#0174

A PHASE III STUDY OF ADJUVANT ENDOCRINE THERAPY WITH OR WITHOUT CHEMOTHERAPY FOR POSTMENOPAUSAL BREAST CANCER PATIENTS WHO RESPONDED TO NEOADJUVANT LETROZOLE: STUDY DESIGN OF THE NEW PRIMARY ENDOCRINE-THERAPY ORIGINATION STUDY[NEOS(N-SAS BC06)]

H. Iwata*[1], N. Masuda[2], T. Toyama[3], N. Taira[4], Y. Yamamoto[5], S. Saji[6], M. Kashiwaba[7], T. Yamaguchi[8], Y. Ohashi[9]

[1]Breast Oncology, Aichi Cancer Center Hospital, Nagoya, [2]Surgery, NHO Osaka National Hospital, Osaka, [3]Breast and Endocrine Surgery, Nagoya City University Hospital, Nagoya, [4]Breast and Endocrine Surgery, Okayama University Hospital, Okayama, [5]Breast and Endocrine Surgery, Kumamoto University Hospital, Kumamoto, [6]Breast Oncology Unit, Tokyo Metropolitan Cancer and Infection disease Center Komagome Hospital, Tokyo, [7]Surgery, Iwate Medical University, Morioka, [8]Clinical Trial Data Management, [9]Biostatistics, School of Public Health, The University of Tokyo, Tokyo, Japan

Rationale

- At the 2007 International Conference on Primary Therapy of Early Breast Cancer in St. Gallen [1] , endocrine therapy alone or chemotherapy followed by endocrine therapy was recommended as adjuvant therapy for highly endocrine-responsive, or incompletely endocrine-responsive and HER2-negative, intermediate-risk breast cancer.
- However, any other characteristics of patients who need addition of chemotherapy remain unknown.
- The TAILORx [2] and MINDACT [3] trials are ongoing and utilize gene expression profiling in order to answer this question (Fig. 1-2).
- Sufficient data have not been available about the long-term prognosis of patients receiving neoadjuvant endocrine therapy so that how the long-term treatment outcome differs between patients responding and not responding to neoadjuvant endocrine therapy and between those receiving and not receiving neoadjuvant endocrine therapy.
- In patients with hormone receptor-positive breast cancer, pathological complete response (pCR), a positive prognostic factor, is difficult to achieve even with intensive neoadjuvant chemotherapy [4,5] .
- Letrozole is a more potent aromatase inhibitor and is more effective than tamoxifen in neoadjuvant and adjuvant settings.

Study Design

- The primary aim of NEOS(N-SAS BC06) is to evaluate the necessity of using adjuvant chemotherapy for the treatment of postmenopausal breast cancer patients with node-negative, ER-positive and HER2-negative tumors who responded to neoadjuvant letrozole.
- This trial is a randomized, open-label, multicenter trial, which aims to recruit a total of 1,700 patients.
- Follow up is planned for 5 years from final recruitments.
- The trial design is shown in Figure 3.
- The eligibility criteria for this trial are as follows:

Eligibility criteria for primary registration

Inclusion criteria

1) Postmenopausal women with histological confirmed primary invasive breast cancer.
2) T1c-T2, N0, M0
3) ER-positive
4) HER2: ≦2+ and FISH negative at registration
5) ≦ 75 years at primary registration
6) ECOG Performance Status: 0 or 1
7) No previous treatments of breast cancer
8) Adequate organ function
9) Written informed consent

Exclusion criteria

1) Positive sentinel lymph node if biopsied before primary registration
2) Synchronous or asynchronous bilateral breast cancer

Eligibility criteria for secondary registration

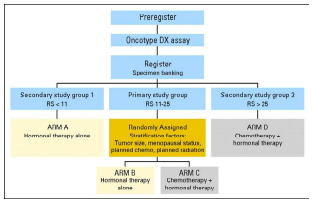
Inclusion criteria

1) Clinical response to the neoadjuvant letrozole evaluated as CR, PR or SD
2) Completion of any surgical resection of breast cancer
3) The following lymph node status found after axillary lymph node dissection:
   i) Patients with CR or PR : Node-negative, or 1-3 involved nodes.
   ii) Patients with SD : Node-negative
   A patient who does not undergo axillary lymph node dissection because of negative sentinel lymph node biopsy will be considered as "axillary node negative".

Exclusion criteria

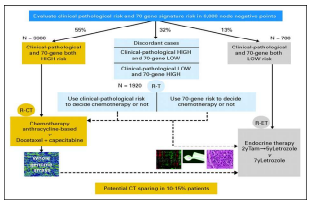
1) FISH positive for HER2 proved after primary registration

Fig. 1 Trial Assigning Individualized Options for Treatment (TAILORx) design[2]



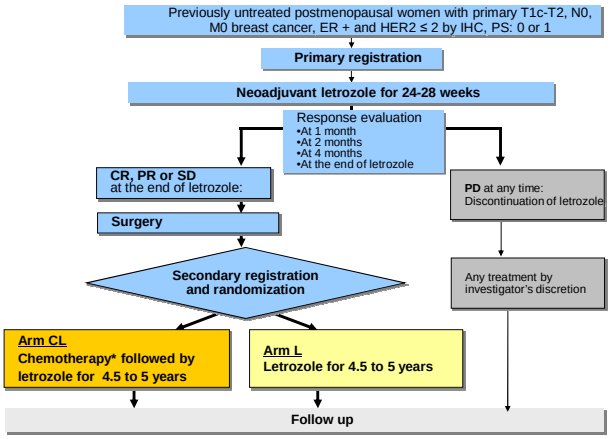
Sparano, J. A. et al. JCO 2008

Fig 2. The MINDACT (Microarray in Node-Negative Disease May Avoid Chemotherapy) trial design[3]



Cardoso, F. et al. JCO 2008

Fig 3. NEOS design



*Standard chemotherapy regimen: CMF, AC/EC, TC, FAC/FEC, AC-T/EC-T, FEC-T or TAC

Stratification factors for randomization

1) Response to neoadjuvant letrozole	CR or PR	/ SD
2) PgR status at primary registration	positive	/ negative
3) Pathological node status	positive	/ negative
4) Age at primary registration	<60	/ 60 ≤
5) Study center		

Trial endpoints

Primary endpoint:

Disease-free Survival

Secondary endpoints:

Overall Survival (OS), clinical response rates, pathological response, breast-conserving surgery rate, DFS/ OS in subgroups of patients according to clinical response (CR, PR, SD or PD), safety, HRQOL, and cost-effectiveness

Planned Sub-studies (in selected centers)

- Gene expression profiling
- Treatment induced-changes in biological markers (Ki-67, ERβ, etc.)

Future Aspect

- Response to neoadjuvant endocrine therapy may become a very useful tool in practice if it can help determine adjuvant systemic therapy for postmenopausal women with endocrine-responsive and intermediate-risk breast cancer.

References

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