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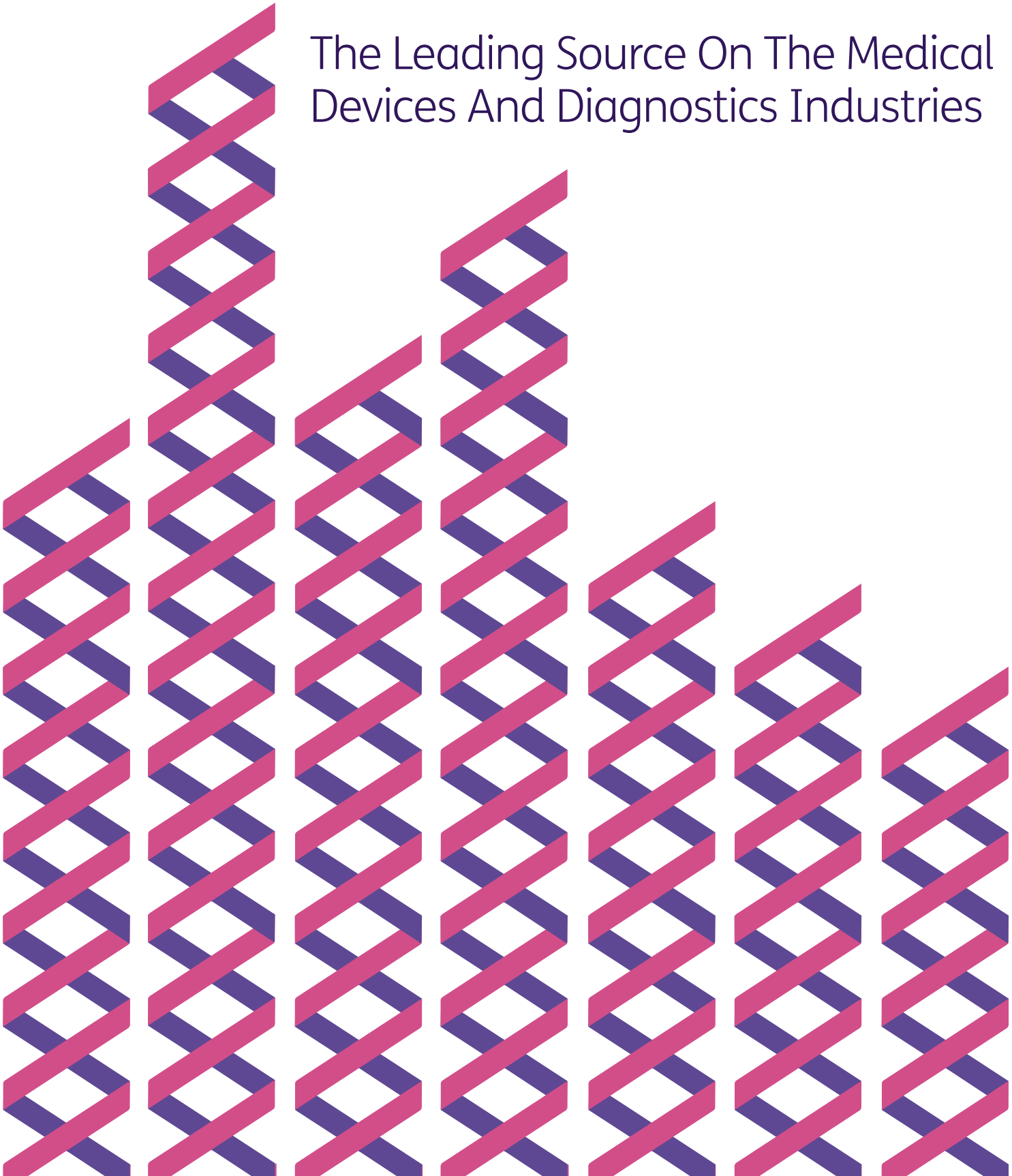

Chronix's new liquid biopsy approach show promise as early predictor of cancer therapies

By Tina Tan, 18 April 2016

A blood-based test which looks at chromosomal gains and losses in cell-free DNA (cfDNA) has demonstrated its potential of being a predictor of how well cancer patients are responding to chemotherapy.

The developer of the Delta Dots test, Chronix Biomedical, is presenting its findings from a blinded proof-of-concept study today at the annual meeting of the American Association for Cancer Research (AACR) currently being held in New Orleans, Louisiana (April 16-20).

Unlike conventional cancer molecular diagnostics, which seek to detect single mutations or rearrangements in the gene, Chronix's technology takes a more holistic approach by calculating what it calls the genomic "copy number instability index (CNI)" of the cfDNA. CEO Howard Urnovitz explained: "The way we got to this point was we took 1,000 samples – half cancer, half matched controls. We sequenced everything and then asked the computer, where's the difference? To our surprise, the difference wasn't at the level of SNPs (single nucleotide polymorphisms) - it was in areas on the genome that had gains or losses [of chromosomal regions] – in other words, when one area has more or fewer DNA fragments compared to the same area in the matched controls." These gains and losses are representative of genomic instability caused by bad DNA repair, which in turn is indicative of cancer. "That's the basis of the CNI score – it measures the mathematical and statistical difference in fragment on each spot on the genome."

