Supplemental Material

Epidemiology, Biology, Treatment and Prevention of Ductal Carcinoma *in Situ* (DCIS)

Highlights from the Dana-Farber/Harvard Cancer Center DCIS Retreat
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Supplemental Table 1. Key Questions Considered

Current Trends, Outcomes, Detection and Pathology
– Does local therapy improve survival outcomes?
– Can we use national populated-based data to describe outcomes for women with low-risk DCIS to inform current trials of de-escalating therapy?
– Is imaging part of the problem or part of the solution?
– Are advances in imaging or shifting trends in interpretation of imaging findings changing rates of DCIS diagnosis?
– Can we distinguish clinically relevant DCIS based on MRI/mammographic features, microenvironment, or overall breast tissue composition?
– Are there clinical, treatment, or tumor related risk factors that can reproducibly predict for local recurrence or progression to invasive disease in patients with DCIS?
– Can factors to assess risk be combined to inform treatment recommendations?
State-of-the-Science
– What are the mechanisms driving the progression of DCIS to invasive cancer?
– How is the microenvironment of DCIS different from that of invasive cancer? How does it change during the progression from DCIS to invasive cancer?
– Are there biologic features that distinguish a “good” DCIS from a “bad” DCIS? Can we predict progression based on biological features alone?
– Is there a role for vaccines in DCIS?
– There are several prevention studies either in development or actively enrolling patients. What can we, as a community, support?
Risk Perceptions, Communication, and Decision-Making
– How are treatment decisions currently being made?
– Does modeling cost-effectiveness among treatment strategies help us to determine which treatments are best for which patients?
– How do we help patients understand the risks and benefits of each treatment?
– What are the tradeoffs for surveillance?
– Are we ready for de-escalation of treatment for DCIS?

DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging

Supplemental Table 2. Future Research Directions

Current Trends, Outcomes, Detection and Pathology
– What are the features of both the lesion and the surrounding tissues on MRI or other advanced imaging that could be combined to better predict future outcomes? These features may include pattern of calcifications (distribution, size, features, adjacent tissue), as well as features of the breast tissue itself: density, microenvironment around the tumor, macroenvironment of the breast, and parenchymal enhancement.
– Could enhanced MRI diffusion imaging improve upon our ability to distinguish high grade from low grade DCIS?
– Can the tumor microenvironment, specifically the myoepithelial and stromal cells, tells us more about which patients with DCIS are more likely to develop invasive cancer?
State-of-the-Science
– Investigate the co-evolution of the cancer cells with the immune environment such as T-cell signatures.
– Further identify antigens on cancer cells that the immune system targets.
– Role of vaccines in boosting or priming the immune response in the premalignant setting. Could consider combining vaccines with checkpoint inhibitors.
Risk Perceptions, Communication, and Decision-Making
– Pilot testing and randomized controlled trial for the www.onlineDeCISion.org decision tool to see if it affects knowledge, the treatment a patient receives, and the quality of decisions.
– Opportunity to change the way we talk about DCIS; standardize the language we use.
– We must reframe the goals of treatment of DCIS; rather than focusing treatment strategies on recurrence, we need to focus on risk of invasive cancer and breast cancer mortality, as well as impact on quality of life and breast cancer free survival.

DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging

Supplemental Figure 1

Projections of Breast Cancer Mortality and Competing Causes of Mortality According to DCIS Management Strategy [1]

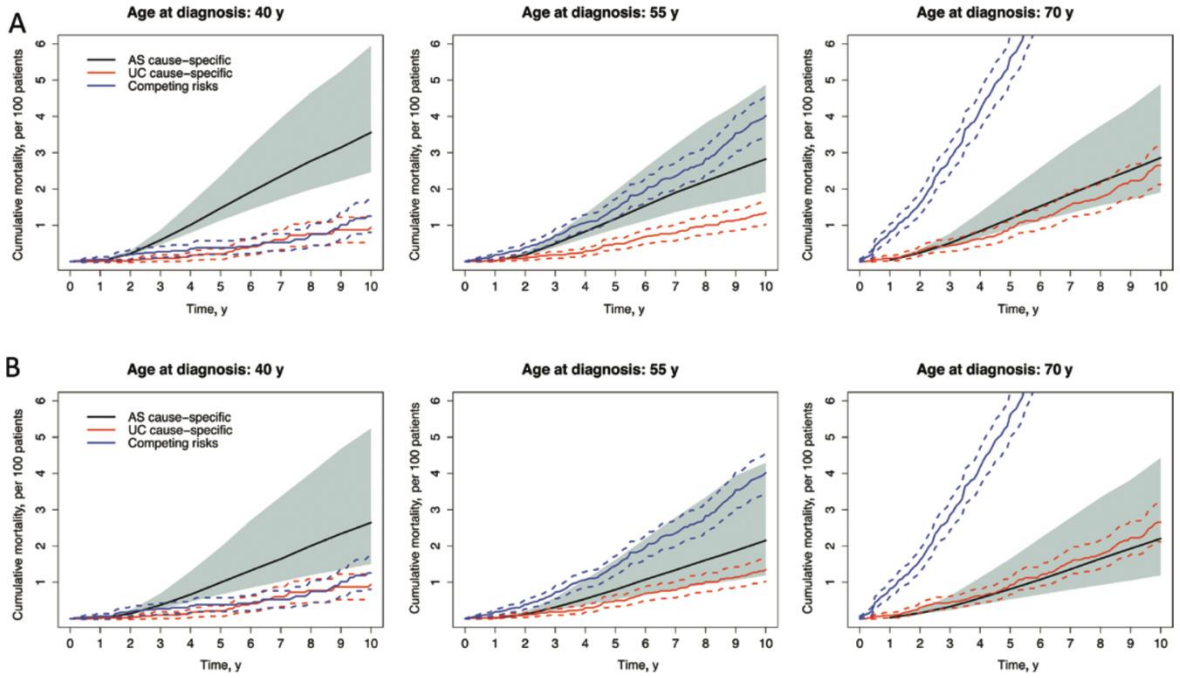

Figure 2. Cumulative mortality—active surveillance (AS) disease-specific projections vs usual care (UC) disease-specific and competing risks. The model-based, projected disease-specific cumulative mortality (DSCM) for the AS strategy (median: **black line**; 95% projection range: **gray shading**) is compared with the Surveillance, Epidemiology, and End Results (SEER)–based DSCM for UC (point estimate: **red solid line**; 95% confidence interval: **red dotted lines**) and the cumulative mortality because of competing risks (point estimate: **blue solid line**; 95% confidence interval: **blue dotted lines**) for two different control parameter sets. **A)** baseline control parameter set with understaging probability p_{inv} = 18.9%, screening sensitivity p_{sen} = 80%, and screening interval Δt = 6 months. **B)** Improved control parameter set with p_{inv} = 10%, p_{sen} = 90%, and Δt = 6 months.

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1. Ryser MD, Worni M, Turner EL, *et al.* Outcomes of Active Surveillance for Ductal Carcinoma in Situ: A Computational Risk Analysis. J Natl Cancer Inst 2016;108(5): pii: djv372.