
UNIVERSITY OF NORTH TEXAS
HEALTH SCIENCE CENTER AT FORT WORTH
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Habib, Nausheen

Master of Science, Biomedical Sciences, December 2005

An Open-Label Pilot Study Evaluating the Effects of Travoprost on Eyebrow Regrowth Among Patients Undergoing Chemotherapy for Cancer

The primary objective of this study is to determine the effect of eyebrow hair growth of a twice daily application of travoprost among patients undergoing chemotherapy or those who have already completed chemotherapy.

Travoprost, used clinically in the treatment of glaucoma, is topically and unilaterally applied to a total of 15 patients to induce eyebrow hair growth. This is an ongoing pilot study in which the screening, treatment and follow-up visits are scheduled on day 0, week 4, week 8, week 12, and week 14.

After an eight week treatment period, 69% of the patients demonstrated increased eyebrow density. This increase in eyebrow hair is consistent with travoprost's ability to prolong the anagen or growing phase of the hair cycle.

AN OPEN-LABEL PILOT STUDY EVALUATING THE EFFECTS OF TRAVOPROST ON EYEBROW REGROWTH AMONG PATIENTS UNDERGOING CHEMOTHERAPY FOR CANCER

Nausheen Habib, B.S.

APPROVED:

Major Professor

Committee Member

Committee Member

University Member

Department Chair, Graduate School of Biomedical Science

Dean, Graduate School of Biomedical Science

AN OPEN-LABELED PILOT STUDY EVALUATING THE EFFECTS OF TRAVOPROST ON EYEBROW REGROWTH AMONG PATIENTS UNDERGOING CHEMOTHERAPY FOR CANCER

INTERNSHIP PRACTICUM REPORT

Presented to the Graduate Council of the

Graduate School of Biomedical Sciences

University of North Texas
Health Science Center at Fort Worth

In Partial Fulfillment of the Requirements

For the Degree of

MASTERS OF SCIENCE

By

Nausheen Habib, B.S.

Fort Worth, TX

December 2005

ACKNOWLEDGMENTS

First and foremost I would like to thank God for always providing me with great inspiration throughout my life.

I would like to thank my mentor, Ray Page, D.O., Ph.D., whose idea inspired this research. His enthusiasm for research gave me great motivation to design and implement this study. Thank you for all your support and help through this whole process. Additionally, I would like to thank Julie Weikel, Jennifer Crawford, Joyce Wallace and the entire staff at The Center for Cancer and Blood Disorders for welcoming and providing me with the resources I needed to accomplish my research.

Thank you to my entire committee, Jamboor Vishwanatha, Ph.D., Harold J. Sheedlo, Ph.D. and Michael W. Martin, Ph.D., for always being there and providing me with support and encouragement when I needed it. I would also like to thank Stephen M. Goode, M.D., for providing the study medication and other necessities needed to carry out the study. To Annita Bens, Ph.D., I would like to say that I appreciate your guidance and advice throughout the past six month and thank you for introducing me to the clinical research field.

Most importantly, I would like to thank my family and friends for always believing in me and being with me every step of the way. Thank you.

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INTRODUCTION

CHEMOTHERAPY

Chemotherapy drugs act by killing all rapidly dividing cells and identifying unique characteristics specific to those particular cells. One of the major advantages of administering chemotherapy is the ability to treat metastatic cancer, while surgery and radiation therapies on the other hand, are very limited to treating cancers in specific areas within the body.[1] There are a variety of chemotherapeutic agents available which can be used by themselves or in combination with others. All chemotherapy drugs are classified according to their mechanisms of action.

Alkylating agents

Alkylating agents are the oldest class of anticancer drugs and include nitrogen mustards, nitrosoureas, and platinum complexes. These agents are active during every stage of the cell cycle and act by forming covalent bonds with negatively charged sites such as amino, carboxyl, phosphate, and sulfhydryl groups on DNA and RNA.[1-3] By binding to DNA sites, these agents alter DNA replication, transcription, base pairing and strand cross-linking along with causing denaturation of DNA, RNA, or protein.[1,3]

Antimetabolites

Antimetabolites for the most part disrupt normal metabolic pathways by acting as competitive inhibitors of enzymatic reactions that take place in intermediary metabolism. They are analogs of purine and pyrimidine bases used to synthesize DNA and RNA. Antimetabolites act during a specific cell cycle phase, most being active during the S-phase of the cell cycle. Methotrexate, the most widely used of these agents is S-phase specific and interrupts the synthesis of thymidylate and purine precursors which are necessary for DNA and RNA synthesis.[1,3]

Natural Products

Natural products are compounds which are derived from substances such as bacteria, plants, and fungi. These products include antitumor agents such as anthracyclines, antitumor antibiotics, epipodophyllotoxins, vinca alkaloids, taxanes, and camptothecin analogs.[2] These agents are usually cell cycle specific and are active mostly during the S-(vinca alkaloids) and M-(vinca alkaloids, taxanes) phases of the cycle. Anthracyclines, epipodophyllotoxins, and camptothecin analogs all act by inhibiting activity of topoisomerases I or II.[1,3] Inhibition of this enzyme does not allow the DNA double strand to unwind and therefore prevents DNA repair, replication, and transcription from occurring.[1] The vinca alkaloids and taxanes interfere with microtubule assembly and disassembly. While the vinca alkaloids bind to the tubulin and prevent polymerization of microtubules, the taxanes (paclitaxel and docetaxel) act by promoting microtubule assembly and blocking the cell cycle during mitosis.[3]

CHEMOTHERAPY AND HAIR LOSS

Chemotherapy agents are specifically designed to target all fast growing cells in the body. Along with cancerous cells, these drugs also affect other fast growing cells such as hair follicles, cells in the gastrointestinal (GI) tract, bone marrow, and skin cells. The destruction of these non-cancerous cells can cause many side effects which include hair loss, mouth sores, difficulty swallowing, nausea, vomiting, diarrhea, constipation, infection, anemia, and bleeding risks.[1]

Hair loss is one of the most distressing side effects of chemotherapy that occurs through disturbance of the growing hair roots. This problem is not recognized in patients unless it is extreme enough to cause alopecia. Hair loss with chemotherapy occurs in growing hairs (anagen) only. The hair follicles of resting hairs (telogen) on the scalp and other areas of the body are left unharmed leading to an increased percentage of telogen hair follicles.[4]

Patients undergoing chemotherapy not only lose their scalp hair but they start to lose hair from their entire body including eyelashes and eyebrow hairs. In this study, patients will be given a topical application of travoprost twice a day for a period of three months. The patients will then be evaluated on the end hair thickness and density compared to their baseline measurements through photographic and microscopic analyses of the hair follicles. The clinical significance of this study is to improve the quality of life for patients enduring chemotherapy along with eliminating infections related to eyelash and eyebrow hair loss.[5]

CHAPTER II

AN OPEN-LABEL PILOT STUDY EVALUATING THE EFFECTS OF TRAVOPROST ON EYEBROW REGROWTH AMONG PATIENTS UNDERGOING CHEMOTHERAPY FOR CANCER

BACKGROUND

Travoprost

Travoprost (Travatan® [Alcon, Ft. Worth, TX]) is a newly discovered drug commonly used for treatment of glaucoma and ocular hypertension (figure 1). The isopropyl ester precursor of this drug undergoes hydrolysis to the biologically active free acid making it a prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) analog selective for the prostaglandin F (FP) receptor.[6] Travoprost lowers intraocular pressure (IOP) of

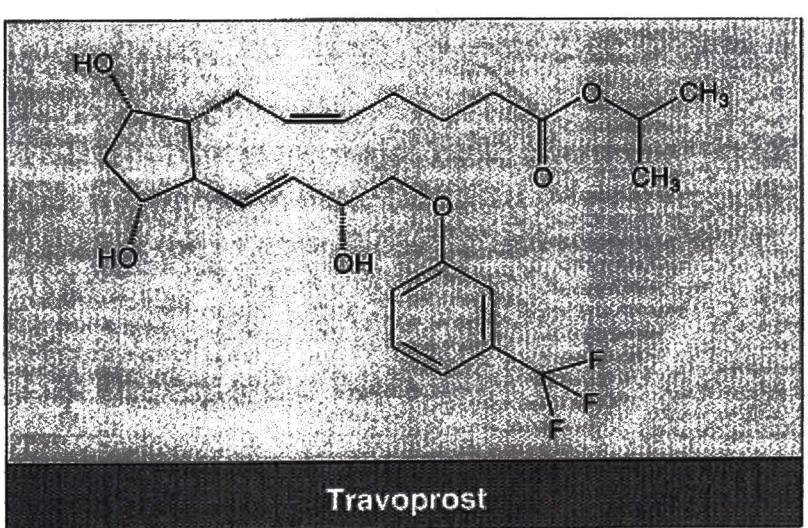


Figure 1: Structure of travoprost. [7]

the eye by increasing drainage of interoculer fluid from the posterior to the anterior chamber and through the canal of schlemm (figure 2). Travoprost also increases the aqueous humor outflow through the trabecular meshwork.[6] The ester portion of travoprost is hydrolyzed into its biologically active free acid state which increases penetration into the aqueous humor.[7] Travoprost is a full agonist of the FP receptor which has higher affinity for the FP receptor than other prostaglandin receptors, and therefore is less likely to activate other prostanoid receptors. After binding to the FP receptor, travoprost triggers a response to activate C-Fos, a regulatory protein, which stimulates metalloproteinase enzymes (MMPs). MMPs hydrolyze the collagen within the extracellular matrix allowing aqueous humor to pass through the ciliary body more freely (figure 3).[8] The aqueous humor is a source of nutrients and oxygen, therefore its flow is extremely important for the health of the lens and cornea. The drainage of aqueous humor from the posterior chamber of the eye occurs via conventional and uveoscleral routes.[8] The uveoscleral outflow is thought to be improved with travoprost.[9]

