² IV q 2 wk x 8

No adjuvant therapy (nil)

Option 2: CAELYX - CM

For patients who, according to the treating physician and/or to the patient’s preferences, are candidates to receive some adjuvant therapy

CAELYX 20 mg/m² IV q 2 wk x 8

Low-dose, metronomic CM

All regimens are 16 weeks’ duration. C = cyclophosphamide 50 mg PO qd x 16 wk; M = methotrexate 2.5 mg PO bid d 1 & 4 q wk x 16 wk.

CAELYX and CM Therapies: Background

Why CAELYX?

- Anthracyclines are highly active and widely used in breast cancer
- Conventional doxorubicin is avoided in the elderly due to cardiac toxicity
- CAELYX maintains antitumor efficacy while improving the safety profile
- CAELYX efficacy is comparable to common salvage regimens in patients with taxane-refractory metastatic breast cancer
- CAELYX 20 mg/m² is used in patients with Kaposis Sarcoma (KS), and other diseases, including CNS tumors and lymphomas
- This schedule is active for patients with advanced breast cancer and is well-tolerated

Why CM?

- Relevant clinical responses were observed with continuous oral low-dose cyclophosphamide and methotrexate in different types of cancer
- Oral cyclophosphamide and methotrexate demonstrated significant efficacy in patients with pretreated metastatic breast cancer
- Active oral treatment is easy to administer and has a low cost

CASA Summary

Population

- Older postmenopausal women (66 years of age or older)
- Histologically proven, completely resected, early-stage breast cancer
- Endocrine-nonresponsive breast cancer
- Patients must not be candidates for endocrine therapy or for an adjuvant chemotherapy program which includes a “standard” anthracycline-containing chemotherapy regimen
- Patients must have VES-13 geriatric assessment prior to randomization

Endpoints

Primary:
- Breast cancer-free survival (events are reappearance of invasive breast cancer at any site, including contralateral disease)

Secondary:
- Tolerability (treatment completion)
- Adverse events
- Quality of life
- Disease-free survival (includes second malignancies and deaths)

Analysis Plan

- Stratified (pooled) analysis combining the results of both randomization options (CAELYX vs non–CAELYX-containing control groups, either nil or CM)
- Separate analyses for each of the two randomization options to assess pair-wise contributions to the overall result (whisker plots)
- 1,296 patients (432 per year for 3 yrs with 1.76 years of additional follow-up; total study duration of 4.76 years) to provide 80% power

CASA is being coordinated by the International Breast Cancer Study Group with participation from other members of the Breast International Group, with support from Schering-Plough.

Activation of the CASA trial is planned for mid-2005.

For further information contact the IBCSG Coordinating Center at www.ibcsg.org.