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San Antonio Breast Cancer Symposium: New Diagnostics From Myriad, Lumicell, Agendia

by Reed Miller

Myriad Genetics, Lumicell, and Agendia were among the companies with diagnostic technologies featured in the scientific presentations at the recent San Antonio Breast Cancer Symposium. New trials show that Myriad's *EndoPredict* can help identify patients who should not have preoperative chemotherapy. New Phase II data support Lumicell's *LUM* system for guiding excision of residual tumor and preventing cancer recurrence. Agendia's *MammaPrint* test proved cost-effective in the MINDACT trial.

The 2017 San Antonio Breast Cancer Symposium featured the latest information on experimental biology, prevention, diagnosis and therapy for breast cancer for industry, academic researchers and oncologists.

The top diagnostics news from the meeting was the results of a 1,617-patient trial showing Myriad Genetics Inc's *riskScore* and *myRisk* breast cancer-risk assessment could potentially provide every patient with an individualized risk assessment. (Also see "*New Data Validates Myriad's myRisk Hereditary Breast Cancer Test, Enhanced With riskScore*" - Medtech Insight, 8 Dec, 2017.)

But the riskScore/myRisk results were only part of the good news for Myriad at the meeting, and the firm was just one of several diagnostics companies touting important new data on their technologies at the meeting, which ran Dec. 5-9 in San Antonio, Texas.

Two Studies Support EndoPredict For Predicting Response To Neoadjuvant Therapy In HR+ Breast Cancer

On Dec. 8, Peter Dubsky from the Medical University of Vienna presented results from *ABCSG-34* – a randomized, Phase II study of Merck's therapeutic cancer vaccine L-BLP25 for the preoperative treatment of women – showing that Myriad's *EndoPredict* test predicts residual cancer burden to neoadjuvant chemotherapy and to neuroendocrine therapy in hormone receptor-positive(HR+)/ human epidermal growth factor receptor 2-negative(HER2-) breast cancer patients.

A low EndoPredict score "is associated with tumor response to endocrine treatment and predicts resistance in the chemotherapy group," the study authors conclude. Preoperative chemotherapy, especially to attain breast conservation in patients who are estrogen-receptor-positive (ER+), HR+, and have a low EndoPredict score "should be reconsidered," they say.

The study analyzed biopsies from 217 women with HR+ breast cancer and assigned 134 patients of those patients to neoadjuvant chemotherapy according to aggressive clinico-pathologic tumor features, and assigned the other 83 patients to neoendocrine treatment based on their luminal A types of breast cancer.

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In the neoadjuvant chemotherapy group, 125 patients had high EndoPredict scores and nine had low EndoPredict scores; 26.4% the high-score group showed good tumor response to neoadjuvant chemotherapy, while all the patients with a low score showed a poor tumor response. In the group treated with neoendocrine therapy, 27.3% of the 44 patients with a low EndoPredict score and 7.7% of the 39 patients with a high score achieved excellent tumor response.

Also at the San Antonio meeting, Ivana Sestak of the Queen Mary University of London and collegues presented a poster on a study of EndoPredict for the prediction of distant recurrence in women diagnosed with invasive lobular carcinoma, compared to those with invasive ductal carcinoma.

The study included 928 women with ER+/HER2- breast cancer, including 141 with invasive

lobular carcinoma, 710 with invasive ductal carcinoma, and 77 with a mixed type of cancer. After a median follow up of ten years, the results of the study show that EndoPredict provides significant power for predicting distant recurrence in patients with both types of breast cancer.

Women with invasive lobular carcinoma who had a high EndoPredict score were at seven times greater risk of distant recurrence of cancer within 10 years after endocrine therapy than patients with a low EndoPredict score. In the women with invasive ductal carcinoma, the patients with a high EndoPredict score were five times more likely to have a distant recurrence within 10 years than comparable patients with a low EndoPredict score.