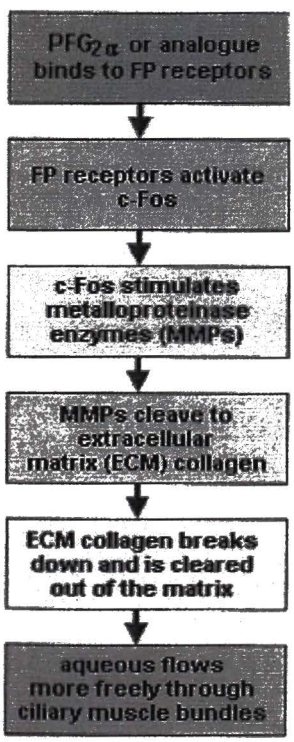


Figure 3: Prostaglandin and Prostaglandin analogue mechanism of action. Adopted from reference 8

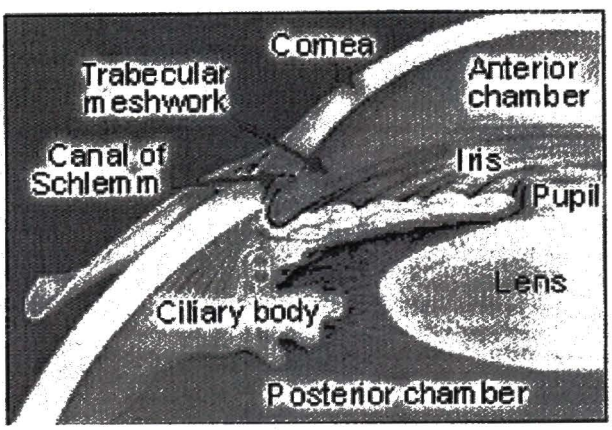


Figure 2:Uveal tract structures
Adopted from reference 8

Hair structure and growth cycle

The entire hair follicle consists of an outer root sheath, an inner root sheath, hair shaft, a sebaceous gland and an arrector pili muscle which is absent in the hair follicles of the eyelashes and eyebrows (fig 4). The outer fibrous sheath is composed of thick collagen bundles and is continuous with cells that line the epidermis. The inner sheath, however, is composed of different cell types organized into Henley's layer, Huxley's layer, and the cuticle of the

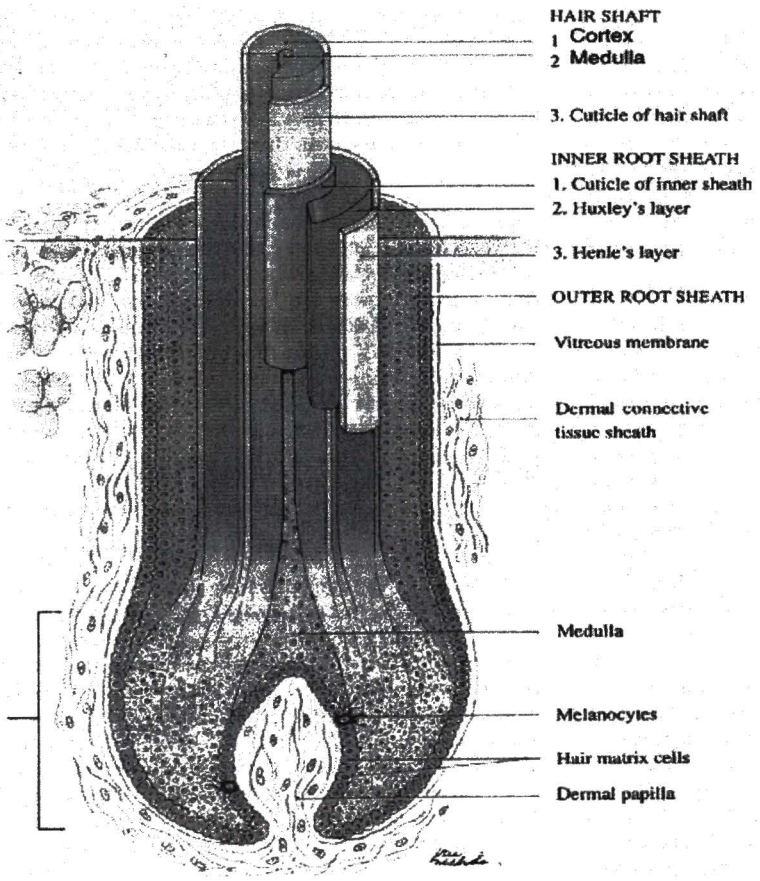
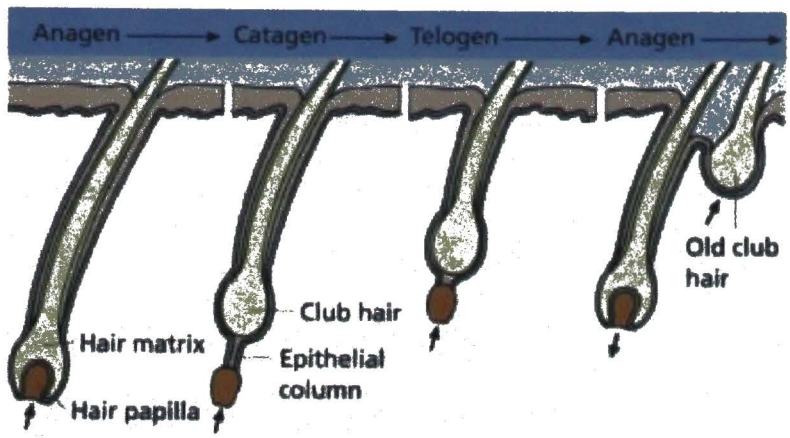


Figure 4: Hair structure during the late anagen phase of the hair cycle showing the differentiated layers of the follicle.
Adopted from reference 10.

inner root sheath. Moving inward within the hair follicle, the hair shaft also consists of the cuticle, cortex, and medulla. The cuticle is the outermost layer and surrounds the skin surface. Below the cuticle is the cortical layer surrounding the medulla of the hair shaft. Located at the lower end of the follicle is the thickest part called the hair bulb. This part of the follicle is where intense metabolic activity takes place during the hair cycle. The bulb contains a proliferative zone of matrix cells which later differentiate into the medulla and cortical fibers of the hair shaft and are shaped into their final shape by the inner root sheath.[10]

Each hair follicle undergoes a cycle which includes anagen (growing phase), catagen (transition phase), and telogen (resting phase) stages (figure 5). During anagen, an unknown stimulus initiates new growth of the hair follicle. Intense metabolic activity takes place and a new hair follicle grows during early anagen which determines the size and shape of the follicle.[10-11] Duration of the anagen stage is suggested to be determined by the volume of the dermal papilla, which is necessary to "induce and maintain the hair follicle," and control the thickness of the fully developed hair follicle.[10] The entire length of the hair fiber is directly proportional the length of the anagen cycle.

Figure 5: Illustration of the stages of growth of hair follicles
Adopted from reference 12



During the catagen or the transition stage the metabolic activity slows down, and the epithelial elements at the base of the bulb migrate upward through the skin and toward the epidermal surface. The new hair follicle is approximately one-third of its original length after late catagen is completed. Through upward migration and dedifferentiation, a club follicle is formed which matures to leave a club hair.

The telogen stage continues for a few weeks. Growth during this period stops and the base of the bulb approaches the level of the sebaceous canal. A new cycle then begins and a new hair begins to grow underneath the telogen follicle, eventually pushing the old fiber out as shed.[10-11]

The hair cycle in humans is asynchronous; it varies in length depending on the location of the hair on the body. Compared to the scalp hair, the anagen phase is much shorter for eyelashes and eyebrows. The growth phase (anagen) for eyebrows is approximately 6 months compared to about 6 years with scalp hair. The telogen or rest stage in eyebrows lasts for approximately 100 days. When compared with scalp hair, eyelashes and eyebrows have the lowest number of

anagen to telogen follicles. Therefore, most of the hairs that make up the eyelashes and eyebrows are in the telogen phase of the hair cycle.[10]

$PGF_{2\alpha}$ and hair growth

One side-effect of travoprost is eyelash hair growth which is due to the effects of PGF2α and its analogs.[13] Prostaglandins, along with thromboxanes, and prostacyclins are molecules which occur naturally in many tissues within the body. They play a major role in physiological processes such as vasodilation and vasoconstriction, body temperature regulation, cardiovascular functions, reproduction, digestion, platelet aggregation and renal functions.[14] $PGF_{2\alpha}$ and its analogs have an effect on hair regrowth because of their vasodilatory effects and ability to "induce DNA replication and stimulate cell division and growth"[13] in many tissues. Prostaglandin analogues act as vasodilators in the skin, including increasing blood flow in the perifollicular vessels. $PGF_{2\alpha}$ had been also shown to be the most effective of the prostaglandins to induce DNA synthesis. $PGF_{2\alpha}$ induces nuclear transcription factors which lead to an increased protease synthesis. These proteases alter the extracellular matrix which is the "central feature of hair formation."[10] These alterations to the extracellular matrix lead to a variety of events eventually leading to $PGF_{2\alpha}$ induced hair growth. First, enhancement of the remodeling of the matrix allows cell proliferation, hair bulb enlargement, and downward migration of the entire follicle. Second, changes in the matrix initiate signals which alter differentiation. Lastly, during the transition from the anagen phase to the catagen phase, changes in the extracellular matrix

delay apoptosis and increase the anagen cycle, thereby increasing the entire hair cycle and the length of the hair shaft.[10]

