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Freezing Cancer: Cryoablation Emerging as Effective Treatment for Low Risk Breast Cancers

Three-year Results of the ICE3 Trials

Abstract: Cryoablation Without Excision for Early-Stage Breast Cancer; ICE3 Trial Update on Ipsilateral Breast Tumor Recurrence

Columbia, MD, April 29, 2021—Non-surgical breast cancer cryoablation, which destroys tumor cells by exposing them to sub-freezing temperatures, is proving to be an effective alternative to surgery for small breast cancers, with low-risk features, in women over 60 years, based on the early three-year results of an ongoing IRB-approved clinical trial. The findings of the multi-center ICE3 trial—the first ever cryoablation trial that does not involve follow-up surgery—was presented at the American Society of Breast Surgeons (ASBrS) annual meeting this week.

“Cryoablation potentially represents a dramatic improvement in care for appropriate low-risk patients, and at three years post-treatment, the ICE3 trial results are extremely positive,” says Richard Fine, MD, West Cancer Center & Research Institute, lead researcher. “The non-invasive procedure is fast, painless and can be delivered under local anesthesia in a doctor’s office. Recovery time is minimal and cosmetic outcomes are excellent with little loss of breast tissue and no scarring. Now, this trial is underscoring the efficacy and safety of the procedure for this patient group.”

Dr. Fine notes that this clinical trial builds on others demonstrating that cryoablation of small, low-grade tumors is effective. The technique also is used routinely as therapy for other types of cancers.

Researchers studied 194 patients 60 years of age or older with unifocal invasive ductal cancers measuring 1.5 cm or less. Tumors were all low-grade, HR+, HER2-, consistent with a low-risk form of the disease. Women were treated with a cryoablation freeze-thaw-freeze cycle for 20 to 40 minutes. Treatment was delivered through a needle-like nitrogen-chilled probe inserted through the skin directly

into the tumor. Freezing temperatures targeted a carefully controlled area, turning the tumor into an ice ball to destroy the diseased cells. No surgical incision and related tissue damage and scarring were involved.

Along with cryoablation, at the discretion of their treating physician, 27 patients received or are receiving adjuvant radiation, 148 with endocrine therapy and one with chemotherapy. All patients were followed at six month intervals with same breast recurrence at five years after cryoablation as the primary trial outcome.

At a mean of 34.83 months from treatment, only 2.06% (4 patients) recurred. Ninety-five percent of patients and 98% of treating physicians reported satisfaction with the cosmetic results. No significant device-related adverse events were reported.

One patient had breast cancer-related positive sentinel lymph nodes at biopsy. That patient remains cancer-free at 60 months follow up.

“Increasingly, precision medicine is helping physicians characterize breast cancer with tools like genomic profiling and hormone receptor status,” Dr. Fine says. “We also are picking up cancers at an earlier stage than ever before. In recent years, healthcare has been deescalating breast cancer treatment, realizing that for some tumors, less aggressive therapies can be as effective and deliver greater patient satisfaction at a lower cost than traditional interventions. In keeping with that trend, cryoablation is a promising, high value treatment for certain forms of less aggressive cancers.”

Abstract, Official Proceedings

Cryoablation Without Excision for Early-Stage Breast Cancer; ICE3 Trial Update on Ipsilateral Breast Tumor Recurrence

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Objective: The ICE3 Trial was designed to evaluate safety and efficacy of cryoablation, allowing women age >60 with low risk, early-stage breast cancers to benefit from a non-operative treatment of their tumor and avoid the associated risks of surgery. Ipsilateral breast tumor recurrence (IBTR) at 5 years was the primary outcome.

Methods: The ICE3 trial is an IRB-approved, multi-centered, single-arm, non-randomized trial including women ≥ 60 years with unifocal, ultrasound visible invasive ductal carcinoma ≤ 1.5 cm in size, HR+, HER2-, and breast size allowing safe cryoablation. Four patients <60 years were added after IRB adjustment to the protocol. The office-based procedure performed under ultrasound guidance with local anesthesia requires 20-40 minutes, for a freeze-thaw-freeze treatment cycle, depending on lesion size. Decision to perform sentinel lymph node biopsy and the choice of appropriate adjuvant treatment was left to the discretion of the treating physician. Patients were followed at 6-month and annually to 5 years with clinical and imaging assessment, as well as patient satisfaction. The NCCN Distress Tool was administered at baseline treatment and again at 6 months. Local Failure Free Probability (FFP) was calculated with Kaplan-Meier estimates and 95% CI.

