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Current Approaches to Reduce the Overtreatment of DCIS

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The introduction of routine mammography has played a key role in early breast cancer detection and subsequently a reduction in breast cancer-related deaths [1]. However, these advancements in screening have also contributed to ~60,000 women each year in the U.S. being diagnosed with ductal carcinoma in situ (DCIS), a 'pre-cancerous lesion' also referred to as stage 0 breast cancer. This accounts for ~25% of all breast cancer diagnoses. DCIS is diagnosed when the cells that line the milk ducts turn abnormal or malignant but are unable to penetrate through the wall of the duct. As long as these cells remain confined to the duct, it is considered non-invasive as they are unable to get into the lymph nodes or blood stream. The goal of therapy for DCIS is to prevent the development of invasive breast cancer. It is estimated that only 20–30% of these pre-cancerous lesions will progress to invasive breast cancer. However, since there is no way to predict whether a case of DCIS will become invasive cancer, it is treated similarly to invasive breast cancer, such that ~97% of women with DCIS undergo a combination of surgery, radiation, and endocrine therapy [2].

Recognizing that approximately 70-80% of women diagnosed with DCIS are being overtreated, oncologists and researchers are earnestly trying to understand why some cases of DCIS develop into invasive breast cancers while others remain stable. Some approaches, including the gene expression analysis tool, Oncotype DX DCIS recurrence score, are used to identify patients that may reasonably omit post-lumpectomy radiation therapy [3]. The data regarding its application remain limited and thus gene expression analyses in DCIS patients are not routine across all cancer centers. Because such prognostic biomarkers are not the standard of care for DCIS, another potential approach to DCIS management is to monitor the lesion carefully and wait—a concept known as active surveillance. This concept of active surveillance is used in other types of low-risk (pre-) cancers, but is underutilized in DCIS with an estimated 3% of patients choosing this management method. To address this, an international collaboration of active surveillance trials for low-risk DCIS has been initiated.

Four prospective phase III clinical trials have launched in the United Kingdom, Europe, Japan, and the United States referred to as LORIS, LORD, LORETTA, and COMET, respectively. Though there are some minor differences across these studies, they similarly only include participants with low-risk, hormone-receptor-positive DCIS. Upon enrollment, participants are randomized to either the control arm in which they undergo the standard of care treatment (surgery +/- radiation and five years of endocrine therapy) or to the experimental arm in which they engage in active surveillance and five years of endocrine therapy if needed (COMET and LORETTA trials only) [4].

Active surveillance, as described by the COMET trial, includes clinical breast examinations every six months, mammogram of the affected breast every six months, and mammogram of the unaffected breast every 12 months. In the event that the original lesion increases in size or if there is a new lesion, a biopsy will be performed. If the new findings are benign or DCIS, active surveillance will resume. If a biopsy reveals invasive ductal carcinoma, the participant will undergo therapy according to standard guidelines [5].

As screening techniques continue to improve and DCIS diagnoses increase, identifying patients who can safely omit invasive treatments will continue to be a major focus for researchers. The conclusion of these four clinical trials has the potential to drastically impact future DCIS management in such a way that may decrease overtreatment among select patient populations.

For more information about the COMET trial, please visit: https://clinicaltrials.gov/ct2/show/NCT02926911

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