Prostaglandins act via many different receptors which can be located within the intracellular, subcellular, or transcellular compartments of the cell. Most of these receptors reside on or within the plasma membrane.[14] The prostaglandin receptors express cellular functions which couple many signal transduction pathways when activated. These signal mechanisms include "(1) stimulation of adenylyl cyclase via the G_s protein, (2) inhibition of adenylyl cyclase via G_i proteins, (3) stimulation of phosphoinositide-specific phospholipase C (PI-PLC) via G_q, and (4) elevation of intracellular free Ca^{2+} through an inositol-1,4,5-trisphosphate-($InsP_3$) independent effect."[15] $PGF_{2\alpha}$ analogues also stimulate cell surface receptors to induce activation of protein kinase C (PKC) which plays a large role in cell growth. Exposure to $PGF_{2\alpha}$ leads to an over-expression of PKC found in the mid-anagen to anagen stages of the hair cycle.[13]

Hypertrichosis or excessive hair growth of the eyelashes and eyebrows after treatment with travoprost is shown to be through the initiation of the anagen phase in follicles which are currently in the telogen phase of the hair cycle. As stated earlier, the proportion of follicles in the eyelashes and eyebrows which are in the telogen phase is normally higher (~50%) than of hair on the scalp (~14%). Therefore, there are more eyelash and eyebrow hair follicles that are available to undergo the transition from the telogen phase to the anagen phase.[10] The effects of PGF2α on hair growth mentioned above suggest that prostaglandin and

prostaglandin analogues may serve as intermediates that regulate the natural hair cycle but its mechanism of doing so must still be further clarified.[13]

Clinical Studies on Travoprost

Many clinical studies have been conducted which show the effect of travoprost on eyelash growth. These studies were all carried out on glaucoma patients and two drops of travoprost was applied directly into the eye in order to see changes in interocular pressure and eyelash hair. In a 9-month randomized trial the effects of bimatoprost and travoprost were compared with an active control (timolol) on 573 patients. 150 (76%) of the 197 patients who received travoprost saw eyelash changes compared with 6 of 186 (3%) who received timolol.[6] Additionally, a 12-month study was conducted using latanoprost (prostaglandin analog) on 75 patients where eyelash changes were 33.8% at three months, 44.4% at six months, and 46.2% after a twelve month treatment.[16] According to another study conducted with bimatoprost, a prostaglandin analog, there were changes seen in eyelashes including increased length, thickness, density, and changes in eye color. These changes are said to be normalized again several months (up to 14) after stopping treatment.[17]

HYPOTHESIS

The hypothesis of this study is that a 12 week topical travoprost treatment will increase eyebrow hair thickness and eyebrow density at least 50% compared to the untreated eyebrow in the same patient. The primary objective of this study is to look at the ability of travoprost to increase eyebrow hair thickness and

eyebrow density. The evaluation of the study will be based upon the following measurement techniques.

1) Density scale numbers assigned by independent reviewers.
2) Measurement of hair thickness through microscopic analysis.
3) Patients' subjective assessment of eyebrow hair growth based on a questionnaire given at the conclusion of the study.

INTERNSHIP OBJECTIVES

1) Design and write study protocol and informed consent.
2) Develop data collection tools.
3) Set up data analysis tools.

SIGNIFICANCE

This study is designed to test the effects of travoprost on eyebrow growth on cancer patients currently in the process of losing their eyebrows, or patients who have already lost all of their eyebrow hair. Hair loss, including eyelashes, eyebrows, and body hair is a common side effect of patients undergoing chemotherapy. Although hair will resume growth approximately six months after completion of chemotherapy, it contributes to the many problems that cancer patients may face. A major problem which can arise due to hair loss is eye infections and inflammation in patients who have lost their eyelashes.

Additionally hair loss, including eyebrow and eyelash hair, can play a role with patient distress and self-image.[5]

MATERIALS AND METHODS

This is a pilot study in patients who have gone through or are currently going through chemotherapy. Patients, who have lost their eyebrows or are in the process of losing their eyebrows while undergoing chemotherapy prior to the screening visit, were screened for study inclusion. All patients who have met the inclusion and exclusion criteria and those who gave consent were enrolled into the study.

The study enrolled enough patients in order to see a 50% increase in hair thickness and/or eyebrow density. In order to calculate the appropriate number of patients, the following assumptions were made:

1. A two-sided t-test will be used.
2. 80% power at a 95% Confidence Interval.

Taking these assumptions into consideration, the total number of patients to be enrolled into this study was 15. All patient data collection was entered into an electronic data entry program (Epi-info).

The eligible patients (over 18 years of age) with uncomplicated reactions to chemotherapy were enrolled into a 14-week long study period. There was no charge to the patients to participate in this study. All study medication was

provided by the sponsor through donations from Alcon. Patients were evaluated at screening (baseline), and at weeks 4, 8, and 12. A post-treatment follow-up visit was held 14 days after the last dose of study medication was taken. All enrolled patients received 2 drops of travoprost twice a day. Travoprost was applied topically and unilaterally at the site of eyebrow growth. The patient's second site of eyebrow growth, was chosen at random, and used as a control measurement. All patients were advised to take their study medication at the same time each day and to document the time of daily dosing in a medication log which was provided. During each visit the following procedures were conducted.

1) Sign and date the informed consent (screening visit only).
2) A complete medical history obtained (screening visit only).
3) All medications, including any over-the-counter drugs, herbal medications, and vitamins used in the prior 4 weeks was documented (screening visit only).
4) A review of concomitant medication was conducted (treatment visits).
5) A brief physical exam, including vital signs (i.e., blood pressure, respiratory rate, pulse, temperature) and weight.
6) A urine pregnancy test was conducted where necessary.
7) A hair sample from each eyebrow was obtained (if available) in order to measure thickness. A

photograph of each eyebrow was also taken in order to measure eyebrow density.

To quantify an increase in eyebrow density, a photograph of each eyebrow site (control and experimental) was presented to 3 independent masked reviewers. Each individual reviewer evaluated the photograph and assigned a number (0-4) to each photograph according to a standardized scale designed by the study coordinator (Appendix G). The three numbers from each evaluator were then averaged and assigned to the photograph as the increase in eyebrow density. Each photograph was taken according to the standardized set procedures (19 cm away from the eyebrow). Growth in eyebrow hair thickness was evaluated through a microscopic analysis of a sample from the patient. A photograph was taken using an Olympus BX51 microscope at a 20x magnification. The photograph of the magnified hair was then measured for thickness. A 50% increase in hair thickness and/or eyebrow density was considered clinically significant. All statistical results were evaluated by carrying out paired t-test analysis using SPSS (statistical analysis program).

RESULTS

The study started on August 3, 2005 when the first patient was enrolled and is expected to end on December 20, 2005 upon completion of the last follow-up visit. The data being presented below are the results of this ongoing study obtained as of November 9, 2005.

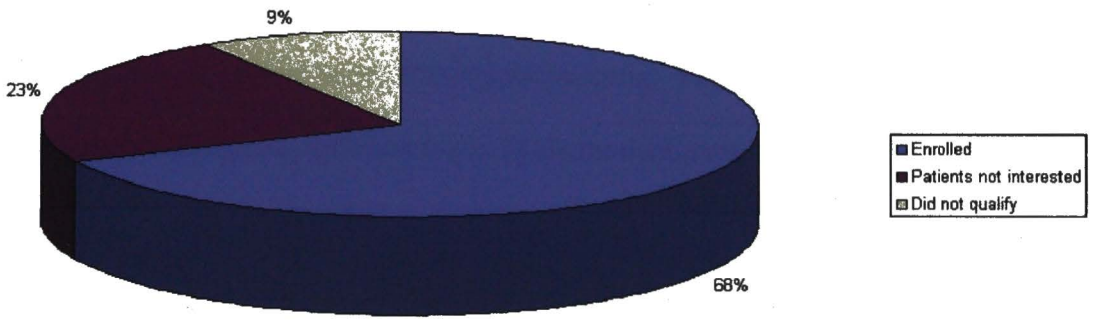


Figure 6: Patients screened
A total of 22 patients were screened of which 15 were enrolled into the study. 5 patients were not interested and two did not qualify. One of the enrolled patients was taken off the study due to an adverse event.

Figure 6 shows the 22 patients which were screened according to the inclusion/exclusion criteria. Of the 15 patients enrolled into the study, 14 (93%) completed the entire study. One (6.6%) of the 15 patients had an adverse reaction (conjunctivitis) and was advised to stop treatment. There were a total of 5 (23%) patients who were not interested in the study and two (9%) patients who did not qualify to be in the study. One of the two had lost hair due to radiation and not chemotherapy and the other patient had already grown most of his eyebrow hairs back after stopping chemotherapy treatment.

