BREAST CANCER COHORT in JAPAN

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Rainbow of KIBOU

Background

- ☐ There are many breast cancer survivors due to high incidence and good prognosis.
- ☐ Patients have strong interests for life style factors to make prognosis better since it can be changed by themselves (diet, smoking, alcohol, exercise, obesity, etc.)
- ☐ Many clinical trials have been conducted for chemo and hormonal therapy, but few studies are available for life style factors and breast cancer prognosis.
- ☐ Several cohort studies has started in foreign countries.

Objective

- ☐ To investigate the effect of life style factors (diet, physical activity), CAM use on the effect of breast cancer prognosis including QOL, we started cohort studies for breast cancer patients.
- ☐ The outline of the design for the cohorts is presented in this report.

Review 1: Risk factors for breast cancer occurrence and recurrence

	Risk factors for breast cancer occurrence				Risk factors for breast cancer recurrense and survival
Data sources	by WCRF / AICR*1 Premenopause	by WCRF / AICR*1 Postmenopause	by NCC*2 Japanese breast cancer	by Japanese Clinical guideline of breast cancer*3	PDQ®*4
Adult attained height	Probable(↑)	Convincing(↑)	–	–	–
Greater birth weight	Probable(↑)	Limited-no conclusion	–	–	–
Body fatness	Probable(↓)	Convincing(↑)	–	Pre: Probable(↓) Post: Convincing(↑)	–
Physical activity	Limited-suggestive(↓)	Probable(↓)	Limited-no conclusion	Pre : Limited-no conclusion Post: Probable (↓)	–
Smoking	–	–	Limited-suggestive(↑)	Limited-suggestive(↑)	–
Alcoholic drinks	Convincing(↑)	Convincing(↑)	Limited-no conclusion	Probable(↑)	(↑?) Beer
Vegetable & Fruits	Limited-no conclusion	Limited-no conclusion	Limited-no conclusion	–	(↓?)
Soya & Soya products	Limited-no conclusion	Limited-no conclusion	Limited-suggestive(↓)	Limited-no conclusion	(?) no evidence for increase nor decrease risk
Vitamin C	Limited-no conclusion	Limited-no conclusion	–	–	(↓?)
Green tea	–	–	Limited-no conclusion	Limited-no conclusion	
Total fat	Limited-no conclusion	Limited-suggestive(↑)	Limited-no conclusion	Pre: Limited-no conclusion Post: Limited-suggestive(↑)	(↑) Total fat / Total energy

1) World Cancer Research Fund / American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective
2) Grant for the Third Term Comprehensive Control Research for Cancer from the Ministry of Health, Labour and Welfare of Japan
"The development and evaluation of cancer prevention strategies in Japan' (Principal investigator; S Tsugane (National Cancer Center))
3) The Japanese Breast Cancer Society
4) National Cancer Institute

Review 2: of the cohort studies being conduced in foreign countries

☐ Pathways (USA)

- Setting: All breast cancer patients registered to Kaiser Permanente Northern California (KPNC, multi-institutions, 3,000 pts)
- Exposure information: Questionnaire and interview, Sample (blood, saliva)
- Endpoints: Disease-free survival, overall survival (mean follow-up: 4 years)
- Follow-up: Periodical questionnaire and telephone to patients and KPNC DB
- Enrollment: 2006.1-2009.6 (1,751 pts registered as of July 2, 2008)

☐ Vitamin D and prognosis (Canada) Goodwin, P et al., Proc ASCO (2008)

- Setting: 512 breast cancer patients diagnosed Toronto U during 1989~96
- Exposure information: Blood sample at diagnosis (frozen)
- Endpoint: Disease-free survival, overall survival
- Follow-up: Until 2006 (follow-up of 10~17 years)
- Results: Recurrence116pts(22.7%), deaths106pts(20.7%)
  - Serum Vitamin D divided into 3 groups; deficient (<50nmol/L), indeficient (50-72nmol/L), sufficient (>72nmol/L)
  - Significant reduction of recurrences and deaths in sufficient to deficient group

Design of our cohort study: Rainbow of KIBOU

☐ Problem of conducting cohort study

- Sample size needed with several hundreds to several thousands
- Confounder information is necessary such as clinical and treatment information
- Follow-up is necessary to obtain endpoint information

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Collaboration with large scale multi-institution clinical trials
⇒Cohort 05, Cohort 06, Cohort 07…

☐ Problems in collaboration with clinical trials

- Dependency of subjects registration to clinical trials

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- Difficulty in collecting qualified samples

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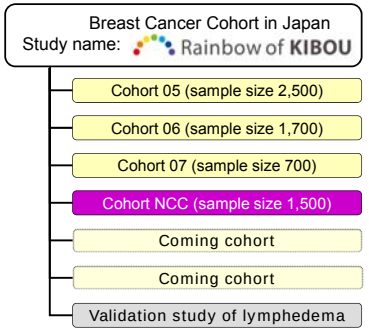
Single institution study with sample collections
⇒Cohort NCC (National Cancer Center Hospital)



