Center for Cancer Research

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U.S. Department of Health
and Human Services
Public Health Service
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TRIAL TITLE

The National Cancer Institute opens "A Randomized, Double-Blind, Phase 2 Trial of GI-6301 (Yeast-Brachyury Vaccine) Versus Placebo in Combination with Standard of Care Definitive Radiotherapy in Locally Advanced, Unresectable, Chordoma"

TRIAL SUMMARY

Researchers at the National Cancer Institute (NCI) are now enrolling patients in a phase 2 clinical trial to determine whether the yeast-brachyury vaccine GI-6301 improves the effectiveness of radiation for patients with localized chordoma. Chordoma patients with inoperable or residual tumor who do not have metastases and are planning to be treated with radiation are eligible to participate. Patients will initially be randomized to receive radiation plus the vaccine or radiation plus a blinded placebo. Those randomized to receive radiation plus placebo will have the option to receive vaccine if their tumor grows while on the study. The study will compare the outcomes of patients treated with radiation with and without the vaccine to determine whether the vaccine can increase the chances of shrinking the tumor and/or preventing further tumor growth.

WHY THIS TRIAL IS BEING DONE

The primary treatment options for chordoma currently consist of surgery and high dose radiation. Radiation has been shown to improve patient outcomes following surgery. Radiation is also sometimes used instead of surgery when surgery would carry unacceptable risks.

The chance of tumor growth after radiation is significantly higher for patients who have residual tumor than for those whose tumor is completely removed. Unfortunately for patients with a tumor that cannot be completely removed, there tends to be a short time until the tumor grows back and eventually causes death. For this reason, our team at the NCI seeks to identify a therapy that can reduce the risk of recurrence and improve survival after radiation for patients who have residual tumor.

One approach we are pursuing is treating patients with a therapeutic vaccine that is intended to stimulate the immune system to fight cancer cells that express the brachyury protein. Brachyury is present at very high levels in nearly all chordomas but is not present in the vast majority of normal tissues, making it a promising target for immune therapy. Research in other cancers suggests that radiation in combination with immune therapy can provide powerful antitumor effects.

We have recently completed a phase 1 clinical trial of a therapeutic vaccine targeting brachyury called GI-6301 in which 11 chordoma patients participated. Through that phase I trial, we learned that this vaccine can be given safely without serious adverse

reactions. In that study, the vaccine was also capable of inducing immune responses against brachyury and one patient had his tumor shrink more than 30% while on study. Some other patients (7 of 10 evaluable) also had stable disease for more than 5 months while on study. However, these clinical findings are not definitive and further clinical testing is required to determine the benefit of this vaccine in chordoma. To that end, we have designed a larger phase 2 clinical trial intended to determine if this vaccine, when given in combination with radiation, improves outcomes for patients with chordoma compared to those who only have radiation.

WHO CAN PARTICIPATE

We have designed this trial for patients who have residual tumor remaining after surgery, who are unable to have surgery, or who have a local recurrence following previous treatment.

To be eligible for enrollment on this study, patients must:

- Have a confirmed diagnosis of chordoma
- Have only localized tumor (no metastases)
- Be able to receive radiation to their localized tumor
- Be willing to travel to Bethesda, MD for treatment and follow-up visits

HOW THE TRIAL WILL WORK

The trial is taking place at the National Institutes of Health Clinical Center in Bethesda, MD. The NCI will pay for transportation costs (including airfare) and a portion of lodging costs for patients after enrollment in this study.

The process of participating in the trial is as follows:

- Patients travel to NIH to receive injections of the vaccine (or placebo) every other week for three doses prior to starting radiation (approximately 4 weeks)
- Patients then complete their radiation treatment with their home radiation oncologist (typically over a 1-2 month timespan)
- Following completion of radiation treatment plan, patients travel back to NIH to resume vaccine (or placebo) injections every 2 weeks until 6 total doses have been given (3 doses after radiation, another 4 weeks)
- At that point, doses spread out to every 4 weeks for 4 doses, and then 1 dose every 3 months until disease progression.
- Between all doses of vaccine, patients may return home and travel back for the next visit. There is no requirement to stay locally in Bethesda at any point in the study outside of clinic visits and dosing days.
- Repeat imaging studies will be performed about 3 months after completion of radiation and then every 3 months for the first year, every 6 months for the second year, and yearly thereafter. Scans can be done earlier if new symptoms develop in the interim between scheduled scans.

HOW TO ENROLL

If you are interested in learning more about the possibility of enrolling in this study, please contact The NCI Patient Referral Office at 866-611-6310 or Cynthia Boyle at cynthia.boyle@nih.gov. You may also contact the principal investigator of this study, Christopher Heery, M.D., directly or through your physician at heerycr@mail.nih.gov.

ABOUT THE VACCINE

GI-6301 is a therapeutic vaccine being developed through a Collaborative Research and Development Agreement (CRADA) between the National Cancer Institute and the biopharmaceutical company, GlobeImmune. Designed to stimulate the human immune system to fight cancer. GI-6301 is composed of heat-inactivated *S. cerevisiae* yeast that expresses human brachyury protein. This product candidate is the fifth of a novel class of yeast-based immunotherapeutics designed to stimulate immune responses to eliminate diseased cells. Spanning cancer and infectious diseases, these products have been evaluated in 10 different Phase 1 and Phase 2 clinical trials. They have shown a good tolerability profile in clinical programs to date. Over 600 subjects have been treated thus far, including some who have received monthly dosing for over 5 years. Expected adverse events from these products are limited to redness, swelling and tenderness at the injection site, and mild, brief flu-like symptoms.

For eligibility criteria and more information about this trial visit:

https://clinicaltrials.gov/ct2/show/NCT02383498