Background: Women with germline BRCA1 or BRCA2 (BRCA1/2) mutations have a 56-80% life-time risk of developing breast cancer. Prophylactic mastectomy provides a valid option to reduce it, but impacts the quality of life [1-3].

Medical prevention by aromatase inhibitors (AIs) has recently been shown to have preventive effect [4]. It may thus be considered as an alternative. LIBER is an ongoing double-blind, randomized phase III trial evaluating the efficacy of 5-years letrozole vs placebo to decrease breast cancer incidence in postmenopausal BRCA1/2 mutation carriers (trial registration NCT00673335).

Methods: We compared characteristics of women in the LIBER trial (n=113) to those of women enrolled in the prospective ongoing national GENEPSO cohort of BRCA1/2 mutation carriers (n=1505). Uptake was evaluated through a survey sent to all active centres, with responses obtained from 17 of the 20 (85%) centres [5].

Enrollment Criteria

- Post-menopausal women (spontaneous menopause or following bilateral oophorectomy)
- Women who carry a characterized BRCA1/2 mutation
- ECOC performance status <2
- Normal hematological, liver, kidney and cardiovascular functions
- No hormone replacement therapy during the 3 months before enrollment
- Eligibility:
  - Women with positive answer and informed during a visit at participating site: N=292 (55%)
  - Women refusal after solicitation or no answer: N=234 (70%)
  - Women deceased: N=58 (17%)
  - Women refusal after information sent to all active centres, with responses obtained from 17 of the 20 (85%) centres [5].

Acceptability

- Women who signed the participation consent: N=75 (56% of orally informed women)
- Women refusal after selection non-center: N=24 (39%)
- Women refusal after information visit: N=237 (44%)

Eligibility

- Without bilateral oophorectomy: N=58 (55%)
- Without bilateral mastectomy: N=134
- Women with invasive cancer history > 5 years from enrollment: N=128 (38%)
- Women with BRCA1/2 mutations: N=176 (52%)
- Women deceased: N=29 (9%)

Results

• According to the characteristics of the women included in the GENEPSO cohort and the survey, approximately one third of BRCA1/2 mutation carriers were eligible for the trial.
• Out of the 534 women eligible from chart review informed by mail about the trial, 44% came to a dedicated medical visit.
• Uptake of drug prevention trial was 32 % of orally informed women and 15 % of overall eligible women.
• The main reasons of refusal were: potential side effects, probability to receive the placebo and lack of support from their physicians.
• Previous unilateral breast cancer and prophylactic oophorectomy were more frequently observed in women enrolled in the trial than in the French cohort (93% vs 66% and 50 % vs 39 %, respectively).

Conclusion

• The overall uptake of the study is 15%, a rate similar to the uptake of other preventive trials [6,7].
• Women with previous unilateral breast cancer or prophylactic oophorectomy are more likely to enter a medical prevention trial.
• A greater and wider information of the trial should be offered to women with BRCA1/2 mutation for better recruitment.
• Breast cancer prevention by AIs deserves to be evaluated since it could provide a precious alternative to bilateral mastectomy in postmenopausal patients.
• The study has been proposed to other countries (Spain, Canada).

References