Siamab's Antibody-drug Conjugates for Ovarian Cancer Seen to Succeed in Animal Models

ovariancancernewstoday.com/2017/11/06/siamab-antibody-drug-conjugates-for-ovarian-cancer-seen-to-succeed-in-animal-models/

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11/6/2017

Siamab Therapeutics' preclinical work with anti-STn antibody-drug conjugates is moving forward, and in animal models — including primates — it showed the conjugates could safely and effectively treat ovarian cancer resistant to chemotherapy.

The treatment blocked tumor progression in all models tested, in which scientists injected patient-derived or lab-grown ovarian cancer cells into mice. Researchers underscored that they observed complete tumor eradication in some treatment groups.

The research team, working with colleagues at Harvard Medical School, presented study updates at the 2017 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Philadelphia two weeks ago.

Their poster, "Humanized anti-Sialyl-Tn monoclonal antibody-drug conjugates inhibit tumor growth in vitro and in vivo," also showed that the levels of STn in these tumors were lowered, indicating that the drugs were specific to their targets.

"Our lead ST1 program shows compelling efficacy and safety across a range of PDX [patient-derived xenograft — a xenograft is transplant of tissue between species] and xenograft studies, underscoring the promise of our anti-STn antibody approach to treating chemoresistant solid tumors," Jeff Behrens, president and chief executive officer of Siamab, said in a press release.

In addition to the efficacy studies, Siamab also tested the safety of the anti-STn antibody-drug conjugates in monkeys. Results showed no organ changes or abnormalities in the function of organs, including the liver and

kidneys. The study, which also explored how the drug behaves in the body, only tested two treatment doses and was considered a pilot study for larger evaluations.

STn or Sialyl-Tn is a tumor marker linked to tumor metastasis, a poor prognosis, and reduced overall survival. In addition to ovarian cancer, the factor is found on the surface of other solid tumors, including prostate, pancreatic, gastric, and colon cancer.

Researchers believe STn is involved in resistance to chemotherapy. It is rarely seen in healthy tissues, but increases in cancerous tissue after chemotherapy.

Siamab's approach is to develop antibodies that bind to STn, and carry with them an anticancer drug. In this way, the anticancer drug becomes concentrated at the tumor site, allowing for fewer treatment side effects.

"The new data from a pilot pharmacokinetic/toxicity study in primates demonstrate the favorable safety and tolerability of ST1 in large animals," said Behrens, who called the monkey data extremely encouraging.

These results will now allow the company to launch the risk and toxicity studies — which Siamab plan to initiate in 2018 — needed to test the treatment in human patients.