The distant recurrence risk in patients with a low EndoPredict score was about the same for both types, suggesting that chemotherapy is not indicated in patients with a low risk score regardless of their tumor type, Sestak et al. conclude.

Myriad launched EndoPredict in the US in March. EndoPredict is included in guidelines from the American Society of Clinical Oncology, European Society of Medical Oncology, and the St. Gallen International Breast Conference, and the Integrated Oncology Network named EndoPredict as its preferred breast cancer recurrence test. (Also see "*Device Debuts: Tryton, Myriad Genetics, Integra Lifesciences, Acelity, And Toyota*" - Medtech Insight, 17 Apr, 2017.)

Lumicell's LUM System On Track For 2019 Launch

Researchers from Massachusetts General Hospital in Boston presented results from the *Phase A-B study* of *Lumicell Inc.*'s *LUM* Imaging System, which assesses *in vivo* lumpectomy cavity walls – rather than excised tissue samples – to guide accurate excision of residual tumor and prevent cancer recurrence.

In the study, led by Barbara Lynn Smith of MGH, the lumpectomy cavity walls of 60 patients undergoing lumpectomy for invasive breast cancer or ductal carcinoma *in situ* were assessed intraoperatively with the LUM Imaging System, which includes Lumicell's proprietary *LUM015* cathepsin-activatable fluorescent optical contrast agent that is cancer- and immuno-activated, a unique handheld imaging device, and proprietary decision software.

The investigators used imaging devices to create digital images of the fluorescence generated at potential sites of residual tumor in lumpectomy cavities. Surgeons then excised the tissue defined by the images and examined the excised tissue with histopathology.

In a Phase A-B trial, Lumicell's LUM Imaging System showed 100% sensitivity and 73% specificity for detection of tumors less than 2 mm from the margin, and could identify invasive ductal cancer, invasive lobular cancer and areas of ductal carcinoma in situ 1 mm.

The mean diameter of tumors treated in the study was 1.2 cm; 71% of the cancers were invasive cancers and 29% were ductal carcinoma *in situ*, the earliest form of breast cancer. The test set included 569 cavity margin surfaces assessed intraoperatively and excised, and the image acquisition for each margin took about one second.

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Eight patients showed positive margins on standard histopathology analysis, and the LUM system correctly identified all positive margins that were identified by standard histopathology and then correctly predicted the negative results of re-excisions in two of the eight patients. There were no serious adverse events.

"What this does is enable improved surgical outcomes by making sure the patients don't have to undergo a second surgery, and that reduces the potential for metastatic disease progress," Lumicell CEO Kelly Londy told *Medtech Insight*. "It reduces health-care costs by minimizing the need for repeat surgery." About 30% of breast lumpectomy patients must undergo a second surgery to remove cancerous tissue that was missed the first time. Those second surgeries – about 70,000 in the US annually – costs the US health-care system about a billion dollars a year, while taking up hospital resources that could be used to treat more patients, she said.

The company is cosponsoring a *Phase C trial* with the National Institutes of Health. That trial, planned for 165 patients, will be completed by late summer 2018, in time for the company to complete regulatory submissions and launch the LUM system commercially in 2019. US FDA is reviewing LUM as a combination product – the imaging device and decision software are devices, but LUM015 is regulated as a drug.

The company is also developing the LUM system to treat prostate, colorectal, esophageal and

pancreatic cancers, Londy said.

"We think it will have wide ability to detect a variety of cancers because of the activation mode of [LUM015]," she explained. "Unlike chemotherapy, which attacks all the cells, ours is different in that it's a protease, so the cancer cells reach out and grab it and pull it in, and when it does that the molecule cleaves and fluoresces. So only the cells around the tumor glow, not all the cells."

The company recently closed a series C round of fundraising worth $27.7m, which will take it through the FDA submission for the breast cancer indication while allowing it to continue funding research and development of the system for other indications. The company is "exploring options" for funding to take it beyond that point and into commercialization of the LUM system, Londy said. (Also see "*Start-Up Spotlight: Lumicell, Shining The Light On Real-Time, Intraoperative Tumor Detection*" - Medtech Insight, 18 Oct, 2017.)

