Compelling in-vitro and in-vivo evidence suggest that aspirin may have anti-tumor effect. Multiple epidemiologic studies have reported improved breast cancer survival among regular aspirin users compared to non-users. Pooled data from randomized trials of aspirin for cardiovascular disease have also reported a decreased risk of metastatic cancer among aspirin users, mainly driven by a decreased risk of metastatic adenocarcinoma (RR 0.52 (95% CI 0.35-0.75)). However in order for aspirin to become standard of care, the exact benefits and risks for breast cancer survivors would need to be confirmed in a randomized controlled trial. Even if clinical effects were modest, the global impact would be substantial since aspirin is inexpensive and widely available.
Alliance A011502: A Randomized Phase III Double Blinded Placebo Controlled Trial of Aspirin as Adjuvant Therapy for Her2 Negative Breast Cancer: The ABC Trial

WY Chen, EP Winer, AH Partridge, LA Carey, T Openshaw, M Carvan, C Matyka, K Visvanathan, B Symington, MD Holmes

Objective

Primary
• To compare the effect of aspirin (300 mg daily) versus placebo upon invasive disease free survival (iDFS) in early stage HER2 negative breast cancer patients.

Secondary
• To compare the effect of aspirin versus placebo on: a) distant disease-free survival; b) overall survival; and c) cardiovascular disease.
• To compare the toxicity of aspirin versus placebo.
• To assess adherence to aspirin and placebo.
• To bank tumor and germline deoxyribonucleic acid (DNA), plasma and urine collected at baseline and sequential plasma and urine collected 2 years later for future measurement of inflammatory markers.
• To determine if there are subgroups of participants characterized by lifestyle factors associates with greater inflammation for whom there is greater benefit of aspirin versus placebo upon iDFS.
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### Study Schema

**ER positive:**
- Node positive within 10 years of diagnosis

**ER negative:**
- Node positive or high risk node negative (> 2 cm) within 18 months of diagnosis

**HER2-negative**
- Age < 70
- Free of recurrence

**R A N D O M I Z E**

**ARM 1**
Aspirin 300 mg daily x 5 years

**ARM 2**
Placebo daily x 5 years

### Target accrual: 2,936

**Power and Sample size:** Assuming 381 iDFS events and 5-year iDFS on placebo of 77%, 80% power to detect HR 0.75

**Key Eligibility Criteria**
- Age < 70
- Free of recurrence
- ER positive:
  - Node positive within 10 years of diagnosis
- ER negative:
  - Node positive or high risk node negative (> 2 cm) within 18 months of diagnosis
- HER2-negative
- Node positive or high risk node negative (> 2 cm) within 18 months of diagnosis

**Follow Up**
- ARM 2
  - Placebo daily x 5 years
- ARM 1
  - Aspirin 300 mg daily x 5 years
<table>
<thead>
<tr>
<th>Study Status</th>
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<tr>
<td>Activated December 2016</td>
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<td>Accrual as of April 2019: 1,347</td>
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<td>1175+ sites approved</td>
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<td>Open in ECOG-ACRIN, NRG, SWOG, and Health Canada</td>
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Key Eligibility Criteria

- HER-2 negative
- ER positive: Node positive within 10 years of diagnosis
- ER negative: Node positive or high risk node negative (> 2 cm) within 18 months of diagnosis
- Prior adjuvant treatment with chemotherapy and/or endocrine therapy, as determined by treating physician
- Regular NSAID/aspirin use allowed if stopped for 30 prior to study entry
- Age 18-70

Exclusion Criteria

- History of prior stroke
- History of significant GI bleeding
- No concurrent anticoagulation with warfarin, heparin, clopidogrel, or oral direct thrombin inhibitors
- History of atrial fibrillation or myocardial infarction
- History of grade IV hypertension
- Chronic daily use of oral steroids
- No prior malignancy in past 5 years
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