The experiment was conducted on one eyebrow site of each patient for a total of 14 sites, while the other 14 eyebrow sites served as control. This gave a total number of 28 sites being studied. Table 1 shows the demographic breakdown of the patient population. All 15 patients were females between the ages of 30 and 80 years old. Forty percent of the patients were between the ages of 60-70 years old. About 47% are patients with breast cancer and 33% with

ovarian cancer. The rest of the patients have a variety of other types of cancers including bladder, lung, and hypogammaglobuliniemia. They all have completed or are currently undergoing different types of chemotherapy with over 53% of the patients being treated with Paclitaxel. After reviewing all concomitant medications being taken by patients, the study coordinator concluded these medications would not conflict with travoprost treatment.

Table 1: Patient Demographics

	Frequency	Percentage
Age		
30-50	3	20%
51-60	4	26.6%
61-70	6	40%
71-80	1	6.7%
81-100	1	6.7%
Gender		
Female	15	100%
Male	0	0%
Eye Color		
Dark (Brown/Hazel)	8	53.3%
Light (Blue/Green/Grey)	7	46.7%

Randomized Eyebrow		
Right	8	53.3%
Left	7	46.7%
Type of Cancer		
Breast	7	46.7%
Ovarian	5	33.3%
Bladder	1	6.7%
Lung	1	6.7%
Hypogammaglobuliniemia	1	6.7%
Type of Chemotherapy		
Paclitaxel	4	26.7%
Docetaxel	2	13.3%
Paclitaxel, cremaphor free	2	13.3%
Carbo-Cytoxan	1	6.7%
CMF	1	6.7%
Etoposide, Cisplatin	1	6.7%
Etoposide, Paclitaxel	1	6.7%
Gemcitabine, Paclitaxel	1	6.7%
Vinorelbine	1	6.7%
Zeloda, Docetaxel	1	6.7%
Paclitaxel (total)	8	53.3%

A total of 13 (86.7%) of the 15 patients enrolled have completed at least 8 (treatment visit 2) of the 12 weeks of this ongoing study. One (6.7%) patient appeared to have an adverse event and was advised to stop study related treatment. One (6.7%) other patient was non-compliant and did not meet the study requirements. Therefore, only a total of 13 patients (n=13) were considered when conducting study results. A graphic representation of the increase in eyebrow hair density from the screening visit to treatment visit 2 is shown for the treated and control eyebrow sites in figure 7 and figure 8. According to the averages calculated from the density numbers assigned (table 2), figure 9 shows that there was a 23% increase demonstrated in the travoprost-treated eyebrow during the first treatment visit and 69% at the second treatment visit. When compared to assigned numbers for the control eyebrow (table 3) only 15% of the patients demonstrated eyebrow density increase at treatment visit 1 and 23% at treatment visit 2 as shown in figure 10. Table 2 also shows that a total of 4 (30.7%) of the 13 patients demonstrated a 50% or greater increase in eyebrow density of the travoprost treated eye. Paired t-test analysis was done on the eyebrow density measurements of the control and treated eyebrow site in order to compare significance of eyebrow hair regrowth. Table 5 shows comparisons between the screening visit, treatment visit 1, and treatment visit 2. Table 6 shows the t-test analysis comparing the screening visit and treatment visit 2 of both the treated and control eyebrow and table 7 shows comparisons between the treatment visit 1 and treatment visit 2 of both the treated and control eyebrow. The microscopic analysis of eyebrow hair thickness does not show clinically

significant results (table 8). Table 10, table 11, and table 12 are paired t-test analysis on the microscopic hair measurements comparing the screening visit, treatment visit 1, and treatment visit 2 between the treated and control eyebrow. There is no statistically significant data shown through these data tables.

Table 2: One photograph of each eyebrow site was taken during each study visit including the screening visit and final treatment visit. A masked evaluation was then conducted of the density measurements during the screening visit (SV), 1st treatment visit (T1), 2nd treatment visit (T2), and the 3rd treatment visit (T3). The average of the three numbers for each visit was then taken and rounded to the nearest tenth.

Photographic Measurements (treated eyebrow)																
Study Number	SV [A]	SV [B]	SV [C]	**SV [avg]**	T1 [A]	T1 [B]	T1 [C]	**T1 [avg]**	T2 [A]	T2 [B]	T2 [C]	**T2 [avg]**	T3 [A]	T3 [B]	T3 [C]	**T3 [avg]**
001	Patient did not complete study															
002	2	1	2	**1.7**	1	1	2	**1.3**	2	2	2	**2**	1	2	3	**2**
003	3	1	2	**3**	1	1	1	**1**	1	1	1	**1**	-	-	-	**-**
004	2	1	2	**1.7**	1	1	1	**1**	-	-	-	**-**	-	-	-	**-**
005	3	2	2	**2.3**	3	3	2	**2.7**	3	3	3	**3**	3	3	3	**3**
006	3	2	3	**2.7**	3	2	3	**2.7**	3	2	3	**2.7**	3	2	3	**2.7**
007	1	1	1	**1**	1	1	1	**1**	2	1	1	**1.3**	2	1	1	**1.3**
008	4	3	3	**3.3**	3	2	3	**2.7**	3	2	3	**2.7**	3	2	3	**2.7**
009	3	2	2	**2.3**	3	3	3	**3**	4	3	4	**3.7**	-	-	-	-
010	3	3	2	**2.7**	3	3	2	**2.7**	4	3	2	**3**	-	-	-	-
011	1	1	1	**1**	1	1	1	**1**	0	0	0	**0**	-	-	-	-
012	0	0	0	**0**	0	0	0	**0**	2	2	2	**2**	-	-	-	-
013	3	2	2	**2.3**	3	3	2	**2.7**	4	4	4	**4**	-	-	-	-
014	3	2	2	**2.3**	2	2	2	**2**	4	3	4	**3.7**	-	-	-	-
015	3	2	2	**2.3**	3	2	2	**2.3**	4	2	2	**2.7**	-	-	-	-

Table 3: Photographic measurements of the control eye during the screening visit (SV), treatment visit 1 (T1), treatment visit 2 (T2), and treatment visit 3 (T3). The numbers assigned to each photograph are shown below. The average of the three numbers was taken for each visit and rounded to the nearest tenth.

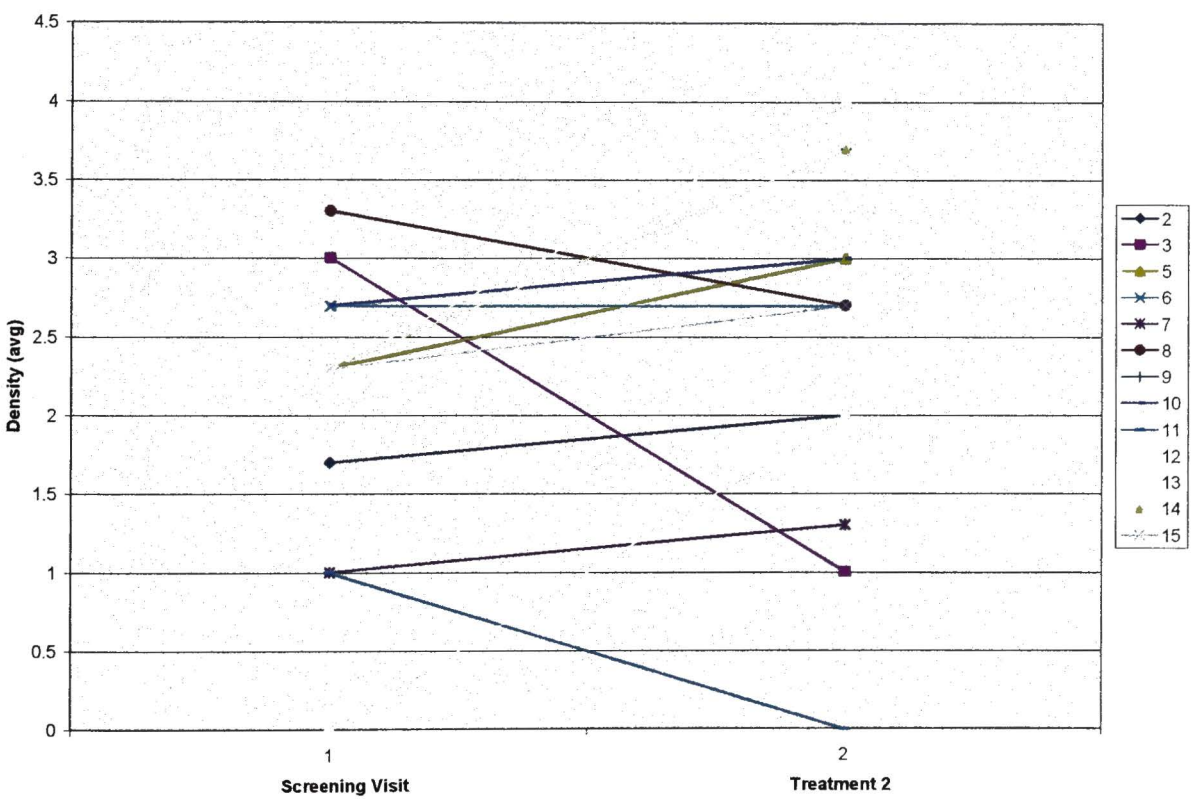
Photographic Measurements (control eyebrow)																
Study Number	SV [A]	SV [B]	SV [C]	**SV [avg]**	T1 [A]	T1 [B]	T1 [C]	**T1 [avg]**	T2 [A]	T2 [B]	T2 [C]	**T2 [avg]**	T3 [A]	T3 [B]	T3 [C]	**T3 [avg]**
001	Patient did not complete the study															
002	1	1	2	**1.3**	1	1	2	**1.3**	1	2	1	**1.3**	2	2	1	**1.7**
003	3	1	2	**2**	2	1	1	**1.3**	1	1	1	**1**	-	-	-	-
004	2	1	2	**1.7**	1	1	1	**1**	-	-	-	-	-	-	-	-
005	3	2	2	**2.3**	2	2	2	**2**	3	3	2	**2.7**	3	2	3	**2.7**
006	3	2	3	**2.7**	3	2	3	**2.7**	2	3	3	**2.7**	3	3	3	**3**
007	1	1	1	**1**	1	1	1	**1**	1	1	1	**1**	1	1	1	**1**
008	4	3	3	**3.3**	3	2	3	**2.7**	4	3	3	**3.3**	3	3	3	**3**
009	3	2	2	**2.3**	3	2	2	**2.3**	3	2	2	**2.3**	-	-	-	-
010	3	3	2	**2.7**	3	3	2	**2.7**	3	3	2	**2.7**	-	-	-	-
011	1	1	1	**1**	1	1	0	**0.7**	1	1	0	**0.7**	-	-	-	-
012	1	1	1	**1**	0	0	0	**0**	1	1	2	**1.3**	-	-	-	-
013	3	2	2	**2.3**	3	3	3	**3**	3	3	3	**3**	-	-	-	-
014	4	2	3	**3**	3	2	2	**2.3**	3	2	3	**2.7**	-	-	-	-
015	3	2	2	**2.3**	3	3	2	**2.7**	3	3	2	**2.7**	-	-	-	-