New Data Support Cost-Effectiveness Of Agendia's MammaPrint Cancer Risk Test

Agendia BV's *MammaPrint* 70-gene breast cancer risk-of-recurrence is a cost-effective test for the pre-selection of patients for the I-SPY 2 trial of drugs to treat breast cancer and adds to the limited evidence available for younger patients with breast cancer, according to new clinical trial data presented at the San Antonio Breast Cancer Symposium.

FDA has defined 'pathological complete response ' and accepted it as a surrogate endpoint for accelerated approval of targeted agents, in combination with chemotherapy based on long-term outcomes. The results of I-SPY 2, a Phase II trial intended to shorten the time required to collect drug-efficacy data, support the inclusion of pathological complete response as a primary endpoint in future clinical trials of neoadjuvant, and personalize adaptive novel agents for breast cancer.

Among stage 2/3 breast cancer patients who are hormone receptor positive and human epidermal growth factor receptor 2 negative, the study only enrolled patients whose MammaPrint tests showed them to be at high risk for early recurrence. So far, more than 1,200 patients have been randomized to one of 14 drugs in the trial. (Also see "*Merck's Keytruda Offers Hope And Risk In Early Breast Cancer*" - Scrip, 6 Jun, 2017.)

Douglas Yee of the University of Minnesota presented the first long-term survival results from the I-SPY 2 trial for patients preselected with the MammaPrint system at the San Antonio meeting on Dec. 7. The results demonstrate that achieving pathological complete response is a very strong surrogate endpoint for improved event-free survival and distant disease-free survival in the high-risk population as identified by MammaPrint, Yee and colleagues concluded.

Results of the *MINDACT* trial, published in 2016, showed the addition of MammaPrint to the traditional clinical and pathological risk factors for breast cancer recurrence can help determine

which patients benefit from adjuvant chemotherapy and can help patients who will not benefit from chemotherapy avoid its toxic side-effects. (Also see "*Agendia Touts ASCO Guideline's Endorsement Of MammaPrint Breast Cancer Test*" - Medtech Insight, 24 Jul, 2017.)

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A new cost-effectiveness study derived from the MINDACT trial, led by Valesca Retel of the Netherlands Cancer Institute, presented as a poster at the San Antonio meeting, shows that MammaPrint is cost-effective compared to traditional clinical risk assessment of early-stage breast cancer.

The study evaluated prospective survival data from MINDACT and US insurance claim data to demonstrate that adding MammaPrint to clinical risk assessment is highly cost-effective compared to clinical risk assessment alone. When the cost of chemotherapy and its consequences exceeds $30,000, MammaPrint is a cost-effective test in all early-stage breast cancer patients. If the costs are below $30,000, MammaPrint is only cost-effective for patients with high clinical risk, Retel et al. conclude.

There are about 250,000 new breast cancer patients every year in the US, so a cost savings of $3,342 per patient would save the system $836m, according to Agendia. The MINDACT results represent level 1A evidence to support the clinical utility of MammaPrint, and these cost-effectiveness data will support reimbursement, according to the company.

In another poster presented at the San Antonio meeting, Kim Aalders of the European Organization for Research and Treatment of Cancer and colleagues presented an analysis of MINDACT showing that MammaPrint classified 48% of the 1,100 patients under age 45 as high-risk based on genomics, while clinical risk-assessment alone identified 61% of these patients as high-risk.

The women deemed to be low-risk based on MammaPrint results had a five-year distant metastasis-free survival rate between 95%-98%. These clinically relevant results add important additional data to limited available evidence on genomic expression in young early-stage breast cancer patients. "Performing the 70-gene signature provides additional information concerning

the prognosis of young early-stage breast-cancer patients categorized as clinical high risk," the authors conclude. "The results add important new data to the limited available evidence on genomic expression in young breast cancer patients."

From the editors of Clinica