Protocol

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Preliminary/background data:

Our prior research and clinical data prior to collaboration with BRANY IRB may be read in the published article int the following link: https://link.springer.com/content/pdf/10.1007/s00403-024-03423-0.pdf.

"Our research presents an innovative approach to treating basal and squamous cell carcinomas through the combination of fractional laser therapy and tirbanibulin ointment. Since the treatment of our first participant, we have observed 100% clinical and/or histological clearance of lesions in all subjects over one year. The joint action of both the thulium and erbium lasers, bulk heating with a heat shock response, and the predicted improved penetration of the tirbanibulin ointment demonstrates an effective strategy for the destruction of these cancerous cells. In addition, the feld effect of the treatment may decrease the risk of recurrence and adjacent cancers in the future. This study holds the potential to positively impact nearly 5 million Americans annually who suffer from basal and squamous cell carcinomas. The advantages of laser treatment, including the absence of scarring and bleeding, quick healing, and non-invasiveness, address the specific needs of various patient populations. In conclusion, the findings of this study ofer a groundbreaking and patient-centric solution for basal and squamous cell carcinoma treatment. The possibility to improve the lives of millions paves the way for a paradigm shift in skin cancer management."

"Fractional laser skin treatment is associated with a relatively low complication rate. Side effects and complications observed in this study were temporary and did not result in long-term or significantly severe sequelae (e.g., scarring)." Per: Graber EM, Tanzi EL, Alster TS. Side effects and complications of fractional laser photothermolysis: experience with 961 treatments. Dermatol Surg. 2008 Mar;34(3):301-5; discussion 305-7. doi: 10.1111/j.1524-4725.2007.34062.x. Epub 2008 Jan 8. PMID: 18190541.

Rationale

Basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) are the most common forms of cancer in the United States. The current most commonly accepted treatments for SCCs and BCCs depending on the location and depth, are surgical removal, electrodessication and curettage, or Mohs surgery. Although these treatments were created to limit the destruction of surrounding healthy cells, all treatments typically leave a scar. Tirbanibulin ointment is one of the leading topical medications for the treatment of actinic keratoses, which can progress into SCCs and less commonly into BCCs. Studies have found that non-ablative fractional laser therapy can be an effective treatment for actinic keratoses. Researchers have also tested the treatment of keratinocyte carcinomas with varying laser types and results. However, in this study we have carefully selected the laser type, settings, and treatment design, and have incorporated the use of tirbanibulin ointment, predicting a field effect response and increased depth of penetration.

Study Objective

We seek to evaluate the effectiveness of fractional laser therapy and tirbanibulin ointment to treat squamous and basal cell carcinomas. We will execute this by using both thulium and erbium lasers on previously biopsy-confirmed SCCs and BCCs and applying bulk heating methods. Then, depending on the level of invasiveness, instruct subjects to apply the ointment over the course of five nights immediately following the treatment. The intention of this study

is to minimize the need for invasive surgical procedures so as to optimize the cosmetic appearance, and provide a treatment option that is beneficial for a wide range of individuals.

Design, Selection Criteria, Data Source

Study design: Longitudinal, forward directed, interventional

Study type: prospective

Methodology: site-based (Bruce Robinson, MD private practice dermatology office)

Patient population: The dermatology office is located in New York, NY but patients may come from any origin. The patient population consists of any patient, new or established, of Dr. Bruce Robinson. Patients must have a biopsy confirmed BCC and/or SCC skin cancer confirmed by a dermatopathologist either under the care of Dr. Robinson or another physician.

Expected study duration: Approximately 5 years. To ensure the clearance of skin cancer, we will track our patients for at least 5 years. All patients with a history of skin cancer, including those in this study, are carefully monitored and instructed to return for biannual skin exams or earlier if they notice any abnormalities at the site of the treatment.

