Dr. Bradley Welling's Doxycycline Injection of Cutaneous Schwannoma in Neurofibromatosis Type 2 Research

In a project entitled "Doxycycline Injection of Cutaneous Schwannoma in Neurofibromatosis Type 2" we have enrolled our first patient and started to study the effect of direct injection of tumors in and just under the skin with doxycycline, a commonly used antibiotic.

What is the rationale for injecting schwannomas with an antibiotic?

Although doxycycline is well known as an antibiotic used for the treatment of a broad range of infections, it is also used to cause contraction and scaring of a variety of conditions such as fluid buildup in the lungs (pleural effusions) [1], excess swelling of the eyelid (festoons)2, malformations in the lymphatic system[3-5], and blood filled cysts within bones (aneurysmal bone cyst)[6]. It has not previously been clinically studied in NF2. Doxycycline was selected because of its safety profile and also because of its anti-tumor role in various cancers including prostate and lung cancer[7,8], colorectal carcinoma[9,10], nervous system tumors[11,12], breast cancer[13], leukemias which develop drug resistance[14], melanoma[15], oral cancer[16], bone cancer[17], and malignant nerve sheath tumors, such as are seen in NF1[18].

Does doxycycline inhibits tumor growth in NF2-associated tumors?

We don't know. We have therefore initiated this pilot study. What we do know that in cell cultures doxycycline has been shown to broadly inhibit certain enzymes (metalloproteinases) which may play a role in the growth of vestibular schwannomas. Doxycycline blocks several growth pathways and may also suppresses the formation of new blood vessels into the tumor much like bevacizumab (Avastin) does. Doxycycline also regulates inflammation which we know plays an important role in other cancers. We have also demonstrated that vestibular schwannomas are associated with activation of inflammation[19-21].

If successful, this study may introduce a novel direct treatment path for NF2 -associated schwannomas and potentially reduce the side effects of other treatments now being used to control tumor growth.

How will the study be performed?

We will be measuring the growth or reduction in tumor size after injection as the primary endpoint of this study. Side effects such as numbness, pain, itching, redness, or discoloration of skin will also be monitored[22].

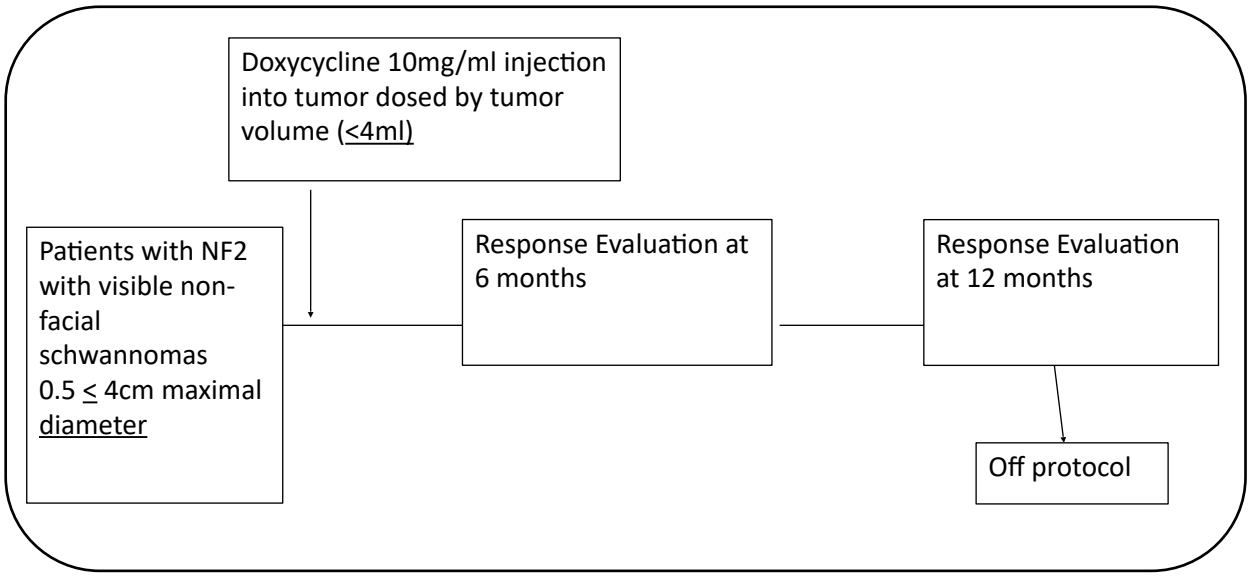
Who can participate in the study?

Patients 8 years of age and older with NF2-associated skin schwannomas between 0.5 cm and 4 cm in greatest diameter who are not on other drugs for NF2. A maximum of three tumors per patient will be injected. Tumors will be measured at baseline, at 6-months and at 1-year follow up. Injection of a local anesthetic (1% lidocaine) can be given prior to doxycycline to block the pain of injection or patients undergoing other surgery can have injections when under anesthesia. Allergies to doxycycline and a few other conditions such as pregnancy may prevent participation.

How can one learn more about the study?

Contact Alyssa Brown, BS who is the study coordinator at:
Alyssa_Brown@meei.harvard.edu or by phone at 203-434-9763
for full screening or
D. Bradley Welling, MD, PhD who is the principle investigator at
Brad_Welling@meei.harvard.edu or by phone at 617-573-3632.

Trial Schema:



Does one need to come in for an examination to determine eligibility?

A pre-screening of potential study subjects over the telephone or in person takes place and consent to proceed may be obtained by phone. The injection does require an in-person visit of course. Financial assistance for transportation and parking of up to $100 per patient may be made to the study subjects to help off-set their cost of participation.

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