Table 4: Table showing the mean and standard deviation calculations for the eyebrow densities of the control and treated eyebrow sites for all patients

Descriptive Statistics

	N	Mean	Std. Deviation
SVcontrol	13	2.092	.7858
SVtreated	13	2.069	.9196
T1control	13	1.900	.9434
T1treated	13	1.931	.9560
T2control	13	2.108	.9014
T2treated	13	2.446	1.1602
Valid N (listwise)	13		

Figure 7: Graphic representation of the increase in eyebrow density between the screening and treatment 2 visits in the travoprost treated eye.



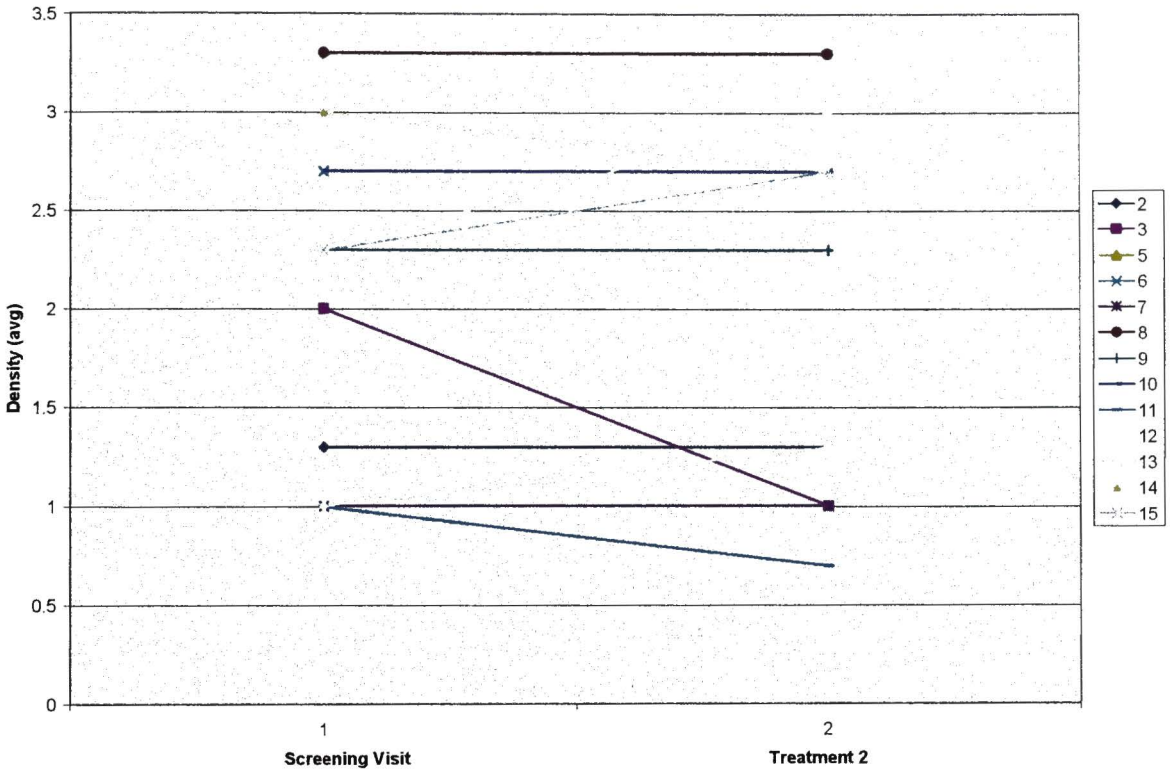


Figure 8: Graphic representation of the increase in eyebrow density between the screening and treatment 2 visit in the control eyebrow site.

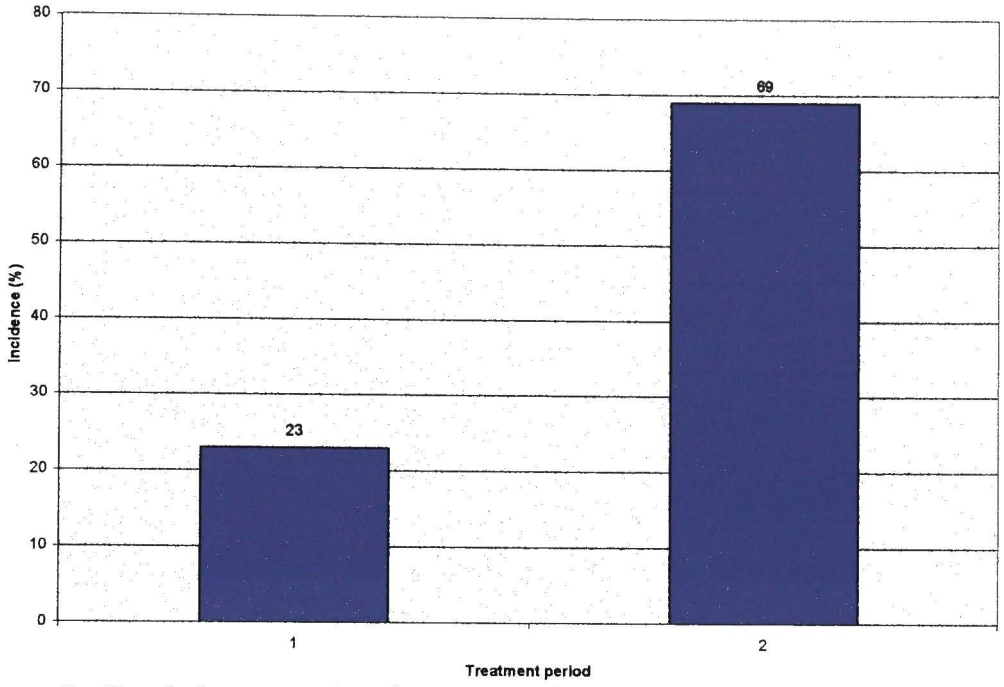


Figure 9: Graph demonstrating the percent of incidence of increase in the density measurements of the travoprost treated eyebrow.

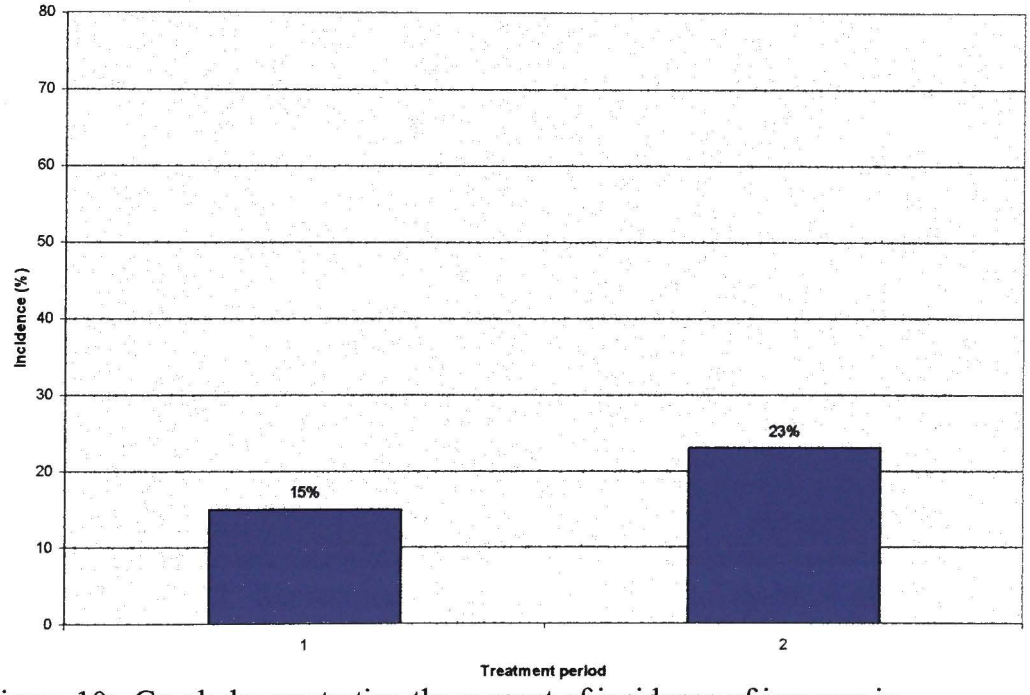


Figure 10: Graph demonstrating the percent of incidence of increase in the density measurements of the control eyebrow site.