Schedule of events/visits:

-Visit #1: In office laser treatment

****For nodular/invasive carcinomas:**

-Night of Visit #1: At home ointment application to treated site

-Night #2- Night #5: At home ointment application to treated site

-For approximately 10-14 days following competition of ointment application: At home wound care performed twice a day at the treated site. Patients instructed to complete wound care until site is completely healed (for some could take up to 1 month)

1 month post-tx: Follow-up to check site (Take biopsy per patient consent)

6 month post-tx: Follow-up for complete skin exam and to check site

1 year: Follow-up for complete skin exam and to check site (Take biopsy per patient consent)

1.5 year: Follow-up for complete skin exam and to check site

2 years: Follow-up for complete skin exam and to check site (Take biopsy per patient consent)

2.5 year: Follow-up for complete skin exam and to check site

3 year: Follow-up for complete skin exam and to check site (Take biopsy per patient consent)

3.5 year: Follow-up for complete skin exam and to check site

4 year: Follow-up for complete skin exam and to check site (Take biopsy per patient consent)
4.5 year: Follow-up for complete skin exam and to check site
5 year: Follow-up for complete skin exam and to check site (Take biopsy per patient consent)
**Advise biannual skin exam thereafter (always recommended to any patients with history of SCC/BCC skin cancer)
**Advise return to office ASAP if abnormalities occur at site at any point in time

Patient recruitment: Established patients will be recruited if they develop biopsy confirmed SCC or BCCs. They will be given the option to participate in the study. For new patients, recruitment will be based on referrals by current patients or other physicians. Additionally, new patients may be recruited through the office website, social media, or other online marketing conducted by employees of Dr Bruce Robinson.

Patient retention: Patients will be instructed of the importance of returning to the office for the scheduled follow ups. Patients will be closely tracked and monitored. We collect cell, home, mobile, and emergency numbers, emails, and addresses from all patients under our care. This provides multiple ways to contact patients. Patients will be instructed to make follow up appointments before leaving the office, if they don't then we will call when they are due. Patients are always called, texted, and/or emailed prior to their appointments to confirm. No show patients will be contacted multiple times. If no response is given after multiple electronic attempts, then letters are mailed to patients. These letters outline the importance of returning to the office for care and the risks associated with not returning.

Patient criteria: Participants must have a biopsy confirmed (by a pathologist or dermatopathologist) BCC and/or SCC and/or an hypertrophic actinic keratosis (solar keratosis) that extends to the base of a specimen and a BCC or SCC cannot be ruled out by the dermatopathologist. The carcinoma can be any level of invasiveness. Patients can be of any skin type, demographic, ethnicity or gender. The carcinoma cannot have been previously treated by any other means (surgical excision, laser, Mohs, electrodissection, topical, etc.) Patients must be 18 years or older. Patients cannot be pregnant. We do not declare any other exclusion criteria in relation to previous or current diagnoses, surgeries, or medications.

Potential bias:
-selection bias: Patients are recruited from an NYC based dermatology office. Patients must have the means to pay for the treatment as it is not covered by insurance (although prices may be discounted or negotiated, and free treatment may be offered, on a case to case bases depending on available resources and patient needs)
-risk of attrition bias if patients do not follow up or drop out of the study
-reporting bias: part of this study requires patients to complete a 5 night course of ointment application. We are trusting that the patient is completing and accurately reporting this in accordance with our detailed instructions provided.

Data source: Collected by Dr. Bruce Robinson or by his medical assistants and inputted into Macpractice electronic medical record.

Outcomes of interest:

primary

1. Successful cure with the experimental method on all participants

   vs. clinical recurrence or worsening

secondary

1. The experimental method successfully treats one type of cancer but not the other (BCCs but not SCCs or vice versa)
2. The experimental method successfully treats early stages of the cancers, but not later stages (ex. Treats superficial SCCs but not invasive SCCs)
3. The experimental method successfully treats only specific parts of the body (ex. Treats areas of the body with thinner skin like the face, but not areas of thicker skin like on the back.)
4. The experimental trial method successfully treats only certain patients (differing results depending on age, skin type, ethnicity, etc).