In the 24-patient study presented at AACR, the performance of the CNI in assessing chemotherapy outcomes was compared against the industry standard for measuring treatment response, RECIST 1.1 (RECIST, Response Evaluation Criteria in Solid Tumors, was recorded using diagnostic imaging). It also assessed CNI's effectiveness in monitoring therapy in five tumor types – advanced esophageal cancer, colorectal cancer, non-Hodgkin lymphoma, pancreatic ductal adenocarcinomas and non-small cell lung cancer. The findings showed that CNI analysis correctly stratified patients as either responders or non-responders to chemotherapy in 92% (22 of 24 patients) of cases compared to RECIST.

Moreover, the study found that for at least 15 patients, CNI change predicted response to the chemotherapy around 3-8 weeks prior to scan response. The study investigators concluded that "CNI change may serve as predictor, potentially an early predictor, of therapeutic chemotherapy to the investigated cancer types."

The Delta Dots test is also being studied for two other types of cancer therapy: immunotherapy and radiotherapy. "The implications of this test are enormous," said Urnovitz. "A lot of chemotherapy is still being used in cancer patients; imagine being able to tell a patient after one cycle that the chemotherapy is not working, then they won't have to go through five more cycles of toxic drugs that could be worse for them. So you can keep using our monitoring test to see how the patient is responding to the therapy until you hit on the right therapy that works.

"With immunotherapy, that has a double impact," continued Urnovitz. Not only could it save the patient from having to continue a toxic therapy that isn't working, with immunotherapy there is also the cost factor as these class of drugs are extremely expensive. "If you are able to tell after the first cycle that it isn't working, it can bring significant savings to the healthcare payor."

Chronix wil be presenting its findings of the Delta Dots/immunotherapy study at the American Society of Clinical Oncology meeting in Chicago in June. The company next plans are to initiate clinical studies to validate the clinical utility of the test and gain reimbursement worldwide.

Second Opinion

Aside from Delta Dots, Chronix also offers the Second Opinion supplemental screening tests for breast and prostate cancer.

Second Opinion is designed not as a replacement for PSA tests or mammograms, but as an additional screening tool in which the CNI score can help guide doctors' decision-making.

Urnovitz outlined how the Second Opinion and Delta Dots could work hand in hand: "There are three potential scenarios when you get the result from Second Opinion. If the CNI score is low and, say, the mammogram is considered low-suspicion, that first scenario is for the doctor to look at the patient again in one year. The second scenario is if the CNI score is in the suspiciously high range, the doctor may say 'we'll look in 3-6 months'. If the CNI score is statistically above the threshold, you would send the patient to biopsy. Then if the biopsy confirms that it is cancer and the patient goes into treatment, that's when you go into this response monitoring area with the Delta Dots to see if the treatment works."

The company is starting to ramp up commercialization of these tests; it has just signed on a distributor for UK and Ireland this month and already has a partner, Amedes, to server the German-speaking countries. "Amedes is a large clinical lab services provider and its business model is to bring disruptive technologies that will make a great impact on patient care and to bring them first to the private payer market and then work towards healthcare reimbursement," Urnovitz told *Clinica*. "Our next model is the US and we are in discussions with groups that have CLIA labs so that we can sell it through their labs there."

"It's the same CNI test each time, with Second Opinion and Delta Dots. We're just simply tracking fingerprints... The data are the data – if you have a spot on chromosome 1 and it's a gain and you fail therapy, it'll still be there. You're always tracking the dynamics of the tumor change, that's the beauty of doing the whole genome sequencing. You are not giving bias in the genes you want to select for, but you allow the patient to tell you what's going on in their unique situation."

One Test To Rule Them All?

Chronix believes that its unique CNI approach to detecting cancer means it can offer a single test to see if asymptomatic patients have cancer.

"It's simple. If you have gains or losses in your blood, you have cancer somewhere," said Urnovitz. The first version of this "pan-cancer test" will be to detect genomic instability in their blood and it would be offered to people who have hereditary cancer mutations. "You find your family does have BRCA genes or EGFR or one of the hereditary panels and people are asking: if I've got the risk, I'd like to know if there are gains or losses in my blood. This would be a risk in real-time test."

The second version of the pan-cancer test would be able to specify which cancer it is and Urnovitz estimates this would take the company 2-4 years of clinical studies to develop and validate. "We want to do the top 17 cancers that have the highest economic and health implications. If we do 500 patients of each of those, and then match controls, we'll get a 10,000 - to 12,000-patient study where the end game is you take the blood out, we would show firstly, whether you have gains and losses and, secondly, the statistical probability of which cancer it is." This second version of the test would require US FDA approval.

When asked if this pan-cancer test would be cheap enough for widespread use as a screening tool, Urnovitz maintained that the savings made in cancer care when the disease is caught early would justify the costs.

"In the US, you're looking at $120bn a year being spent on care of cancer patients. If you could screen people for the earliest stages of cancer and bend the arc towards more success stories you are bringing down tens of billions of dollars of cancer care that you don't need to administer because you caught it early."