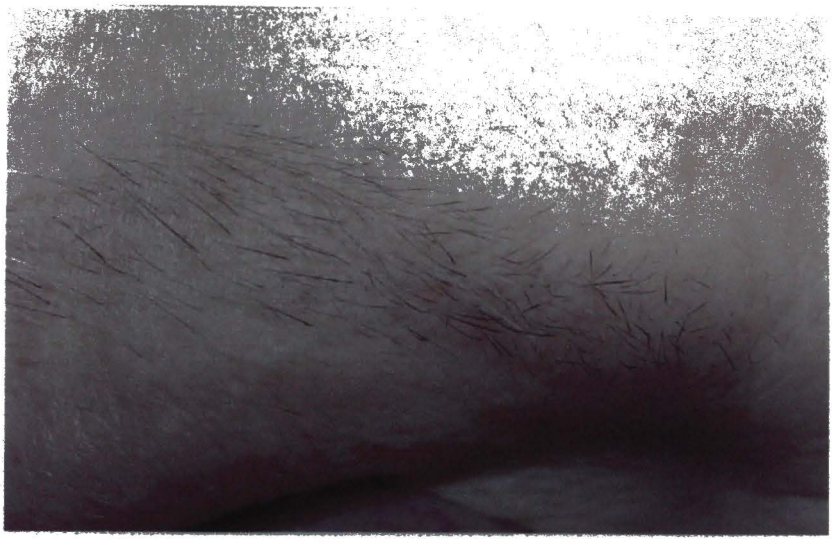


Figure 11: Representative sample of the treated eyebrow of a patient taken during the screening visit.

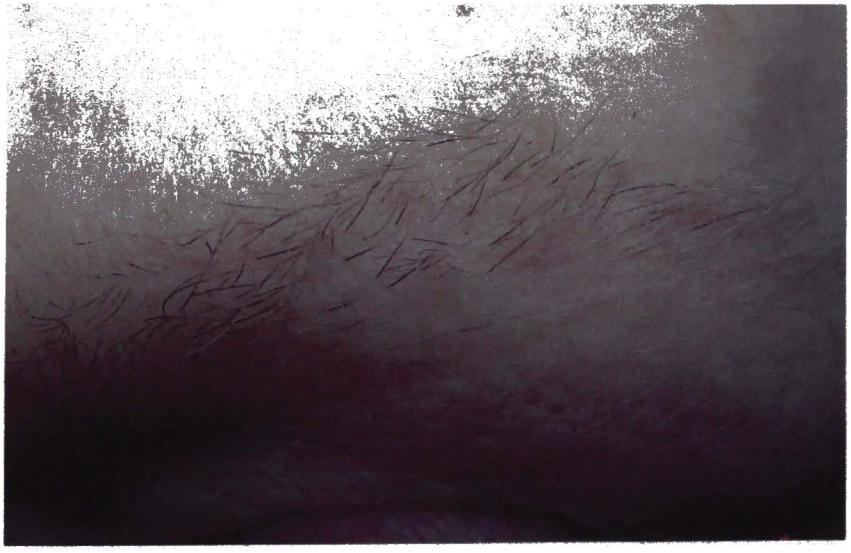


Figure 12: Representative sample of the control eyebrow of a patient taken during the screening visit.

Figure 13: Representative sample of the treated eyebrow of a patient taken during treatment visit 2.

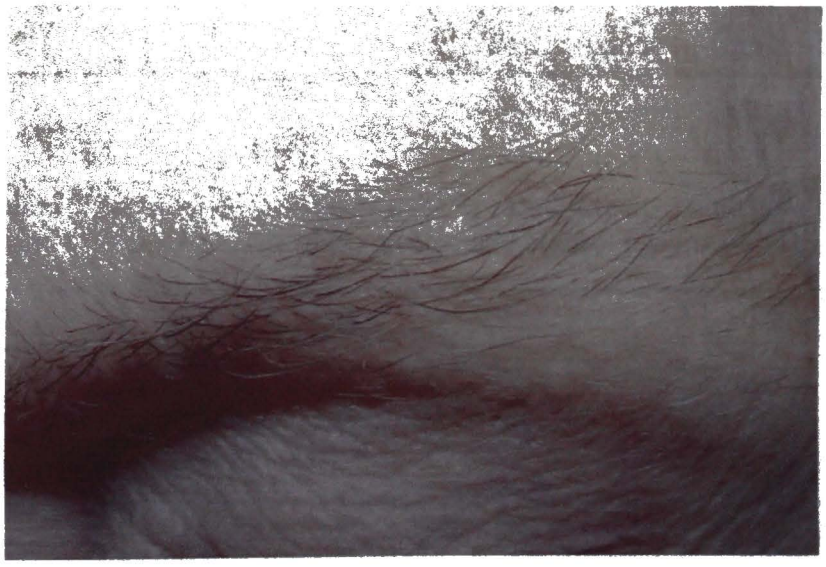


Figure 14: Representative sample of the control eyebrow of a patient taken during treatment visit 2.

Table 5: Paired T-test analysis comparing the eyebrow density results of the screening visit (SV), treatment 1 (T1) and treatment 2 (T2) visits of the treated and control eyebrow sites.

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SV treated SV control	-.0231	.4693	.1302	-.3067	.2605	-.177	12	.862
Pair 2	T1treated T1control	.0308	.3521	.0977	-.1820	.2435	.315	12	.758
Pair 3	T2treated T2control	.3385	.6172	.1712	-.0345	.7114	1.977	12	.071

Table 6: Paired T-test analysis comparing the eyebrow density results of the screening visit and treatment 2 visit of the treated and control eyebrow sites.

		Paired Differences					T	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SVtreated T2treated	-.3769	1.1271	.3126	-1.0580	.3042	-1.206	12	.251
Pair 2	SVcontrol T2control	-.0154	.4160	.1154	-.2668	.2360	-.133	12	.896

Table 7: Paired T-test analysis comparing the eyebrow density results of treatment 1 and treatment 2 visits of the treated and control eyebrow sites.

		Paired Differences					t	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	T2treated T1treated	.5154	.7925	.2198	.0365	.9943	2.345	12	.037
Pair 2	T2control T1control	.2077	.4310	.1195	-.0528	.4681	1.737	12	.108

Table 8: Microscopic analysis of hair thickness of the treated eye and control eye of each patient was conducted at 20x magnification. A photograph of each hair follicle was taken through the microscope. The measurements above were obtained directly by measuring the hair thickness on the photographs and are represented as arbitrary values.

Microscopic Hair Thickness Measurements

Study Number	SV control	SV treated	T1 control	T1 treated	T2 control	T2 treated	T3 control	T3 treated
001								
002								
003		2	1	1.8				
004								
005	1.9	1.6	1.4	1.5	1	1.5	1.1	1.5
006	2.3	2.1	1.5	1.5	1.5	2	2.5	2.2
007		2	1.8	1.9	1.3	1.1		
008	1.7	1.6	1.4	0.8	2	0.9	1.6	1.4
009			0.6	0.6	0.7	0.8		
010	1.1	1.9	1.2	1	1.5	1.4		
011								
012								
013	2.2	2	2	1.4	1.5	2.2		
014	1.2	1	1.9	1.8	1.4	1.7		
015	0.6	0.8	0.7	0.8	0.7	1.2		

Table 9: Table showing the mean and standard deviation calculations for the eyebrow hair thickness of the control and treated eyebrow sites for all patients.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
SVcontrol	9	.0	2.3	1.222	.8800
SVtreated	9	.0	2.1	1.444	.7073
T1control	9	.6	2.0	1.389	.4936
T1treated	9	.6	1.9	1.256	.4693
T2control	9	.7	2.0	1.289	.4226
T2treated	9	.8	2.2	1.422	.4790
Valid N (listwise)	9				

Table 10: Paired T-test analysis comparing the eyebrow hair thickness results of screening visit, treatment 1 and treatment 2 visits of the treated and control eyebrow sites.

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SVcontrol SVtreated	-.2222	.7463	.2488	-.7959	.3514	-.893	8	.398
Pair 2	T1control T1treated	.1333	.2828	.0943	-.0841	.3507	1.414	8	.195
Pair 3	T2control T2treated	-.1333	.5523	.1841	-.5578	.2912	-.724	8	.490

Table 11: Paired T-test analysis comparing the eyebrow hair thickness results of screening and treatment 2 visits of the treated and control eyebrow sites.

