What Cancer Patients Need to Know About Enrolling in The BioEclipse CRX100 Clinical Trial

Additional information about this study and general information about participating in clinical trials can be found at ClinicalTrials.gov.

This is a Phase 1 trial to evaluate the safety and tolerability of CRX100 in participants 18 years or older with advanced solid tumors that do not respond to standard of care. This trial will also investigate the effect CRX100 has on participant's tumor progression and overall immune response.

CRX100 Clinical Trial Overview

- **Phase 1 of this clinical trial opens in Fall of 2020 and will enroll up to 24 participants with the following tumor types:**
  - Colorectal
  - Epithelial Ovarian Cancer
  - Gastric Cancer
  - Hepatocellular Carcinoma
  - Osteosarcoma
  - Triple Negative Breast Cancer

- **Clinical Trial Identification Information**
  - **Formal Trial Title:** A Phase 1, Open-Label, Dose-Escalation Study of CRX100 in Patients With Advanced Solid Tumors
  - **Clinical Trials Identifier:** NCT04282044
  - **Other Study ID Number(s):** CRX100-001
  - **Sponsor:** BioEclipse Therapeutics

About Your Clinical Trial Sponsor

The mission of BioEclipse Therapeutics is to develop a new generation of therapies. Patients diagnosed with advanced solid tumors, that are resistant to standard of care, urgently require new treatment options. Our goal is to address this unmet need by providing multi-mechanistic therapies aimed at eradicating tumors.

About CRX100

This clinical trial is testing CRX100, a combined immunotherapy designed to target and kill cancer cells throughout the body while triggering an immune response that may prevent relapse. The two agents of CRX100, the immune (CIK) cells and virus, have been tested in clinical trials separately as stand-alone cancer treatments. Based on preclinical animal model results, combining CIK cells and virus has the potential to become a viable treatment option. Preclinical animal studies demonstrated that CRX100 migrates to the tumor site, targets tumors cells and delivers the cancer destroying virus while healthy cells are not targeted.

Frequently Asked Questions

Q: How do I enroll in this trial?
A: BioEclipse is the trial sponsor, but the individual trial sites will manage patient recruitment and enrollment based upon established inclusion criteria. Complete information about these criteria can be found on the FDA website, ClinicalTrials.gov.

Q: Is there a chance I will receive a placebo?
A: No, this is an open label dose-escalation trial which means there is no placebo arm in the trial. This trial tests our therapy at different doses.

Q: What is the purpose of a Phase 1 clinical trial?
A: A Phase 1 clinical trial is primarily intended to establish safety, tolerability and dosing parameters, though early efficacy can be a secondary endpoint. Even though a drug has been cleared by the FDA to advance into clinical trials, there is no guarantee that it will work in humans. It is important to know that efficacy can only be established when a trial is statistically significant in size.

Q: How many patients are being enrolled in the Phase 1 trial?
A: Generally, a Phase 1 clinical trial will enroll anywhere from 10-30 patients. It is the first time a drug candidate is administered in humans with the primary purpose being to establish that the treatment is safe and to look at potential side effects that patients may experience when taking the drug. We also need to evaluate how much drug we can safely administer, known as a dose-range assessment. Establishing these initial parameters does not require a large number of patients, so a Phase 1 trial is usually limited to a small group of participants.

Q: When will patient enrollment begin?
A: Fall 2020. BioEclipse will issue a press release to announce when enrollment begins and will place that press release on the news tab on our website. Also check ClinicalTrials.gov.

Q: When is the trial expected to be completed?
A: Trial completion is highly dependent on how long it will take to enroll patients. This trial will enroll 24 patients and the active time for each participant is six months after dosing with up to two infusions of CRX100.

Q: What are adverse events and dose limiting toxicities?
A: An adverse event (AE) is any harmful medical occurrence in a clinical trial participant whether or not the medical occurrence is related to treatment with the product. A dose limiting toxicity is a side effect that is so severe it prevents the administration of that drug at a given dose or higher. This is a critical parameter to establish, especially in the treatment of cancers that frequently require high dosing levels to maximize efficacy. The evolving safety profile of CRX100 will be closely monitored by the participating physicians and BioEclipse Therapeutics.

