CAC- Biomarker Testing for Risk Stratification in DCIS Questions

1. What clinical outcomes are considered relevant in breast ductal carcinoma *in situ* (DCIS) patients for the use of Radiation Therapy (RT)? Is the appropriate endpoint for consideration ipsilateral breast tumor recurrence (IBTR), invasive cancer, mortality, or some other metric? Why?
2. Do you accept that some low-risk Medicare patients should be treated with Breast Conserving Surgery (BCS) only, and if so, how would you identify this population? What variables/clinical information is relevant for this decision?
3. What is a reasonable risk of IBTR (or other metric) to warrant BCS-only treatment for DCIS in the Medicare population? What is a reasonable risk reduction that would result in a change in recommendation from BCS-plus RT (BCT) to BCS treatment? What variables should be considered?
4. Studies have shown that clinical factors such as negative margins> 2mm, tumor size <2.0/2.5cm, lack of comedonecrosis, and tamoxifen use are associated with lower IBTR. Why is there no consensus on determining a "low risk" population based on these factors? How would you define this?
5. Are the Van Nuys Prognostic Index (VNPI or modified VNPI), MSK nomogram, Patient prognostic score, or MD Anderson Nomograms (for invasive cancer) accepted and currently used means of risk-stratifying DCIS patients? What are the known limitations? Why are these not broadly implemented?
6. Is there sufficient clinical evidence supporting the use of biomarkers for determining what Medicare patients would NOT benefit from RT and should forgo its use (BCS-only)?
7. What are the differences between clinical-only risk stratification modalities and biomarker-based ones in terms of accurate risk assessment? When would you consider one or the other?
8. If "yes" to question 7 above, in what patient populations specifically have demonstrated improved outcomes from these services (improved outcomes here can mean avoiding unnecessary interventions)? Is there any evidence that biomarker testing improves risk stratification or outcomes above clinical stratification methods?
9. If a biomarker identifies a "low-risk" group of 10% IBTR that is not statistically associated with RT response, and clinical-only features strategy can predict LR in a "low-risk" group of 10% without claims to statistical lack of RT response in that group, does this carry any significance to decision making?
10. If a biomarker identifies a "low risk" group of 10% IBTR and further identifies a defined group of patients who are additionally less likely to have invasive cancer recurrence, how would this information impact decision making regarding testing and making BCS vs BCT?
11. Are there any other considerations regarding the clinical validity and utility of biomarker testing for RT use in DCIS patients we should consider and did not discuss?

12. Is there published evidence that we did not consider but should review as part of this analysis?