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SVcontrol T2control	-.0667	.7399	.2466	-.6354	.5021	-.270	8	.794
Pair 2	SVtreated T2treated	.0222	.6016	.2005	-.4402	.4847	.111	8	.914

Table 12: Paired T-test analysis comparing the eyebrow hair thickness results of Treatment 1 and Treatment 2 visits of the treated and control eyebrow sites

		Paired Differences					T	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	T1control – T2control	.1000	.4000	.1333	-.2075	.4075	.750	8	.475
Pair 2	T1treated T2treated	-.1667	.4555	.1518	-.5168	.1835	-1.098	8	.304

CONCLUSION

The purpose of this pilot study was to evaluate the effects of travoprost on increasing eyebrow hair thickness and eyebrow density. In order to evaluate the eyebrow hair thickness, sample hairs were taken from each eye of the patient during each study visit (when applicable). The eyebrow hair was then individually photographed under a microscope at 20x magnification. Eyebrow thickness was measured by measuring the thickness at the center of the photograph of each eyebrow hair. Eyebrow density evaluation was also made through analysis of photographic images. A photograph of each eyebrow was taken with a Sony Mavica camera at a distance of 19 cm from the patient's eyebrow. Each picture of the control and treated eye from each visit was individually evaluated by 3 independent masked reviewers. A number from 0-4 was assigned to each photograph accordingly (appendix G). All three numbers were then averaged together and assigned to that particular picture.

The findings of this pilot study show that clinically there was an increase in eyebrow density in 69% of the patients after completing the 2nd treatment. After completion of treatment visit 2 there was an 18% increase in eyebrow density of the travoprost treated eyebrow compared to less than 1% of an increase seen in the control eyebrow. Previous studies which have been done to demonstrate the side-effects of travoprost on eyelash growth were carried out for at least a 3 month long period during which a 34% change in eyelash hair was observed. There was also a statistically significant relationship between the treatment visit 1 and treatment visit 2. This relationship was shown through a T-test analysis (table 7). The p-value, when comparing density increase from the treatment visit 1 to treatment visit 2 came out to be 0.037. Since this value is less than 0.05 the T-test shows that the increase in hair density is due to travoprost treatment. Therefore the true hypothesis was accepted. Though the clinical findings (figures 7 & 8) demonstrate an increase in the eyebrow hair growth of the travoprost treated eyebrow the statistical findings (tables 5, 6, & 7) only show statistical significance between treatment visit 1 and treatment visit 2. No statistically significant differences were seen when comparing eyebrow density measurements between the screening visit and treatment visit 2 (table 6). Additionally no statistically significant differences between treated and control was seen when measuring eyebrow hair thickness.

According to current results from this ongoing pilot study, it is anticipated that there will be an increased percentage of patients demonstrating eyebrow hair growth. Four of the 13 patients in this study demonstrated at least a 50% increase

in eyebrow hair growth which suggests that further research should be done to evaluate the eyebrow hair along with eyelash growth with a larger patient population. Regrowth of eyebrow hair along with eyelash hair regrowth will benefit chemotherapy patients by decreasing infections in the eye which occur because of hair loss. Though travoprost has been known to cause many adverse reactions when used directly in the eye, most of these reactions are rare and occur only in a few patients. Therefore, treatment with travoprost for chemotherapy patients is recommended for eyebrow and eyelash hair regrowth for preventative purposes.

CHAPTER III

INTERNSHIP DISCUSSION

The internship site was at The Center for Cancer and Blood Disorders in the research department working with Ray Page, D.O., Ph.D. and Julie Weikel (research coordinator) as my on-site mentors. The purpose of this internship was to gain hands-on experience in the research aspect of the medical field along with a complete look at the entire aspect of patient care.

As an intern, I was given the opportunity to plan and carry out a research study. My objective was to evaluate the effects of $PGF_{2\alpha}$ on hair regrowth. In order to accomplish this task I completed a literature review and developed a protocol and informed consent for a clinical trial. I was also responsible for developing the study design including data entry, evaluation, and analysis tools.

Additionally, I was fortunate enough to gain knowledge on the overall process of patient care at The Center for Cancer and Blood Disorders. I was able to shadow and spend time with oncology nurses and medical assistants in areas such as radiology, medical oncology, and chemotherapy. I also shadowed physicians and nurse practitioners at other cancer centers clinics in Weatherford, Mineral Wells, and Huguley. I also attended tumor board meetings and weekly research meetings every Tuesday morning at the downtown clinic.

During the course of my internship, I observed the interactions between various departments at The Center for Cancer and Blood Disorders. By attending the weekly tumor boards, I also observed how the physicians come together to gain a better perspective on treating their patients with the best treatment options available to fit patient lifestyle. Overall, I am extremely pleased by the commitment of the research department and physicians to excellence at The Center for Cancer and Blood Disorders. My experience at the clinic has given me better insight on the entire clinical research process. Additionally, I had a chance to expand my experience working with medical professionals and cancer treatment.

DAILY JOURNAL

Tuesday May 24, 2005

Today was my first meeting with Dr. Page and Julie Weikel, the clinical research coordinator. The meeting was held at The Center for Cancer and Blood Disorders at 10:00 where Dr. Page, Julie and I discussed the topic for my research project. During the meeting, Dr. Page explained the topic to my project, which was to evaluate the effects of $PGF_{2\alpha}$ on hair growth. He further explained that this prostaglandin was developed into eye drops which are currently used for treating glaucoma. My task was to research $PGF_{2\alpha}$, and the eye drops and come up with a study design in order to test the effects of this drug on patients currently losing their eyelashes due to chemotherapy drugs, mainly docetaxel and paclitaxel.

Later that day, I went to the library in order to start my research where I found many articles related to this particular study

Wednesday May 25, 2005

Today I went to the clinic in Weatherford to shadow Dr. Page. I shadowed him while he saw several patients. During lunch, I got a chance

to meet the pharmaceutical representative. Later that day, I continued working on researching the project.

Thursday May 26, 2005

Today at the office I continued to work on researching my topic. I also started writing up the informed consent and worked on an outline for the study protocol.

Friday May 27, 2005

Today I went to the clinic in Weatherford to shadow Dr. Page. I shadowed him while he saw several patients. During lunch, I talked with Dr. Page about my research findings. He suggested that I do more research on Travatan®, manufactured by Alcon, Fort Worth, TX. This way we would have an easier time in getting the drug for the patients.

Monday May 30, 2005

Today, I completed the first draft of the informed consent and started to write up the protocol using the research I had conducted on the topic.

Tuesday May 31, 2005

I worked on finishing up the first draft of the protocol and finalizing the informed consent before the committee meeting took place at 2:00. During the committee meeting, I explained to Julie Weikel, Dr. Sheedlo and Dr. Bens about the study and some background information about $PGF_{2\alpha}$ and Travoprost. They discussed with me the deadlines for the proposal and what needs to be included in it. Dr. Bens also suggested that we speak with Dr. Goode who is an ophthalmologist currently working for

Alcon. Later that day, I spoke with Sharon from the UNTHSC IRB about the study and what I would need to do in order to proceed with it. She said that she would speak to someone about it and get back to me. I also went to Dr. Bens office in order to look at sample research proposals and internship reports.

Wednesday June 1, 2005

Today, I spoke with Sharon from the IRB who referred me to Dr. Jerry McGill. I spoke with Dr. McGill who informed me via e-mail that an IND must be submitted to the FDA before the study can be approved by the IRB. Later, I continued to work on my proposal by doing a literature search.

Thursday June 2, 2005

I spoke with Jennifer Crawford and Julie Weikel about what Dr. McGill had said about submitting the IND form to the FDA. Jennifer had also informed me today that I would only have to submit to the UNTHSC IRB. Today, I also continued working on the protocol and finished the final draft.

Friday June 3, 2005

Today I went to the Weatherford Clinic and shadowed Dr. Page. Later, during a quick meeting, he informed me that he spoke with Dr. Goode. Dr. Goode suggested that we continue the study by applying the drug on their eyebrows instead of directly into the patient's eyes in order to reduce the side effects of the drug.

Monday June 6, 2005

Today I called the FDA and spoke with Melony about the IND. She did give me some information about how long it would take and what I would need to submit. I also e-mailed Dr. McGill in order to set up a meeting. I continued to work on and finished writing up a protocol synopsis in order to submit to Alcon. I also changed the informed consent, made a medication log, and a flyer advertising the trial.

Tuesday June 7, 2005

Today, I attended the tumor board meeting and the research meeting during the morning hours. Throughout the day I worked on finishing the protocol and later met with Dr. Bens to discuss the project more extensively.

Wednesday June 8, 2005

This morning Dr. Bens and I met with Dr. McGill who informed us about the three options we had in order to continue this project. We later spoke with Carla Lee in the graduate school admissions office about extending the internship. Later, Dr. Bens and I worked out the plans and made an outline for another committee meeting during lunch.

Thursday June 9, 2005

From 9:00am until 12:00pm I was in the radiology front office and the front office at the downtown clinic. I got a basic understanding as to how patients are scheduled in and how they are checked into the system. Later,

I worked on the informed consent and the protocol. I also called Melony at the FDA again in order to get more information about submitting the IND form.

Friday June 10, 2005

This morning from 9:00am until 12:00pm I shadowed Dr. Mendel at the downtown clinic. Later that day I worked on completing the protocol.

Monday June 13, 2005

This morning I shadowed Dr. Jordon. I got a chance to speak to a few of his patients about how they were doing with the progression of their disease. I later finished up the final draft of the protocol and informed consent and filled out the IND submission forms.

Tuesday June 14, 2005

This morning I attended the tumor board meeting and the research meeting at 9:00. At 1:00 there was another committee meeting set up with Dr. Bens, Dr. Page and Julie Weikel. During this meeting we further discussed the project and decided to go on with the project and submitting the IND form. I edited the final draft of the protocol and gave it to Dr. Page for any additional recommendations.