Q: Where can I find more information about the trial?
A: For more information about the trial design and protocols visit ClinicalTrials.gov.

Scientific References

1. Jiang JT, Shen YP, Wu CP, et al. Increasing the frequency of CIK cells adoptive immunotherapy may decrease risk of death in gastric cancer patients. *World J Gastroenterol*. 2010;16(48):6155-6162. doi:10.3748/wjg.v16.i48.6155 [PubMed]

2. Bartlett, D. A Phase I Dose-escalation Trial of vvDD-CDSR (Double-deleted Vaccinia Virus Plus CD/ SMR) Administered by Intratumoral Injection or Intravenous Injection. Available from: https://clinicaltrials.gov/ct2/show/NCT00574977. NCT Identifier: NCT00574977 Last Update: December 25, 2015 [ClinicalTrials.gov]

3. Chalikonda S, Kivlen MH, O'Malley ME, et al. Oncolytic virotherapy for ovarian carcinomatous is using a replication-selective vaccinia virus armed with a yeast cytosine deaminase gene. *Cancer Gene Ther*. 2008;15(2):115-125. doi:10.1038/sj.cgt.7701110 [PubMed]

4. Contag CH, Sikorski R, Negrin RS, et al. Definition of an enhanced immune cell therapy in mice that can target stem-like lymphoma cells. *Cancer Res*. 2010;70(23):9837-9845. doi:10.1158/0008-5472.CAN-10-2650 [ResearchGate]

5. Downs-Canner S, Guo ZS, Ravindranathan R, et al. Phase 1 Study of Intravenous Oncolytic Poxvirus (vvDD) in Patients With Advanced Solid Cancers. *Mol Ther*. 2016;24(8):1492-1501. doi:10.1038/mt.2016.101 [PubMed]

6. Laport GG, Sheehan K, Baker J, et al. Adoptive immunotherapy with cytokine-induced killer cells for patients with relapsed hematologic malignancies after allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2011;17(11):1679-1687. doi:10.1016/j.bbmt.2011.05.012 [PubMed]

7. Leemhuis T, Wells S, Scheffold C, Edinger M, Negrin RS. A phase I trial of autologous cytokine-induced killer cells for the treatment of relapsed Hodgkin disease and non-Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2005;11(3):181-187. doi:10.1016/j.bbmt.2004.11.019 [PubMed]

8. McCart JA, Ward JM, Lee J, et al. Systemic cancer therapy with a tumor-selective vaccinia virus mutant lacking thymidine kinase and vaccinia growth factor genes. *Cancer Res*. 2001;61(24):8751-8757 [PubMed]

9. Nishimura R, Baker J, Beilhack A, et al. In vivo trafficking and survival of cytokine-induced killer cells resulting in minimal GVHD with retention of antitumor activity. *Blood*. 2008;112(6):2563-2574. doi:10.1182/blood-2007-06-092817 [PubMed]

10. Sampath P, Li J, Hou W, Chen H, Bartlett DL, Thorne SH. Crosstalk between immune cell and oncolytic vaccinia therapy enhances tumor trafficking and antitumor effects. *Mol Ther*. 2013;21(3):620-628. doi:10.1038/mt.2012.257 [PubMed]

11. Schmeel LC, Schmeel FC, Coch C, Schmidt-Wolf IG. Cytokine-induced killer (CIK) cells in cancer immunotherapy: report of the international registry on CIK cells (IRCC). *J Cancer Res Clin Oncol*. 2015;141(5):839-849. doi:10.1007/s00432-014-1864-3 [PubMed]

12. Thorne SH, Liang W, Sampath P, et al. Targeting localized immune suppression within the tumor through repeat cycles of immune cell-oncolytic virus combination therapy. *Mol Ther*. 2010;18(9):1698-1705. doi:10.1038/mt.2010.140 [PubMed]

13. Thorne SH, Negrin RS, Contag CH. Synergistic antitumor effects of immune cell-viral biotherapy. *Science*. 2006;311(5768):1780-1784. doi:10.1126/science.1121411 [PubMed]