Results: Of the two hundred eleven patients screened, 5 failed screening, and an additional 9 were enrolled but ineligible by protocol. Thus 197 patients were in the intension to treat cohort, three of whom did not receive complete protocol mandated treatment. One hundred ninety-four patients meeting eligibility, received successful cryoablation treatment per protocol and are included for analysis. The mean age is 75 (55-94) and the mean tumor size is: 7.4 mm Transverse (2.8 mm-14 mm) and 8.1 mm Sagittal (8 mm-14.9 mm).

Among the protocol treated patients there were no significant device related adverse events or complications reported. Most of the adverse events reported were minor (ex: bruising, localized edema, minor skin freeze burn, rash, minor bleeding from needle insertion, minor local hematoma, skin induration, minor infection and pruritis).

Two of 15 patients who underwent sentinel lymph node biopsies had a positive sentinel node (1 with CLL and one with adenocarcinoma, consistent with breast primary and is without recurrence at 60 months follow up). Twenty-seven patients underwent adjuvant radiation, and 1 patient received chemotherapy and 148 began endocrine therapy. Over 95% of the patients and 98% of physicians reported satisfaction from the cosmetic results during the follow up visits. With a mean of 34.83

months, only 4 of the protocol treated patients have recurred (2.06% overall recurrence rate). The 36-month local FFP is 99.22% (95% CI 94.58-99.89%).

Conclusions: The ICE3 trial is the largest controlled liquid nitrogen-based cryoablation trial of early-stage, low-risk breast cancer without subsequent tumor excision. Breast cryoablation, an office-based procedure performed under local anesthesia is a promising treatment alternative to surgery and offers the benefits of a minimally invasive procedure with minimal risks. Further study within a clinical trial or registry is needed to confirm cryoablation as a viable alternative to surgical excision in the appropriately selected patients.

Table 1: Summary of clinical, imaging, and pathological data of total eligible cryo-ablated patients

<i>Patients Characteristics</i>	<i>(n=194)</i>
N = 194	
Age (years)	
Mean (range)	75 (55-94)
Median \pm SD	75.7 \pm 7
Race	
White	159 (82%)
African-American	15 (7.7%)
Hispanic or Hispanic origins	12 (6.2%)
Asian	1 (0.5%)
Not specified/ decline to answer/ unknown	5 (2.6%)
Tumor characteristics	
Histology	
Infiltrating ductal	194 (100%)
Other	0 (0%)
Nottingham tumor score (combine histologic grading)	
Low - I (3-5)	98 (51%)
Intermediate - II (6-7)	96 (49%)
High – III (8-9)	0 (0%)
Receptor status	
ER+	194 (100%)
PR+	184 (92.9%)
Her 2-*	194 (100%)
Tumor size by US (day of procedure)	
Mean (range), mm	Sagittal: 8.1 (8 -14.9) Transverse: 7.4 (2.8 -14)

<i>Patients Characteristics</i>	<i>(n=194)</i>
Median \pm SD, mm	Sagittal: 8.0 \pm 2.9 Transverse: 7. \pm 2.7
Sentinel node bx	15
Positive	2 ^[1]
Clinically LN Negative**	194 (100%)
<p>Data are expressed as n (%) unless otherwise specified. <i>SD</i>, standard deviation. <i>ER</i>, estrogen receptor, <i>PR</i>, progesterone receptor, <i>HER2</i> human epidermal growth factor receptor 2</p> <p>*Her2 was tested with IHC and if equivocal was add a FISH assay</p> <p>[1] Positives were found in biopsies performed after study enrollment 1patient with adenocarcinoma, c/w breast, 1 + with CLL (chronic lymphocytic leukemia</p> <p>**Clinical lymph node was assessed per US and clinical exam</p>	