CLINICAL STUDY PROTOCOL SUMMARY

Protocol Title: A PROSPECTIVE TRIAL OF IMMUNOTHERAPY AND STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR THE TREATMENT OF METASTATIC LUNG CANCER: SBRT SENSITIZATION OF THE PROGRAMMED DEATH-1 (PD-1) EFFECT

Metastatic lung cancer continues to carry a dire prognosis despite advances in systemic therapy. A subset of patients with metastatic lung cancer with 5 or fewer metastatic foci may have long term survival with aggressive treatment. The advent of immunotherapy in the last few years has expanded systemic therapy for metastatic lung cancer with greater efficacy and reduced toxicity compared to conventional systemic chemotherapy.

This study seeks to combine immunotherapy which has shown to be superior to chemotherapy in metastatic lung cancer with stereotactic body radiation therapy (SBRT). In has been demonstrated in small studies that SBRT can work in concert with immunotherapy to induce robust immune response and increased anti-cancer effectiveness. Data regarding the safety and efficacy of combined SBRT to multiple lesions with sequential immunotherapy is limited. There is no compelling evidence that toxicity is increased when SBRT is delivered prior to immunotherapy in the treatment of metastatic lung cancer.

Immunotherapy will be delivered and supervised per standard of care by the treating medical oncologist. Risks and side effects associated with immunotherapy are known and will be discussed in standard fashion by the treating physician. In this study, radiation therapy delivery is being investigated and immunotherapy is considered standard of care.

This study is designed as a combined Pilot/Phase II study. It is not clear if combined SBRT and immunotherapy to the lung will to increased lung side effects. The pilot phase of the study will evaluate the first 20 patients in real time for increased lung side effects within the first 15 weeks of treatment. If no additional lung side effects are noted (grade 3 pneumonitis >5%), lung radiation will be allowed for the remainder of the study. Study treatments include standard of immunotherapy and SBRT to the lung and metastatic sites. The interim evaluation will also assess any increased toxicity to areas and adjacent tissues treated with SBRT.

Radiation therapy dosing will be similar to the ongoing NRG BR001 trial for oligometastic cancer. The dosing guidelines are not proprietary and are published dose guidelines. Using similar dosing will allow direct comparison for a similar treatment setting where immunotherapy is not being used. We expect to see improvements in PFS and perhaps OS due to increased antigen presentation to the immune system.

The potential benefits to study participants could be significant. If SBRT enhances immunotherapy response for metastatic lung cancer there could be a slowing of cancer spread or patients could live longer. The most significant risk for participants is potential increase in side effects when both treatments are combined. These risks will be minimized by rigorous radiation therapy planning and adherence to safety guidelines and limits. Outside review will be performed to ensure compliance.

Participants will be monitored 4 weeks after treatment and every 3 months for development of side effects.

The study will last for 2 years and participants will be followed for at least 24 months from the conclusion of treatment. Patients may withdraw from the study at any time. Clinical care and routine follow-up will continue in this scenario but patient data will no longer be collected for study purposes.

Participants will not be reimbursed for participation, treatment costs and or injuries related to their participation.