☐ **Participants:**

- women diagnosed with breast cancer participating in the clinical trials (Cohort 05, 06, 07)
- being treated at National Cancer Center Hospital (Cohort NCC)

☐ **Planned sample size:** 10,000

☐ **Endpoints:**

- Primary endpoint: disease-free survival
- Secondary endpoint: overall survival and the health-related QOL

☐ **Exposure information:**

- common self-administered questionnaire (Cohort 05, 06, 07)
- common self-administered questionnaire, sample (blood and tissue), bone density (Cohort NCC)

☐ **Endpoint information and clinical & treatment information:**

- information from clinical trials (Cohort 05, 06, 07)
- information from charts

☐ **Enrollment period:** 3 years to 5 years

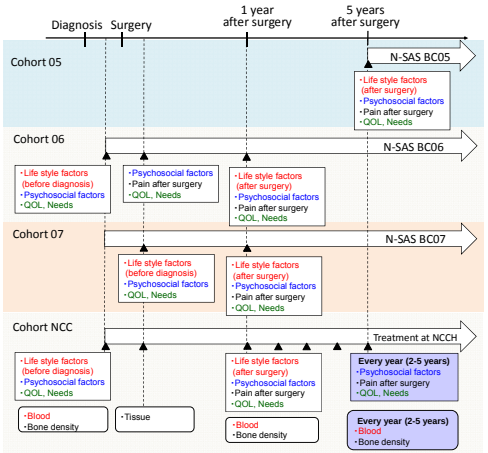
☐ **Follow-up period:** at least 5 years

☐ **Statistical analysis:**

association between prognosis and items below

- information from the questionnaire
- information from blood and tissue sample including genetic polymorphism

Survey items & study points



Survey items (Common questionnaire)

- Life style factors (Diet, physical activity, CAM use…)
- Psychosocial factors (stress, depression, HOPE, Perceived Positive Change, support, social network…)
- Pain after surgery (lymphedema, PMPS…)
- Needs for information and support
- QOL

Cohort 05: Collaboration with clinical trial `N-SAS BC05`

☐ N-SAS BC05: Randomized Study to Assess the Efficacy of a Further 5 Years of Anastrozole Treatment for Postmenopausal Women
- Conducted by CSPOR: Comprehensive Support Project for Oncology Research

☐ Enrollment: November 2007 ~

☐ Current condition (As of October 25, 2010)
- IRB approved at National Cancer Center and 107 of 122 participating institutions
- Questionnaire delivered to 608 among 639 participants of clinical trial
- Baseline data is obtained from 544 pts (Response rate: 89.5%)

Cohort 06: Collaboration with clinical trial `N-SAS BC06`

☐ N-SAS BC06: Randomized Phase III Study of Adjuvant Endocrine-Therapy with or without Chemotherapy for Postmenopausal Breast Cancer Patients who Responded to Neoadjuvant
- Conducted by CSPOR: Comprehensive Support Project for Oncology Research

☐ Enrollment: May 2008 ~

☐ Current condition (As of October 25, 2010)
- IRB approved at National Cancer Center and 105 of 129 participating institutions
- Questionnaire delivered to 250 among 304 participants of clinical trial
- Baseline data is obtained from 230 pts (Response rate: 92.0%)

Cohort 07: Collaboration with clinical trial `N-SAS BC07`

☐ N-SAS BC07 (two studies)
- Evaluation of Trastuzumab without Chemotherapy as a Postoperative Adjuvant Therapy in HER2 Positive Elderly Breast Cancer Patients: Randomized Controlled Trial
- Cohort Study to Evaluate the Efficacy and Safety of Postoperative Adjuvant Therapy in HER2 Positive Elderly Breast Cancer Patients
- Conducted by CSPOR: Comprehensive Support Project for Oncology Research

☐ Enrollment: October 2009 ~

☐ Current condition (As of October 25, 2010)
- IRB approved at National Cancer Center and 59 of 64 participating institutions
- Questionnaire delivered to 26 among 27 participants of clinical trial
- Baseline data is obtained from 24 pts (Response rate: 92.3%)

Cohort NCC

☐ Being conducted at NCCH (National Cancer Center Hospital)

☐ Exposure information: Common cohort questionnaire and sample (blood and tissue)

☐ Enrollment: November 2010 ~ (in preparation)

☐ Current condition (As of October 25, 2010)
- IRB approved at National Cancer Center

Advantage of Cohort NCC
- Most of the breast cancer pts who get surgery in one institution can be registered
- Association between prognosis and biomarker in blood
  /Endogenous hormone level /Insulin registance, chronic inflammation, etc.
  /Biomarker representing nutrient intake, obesity, physical activity
  /Nutrients in blood reflecting metaboism and absorption in body isoflavone, Vitamin D, etc.
- Association between prognosis and genetic polymorphism
  /Direct effect of genetic factors /gene-envirionment, gene-treatment interaction
  /CYP2D6: possible association with tamoxifen effect/ CYP19A1: possible association with AI effect
- Availability of sample
  /Storage for future use /biobank with clincical information

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