Data Collection/Data Management, Quality Control of Data

-All data will be tracked by Bruce Robinson and his medical assistants

-Detailed visit information, treatment and follow-up notes will be documented through the EMR program Macpractice and we will utilize other data management methods such as google sheets

-Any missing data will be accordingly documented

-Missing data will be noted in results section/ likely to be reported in a table format

-Data will be collected at the initial treatment including patient demographics, location of lesion, invasiveness of carcinoma and treatment settings. Each subsequent follow up visit will include data in the format of "clinical recurrence or no clinical recurrence of carcinoma" at each follow-up visit. If a biopsy is taken and is clear then "no histological recurrence" will be reported. If the biopsy shows evidence of carcinoma, then the detailed pathological results will be reported. Any additional necessary data including complications will be tracked and reported.

-Written consent will be obtained by each patient prior to treatment and scanned electronically into their EMR patient file.

-Thermal data and images will be collected through TopDon thermal imaging camera application on an IPad, then exporting in graph form to google sheets.

Statistics

-Subgroups will be defined by cancer type, cancer invasiveness, skin type, and gender

-The sample size is likely to be 20-100 participants as estimated by the established patients at the office of Bruce Robinson MD and the frequency of carcinoma diagnosis.
-On a per-case basis, treatment is considered effective if there is no clinical/histological recurrence in 5 years.
-For the study as a whole, the treatment is considered effective if the recurrence rate is lower or approximately equal to the comparison groups: other FDA approved/traditional treatment options. For example, studies have shown that after surgical excision, over 5 years, superficial BCC recurrence rate is between 2% and 5%, nodular BCC 2-8%, SCC in situ ~0.8%, and invasive SCC between 1.7% and 6.4%. And, most surgical excision recurrences occur within 2 years. Other methods such as electrodessication and curettage have higher recurrence rates. So, we would consider our treatment successful if our recurrence rates are lower or approximately equal to any of the approved treatment options.
-Treatment is not randomized. Participation is determined by the patient's willingness to participate. If they participate they are given the treatment. No placebos or control groups.

Ethics, Privacy, and Pharmacovigilance Reporting

-ethical consideration is important for this study. We use human participants. If not monitored closely, the skin cancers have a risk to progress and cause damage to the patient's skin at the affected area. Survival rate for BCCs and SCCs is almost 100% therefore there is a very low risk of death. We will be submitting our study for ethics approval prior to starting.
-We will protect patient personal data and confidentiality in accordance with HIPAA guidelines. Our office already follows HIPAA and all employees are well informed of the policy. No PHI as outlined by HIPAA will be reported or shared from our study in any publications or shared with any individual not responsible for the direct care of the patient. Letters and/or numbers will replace names when referring to subjects when reporting or referring to data. Photos or videos taken of participants will not include identifying characteristics unless rights were signed off by the patient. Informed consent will be obtained prior to any individual's participation in our study. A detailed consent form will be reviewed with the patient and the patient will be required to sign before being treated. If the patient has caretakers or family members that are responsible for assistance with their care they will also be present in the review of consent.
-Patients will be instructed of the importance of returning to the office for the scheduled follow ups. Patients will be closely tracked and monitored. We collect cell, home, mobile, and emergency numbers, emails, and addresses from all patients under our care. This provides multiple ways to contact patients. Patients will be instructed to make follow up appointments before leaving the office, if they don't then we will call when they are due. Patients are always called, texted, and/or emailed prior to their appointments to confirm. No show patients will be contacted multiple times. If no response is given after multiple electronic attempts, then letters are mailed to patients. These letters outline the importance of returning to the office for care and the risks associated with not returning. If after all attempts to contact the patient are unsuccessful, they will be labeled as withdrawn from the study. This will be noted in our data. If the study is terminated, all participants will be closely monitored as outlined in the study protocol. If the site is terminated, participants will be instructed to find another dermatologist to track the recurrence of their

skin cancer. Medical records and research data will be sent to their new dermatologist once a patient signs a medical record release. Care will then be transferred over to their new dermatologist.

-For adverse reactions/adverse events: All adverse reactions will be noted and reported in our study. A new plan of care will be designed for the patient ensuring the proper treatment of their skin cancer.

-We plan to publish this study in a scientific journal.