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NewLink's Phase II NSCLC Data Another Immunotherapy Boost

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While last year's American Society of Clinical Oncology (ASCO) meeting ended on cautiously encouraging advances in the cancer immunotherapy space, this year's meeting has put immunotherapy front and center, thanks in part to much-awaited data on and anti-PDL-1 and anti-PD-1 drugs from Roche AG and Bristol-Myers Squibb Co., respectively. (See *BioWorld Today*, June 6, 2012.)

Those drugs, both check point inhibitors, generated significant buzz going into the ASCO meeting in Chicago. Between that news, last year's approval of BMS' Yervoy (ipilimumab) and up-and-coming late-stage players, immunotherapy looks like it has finally shaken off the failures of several years ago. (See *BioWorld Today*, May 16, 2013.)

"It's taken a long time, but it's finally arrived," said Charles Link, chairman and CEO of NewLink Genetics Corp. "It's encouraging for those of us who have been working in the field for 10 or 15 years."

The success of ipilimumab "clearly showed that if you got the right immune response, you can have a very effective treatment," he added. Best of all, that response appears to be long-lived, which might prove immunotherapy's most effective trick against cancer.

NewLink presented data Saturday from a trial testing tergenpumatucel-L, a candidate emerging from the firm's HyperAcute immunotherapy platform, as a single-agent in 28 previously treated – second-line and third-line – patients with metastatic or recurrent non-small-cell lung cancer (NSCLC). Results showed that the immunotherapy produced long-term stable disease (16 weeks or longer) in eight patients, including one who survived 50 months. Median overall survival was 11.3 months.

Industry experts usually ask whether there is "evidence that an immune response correlated with the survival data seen in the Phase II [trial], and the answer is yes," Link told *BioWorld Today*, with company confirming clear immune responses in patients who showed survival benefits.

Patients who did not generate responses – often because their bone marrow had been too severely damaged by prior rounds of chemotherapy – showed no survival benefit. That lesson was important for NewLink as the firm designed its ongoing Phase IIb/III study in NSCLC with specific enrollment criteria. For example, only second-line patients can enroll, and they must have lymphocyte counts exceeding 1,000.

"We need patients with their immune systems intact to have an effect," Link explained.

The Phase II study presented at ASCO also was designed to test what kind of effect tergenpumatucel-L had in patients receiving subsequent rounds of chemotherapy, specifically whether it was able to enhance the effect of chemo. And the results showed that it did. Sixteen patients were given salvage chemo post tergenpumatucel-L treatment and progression and, in those subjects, the overall response rate was 31 percent (five of 16) and stable disease was 25 percent (four of 16).

"So there's not just a survival benefit," Link said. "There's an interplay between immunotherapy and chemotherapy."

The ongoing Phase IIb/III trial in NSCLC is designed to compare tergenpumatucel-L to docetaxel in previously treated patients, with a primary endpoint of overall survival. But the firm also set a pre-defined third-line treatment, with patients receiving Alimta (pemetrexed, Eli Lilly and Co.) or Gemzar (gemcitabine) as salvage chemo after tergenpumatucel-L treatment to measure chemosensitization.

NewLink is conducting the study under an adaptive design, so that, depending on initial results, the firm can adjust the trial to include hundreds of additional patients, "hopefully in agreement with the FDA," Link said.

Founded in 1999, Ames, Iowa-based NewLink stayed mostly under the radar for its first decade, emerging from stealth in 2010 with the launch of a large, Phase III trial of lead immunotherapy, HyperAcute-Pancreas (algenpantucel-L). That trial, which is being conducted under a special protocol assessment and set to enroll up to 722 patients, is designed to test the immunotherapy

in combination with chemotherapy in pancreatic cancer patients who have undergone surgical resection. The aim is to prevent or delay the recurrence of the tumor after resection, with the specific goal of increasing median survival by 22 percent. (See *BioWorld Today*, May 28, 2010.)

Like other immunotherapies in development, NewLink's technology is designed to work by stimulating the immune system, directing it to recognize and attack cancer cells. But what sets the HyperAcute approach apart is its ability to stimulate not only antibody production and T cells, but also eosinophils, a type of immune system cell normally recruited to attack parasitic infections. NewLink has pointed to similarities between cancer and parasite-infected cells, both of which have tolerance-inducing antigens.

The company's candidates contain engineered human cancer cell lines containing alpha-galactosyl, a carbohydrate for which humans have pre-existing immunity.

Today at ASCO, the firm is slated to present additional data, including Phase II results of algenpantucel-L in combination with standard-of-care adjuvant therapy (gemcitabine and 5-FU-modulated radiation therapy) in resected pancreatic cancer.

Data also are expected from Phase I studies testing indoximod, an IDO (indoleamine-(2,3)-dioxygenase) pathway inhibitor.

The small-molecule compound currently is in Phase II testing in metastatic breast cancer. Like antibodies targeting PD-1 or CTLA-4 (BMS' nivolumumab and ipilimumab, respectively), indoximod is a check point inhibitor, meaning it's designed for local immune suppression in the tumor.

But IDO inhibitors are a brand new class. "We're pretty excited about it," Link said of indoximod. "We're getting a lot of interest from big pharma." ■