Wednesday June 15, 2005

This morning I shadowed Dr. Chris Jordan between 9:00am-12:00pm. I later spoke with Debbie from the UNTHSC-IRB who advised me to speak with Dr. Bens about the study. Dr. Bens informed me that she had decided not to continue on with the project due to the many risks involved.

She further informed me that there is a meeting set up with her to meet with Dr. Yorio and Dr. Vishwanatha to finalize that conclusion.

Thursday June 16, 2005

Dr. Bens informed me today that we will continue with the study without IRB approval. Additionally, neither Dr. Page nor I will be able to publish any of the results obtained from the study. Later that afternoon, I worked with Jennifer Crawford on other IRB submissions for other ongoing research studies.

Friday June 17, 2005

Today I met with Dr. Page at the clinic in Weatherford. I was in the front office between 10:00am and 1:00pm observing the process of patient check-in. During lunch Dr. Page and I met with the pharmaceutical representative and later discussed in great detail about the study and the internship. We both agreed on continuing the same project without publication.

Monday June 20, 2005

This morning I shadowed Dr. Friess along with a resident doctor who was also shadowing him. In the afternoon, I met with Cindy Glutman who taught me to use the MedOnc computer system and searching the patient's charts. I later finalized the protocol and worked on forming a list of possible study patients.

Tuesday June 21, 2005

This morning I attended the tumor board conference and the research meeting. Between 10:00am and 12:00pm there was a site initiation visit by Genentech at the downtown office which I attended.

Wednesday June 22, 2005

I finalized the protocol synopsis for Alcon and started working the research proposal.

Thursday June 23, 2005

I worked on writing my research proposal all day today.

Friday June 24, 2005

I went to the weatherford clinic and shadowed Dr. Young who saw many breast cancer patients. I asked her about shadowing her again when she sees the prison inmates at the downtown clinic. During lunch, I met with Dr. Page and talked a little more about the project.

Monday June 27, 2005

Today I was at the library working on my research proposal.

Tuesday June 28, 2005

I worked on researching for my proposal more and started organizing and writing the proposal.

Wednesday June 29, 2005

I went to the Huguley Clinic and shadowed a nurse practitioner, Sandy Laird. We saw a variety of patients ranging from patients with breast cancer to colon cancer.

Thursday June 30, 2005

This morning I shadowed Dr. Ross from 9:00am to 12:00pm. After lunch, I looked through patient charts in order to recruit more patients.

Friday July 1, 2005

I went to the Weatherford clinic today and shadowed Dr. Page. Today he was seeing many patients including a couple of new patients. I gained a better perspective on the differences between new patient visits versus visits with existing patients.

Monday July 4, 2005

Out of office. All TCC clinics were closed.

Tuesday July 5, 2005

The tumor board and research meetings were cancelled today. I looked through patient charts today and try to meet with a couple of patients. I also spoke with the radiology staff about my study and asked them to keep an eye out for possible patients.

Wednesday July 6, 2005

Today, I worked on collecting additional background research for the research proposal.

Thursday July 7, 2005

I went to the clinic in Huguely and shadowed Dr. Clibon and Sandy Laird. It was a very fast paced clinic and I observed her talk to a large variety of cancer patients. During the afternoon, I worked on writing my proposal.

Friday July 8, 2005

Out of Office today; Dr. Page on vacation. I worked on the research proposal most of the day.

Monday July 11, 2005

This morning I went to the office and searched for certain patients with appointments. I informed two patients about the study and they seemed interested in being a part of it. Additionally, I told them that we were waiting on getting the drug donated and they will receive additional information as soon as that goes through.

Tuesday July 12, 2005

This morning I attended the tumor board and the research meeting. Later, I worked on the research proposal at the office in downtown.

Wednesday July 13, 2005

Today, I went to the lab in the medical office in downtown and observed the lab technicians working there. I was able to see who they run the various lab tests which need to be done and also saw some samples on the slides. I was there for about 3 hours. Later, I worked on completing my density log and the rest of the proposal.

Thursday July 14, 2005

I worked on making the title page for the proposal and organizing all the items in the appendix.

Friday July 15, 2005

I went to the clinic in Weatherford and followed Dr. Page throughout the morning where he saw many patients with colon and lung cancer. Later that afternoon, I continued working on finishing my proposal which Dr. Page looked over.

Monday July 18, 2005

Today I went to the clinic in Weatherford and shadowed Mary Hiatt, the nurse practitioner. I got a different perspective on patient care and was able to also see how patients respond differently sometimes to nurse practitioners rather than physicians. I was also able to get a better understanding of what nurse practitioners are able to do such as prescribing drugs and diagnosing patients.

Tuesday July 19, 2005

I attended the tumor board in the morning along with the research meeting at 9:00am. In the afternoon, I went up to the campus and spoke with Dr. Vishwanatha about my proposal and gave him a copy to look over and approve. I also tried to get a hold of Dr. Sheedlo, but he was out of town.

Wednesday July 20, 2005

I went to Dr. Good's office in order to speak to him about the study and get samples of Travatan which he had in his office. He informed me that Alcon would have the drugs to him by next week and he would then also

lend me a camera in order to take my pictures. I got 4 samples of Travatan® from him which I can start using for the study.

Thursday July 21, 2005

I worked on the proposal; mostly editing

Friday July 22, 2005

I went to the clinic in Weatherford and followed Dr. Page while he visited his patients. Later, I spoke to him about what Dr. Goode had said about the drugs being donated from Alcon.

Monday July 25, 2005

Today, I worked on editing my research proposal checked by Dr. Page and Dr. Vishwanatha. I also changed the density measurement sheet. Additionally I printed out new medication log sheets for the patients along with informed consents and information packets.

Tuesday July 26, 2005

I attended the tumor board meeting and the research meeting in the morning. Later, I looked on MedOncology in order to search for more patients to enroll in the study.

Wednesday July 27, 2005

I completed and turned in my research proposal to Dr. Bens via e-mail. It had been approved by all the committee members except for Dr. Sheedlo. I later worked on getting all papers together to give to my patients throughout the duration of the study.

Thursday July 28, 2005

Today, I went to pharmacy and shadowed the two pharmacy techs. I learned about how they get the orders for the drugs and which ones they mix to send out to the chemo patients. I later spoke with the pharmacist who went through his job responsibilities with me. Later today, I worked on recruiting more patients for the study.

Friday July 29, 2005

Today, I went to the clinic in Weatherford and shadowed Dr. Page while he visited with his patients. I stayed there until about 1:00 and also looked for more patients to recruit.

Monday August 1, 2005

I made and put together charts in order to organize all the paperwork for different patients.

Tuesday August 2, 2005

This morning I attended the tumor board meeting at 7:30am. There were many interesting cases to be discussed involving ethical issues in concern. At about 9:00am, there was a weekly research meeting which I attended. The rest of the day, I looked up patients schedule for tomorrow and continued on collecting additional research.

Wednesday August 3, 2005

I went to Weatherford today at 8:00am to see 2 study patients. I took pictures of both of them and got sample lashes. I then drove to the clinic in downtown and worked on printing and organizing all of my pictures.

Thursday August 4, 2005

Out of office.

Friday August 5, 2005

I went to Weatherford again today to visit with a new patient who Dr. Page thought would be a good candidate. I went to the clinic at 9:00am and saw the patient at 11:30am. She did not seem interested in the study. I later went to school in order to find out about the use of the microscope and to turn in my research proposal. I also made a patient follow-up phone call today.

Monday August 8, 2005

Today, I went to the weatherford clinic at 8:30am and met with a patient. I took her pictures and sample eyebrow hairs. I then waited for another patient while checking and responding to e-mail and organizing patient information. I met with the second patient and explained to her what the study consisted of. She seemed interested and signed the informed consent. I gave her a bottle of Travatan® and took pictures of both of her eyes. I later went to the clinic in downtown and met with two potential study candidates. One of the patients did not seem interested in the study. I spoke with the other patient and explained the study to her. She informed me that she will let me know by tomorrow if she was interested.

Tuesday August 9, 2005

At 7:30am today, I attended the tumor board conference and immediately following was the weekly research meeting. I then met with my patient

from yesterday and she informed me that she was not interested in the study. I met with another study candidate at 11:30am and she said that she will speak to her doctor about the study before giving me a confirmed answer on whether she wants to join or not.

Wednesday August 10, 2005

I went to the clinic in weatherford today to visit with a potential study candidate. I spoke with her and explained the study to her. She seemed interested and signed the informed consent. She visited with Dr. Page in order to get her required physical exam completed. I then took pictures of her eyebrows and gave her a bottle of the eye-drops. I then went to the downtown clinic and worked on making the view in epi-info for my data collection.

Thursday August 11, 2005

I worked on entering data into epi-info and getting more familiar with the program. In the afternoon, I went to the school to give the research proposal to Dr. Vishwanantha to review.

Friday August 12, 2005

Most of the day today, I worked on printing out patient notes and organizing their information into their folders. I also worked on printing out the pictures which I had taken and organizing them into the album.

Monday August 15, 2005

Today, I worked a little more on epi-info and getting more familiar with the program. I then wrote up specifics on measuring the eyebrow hairs

and how it would be judged. Later, I printed out the pictures I had so far and organized them into the album. I also made a 2 week follow-up phone call to a patient.

Tuesday August 16, 2005

I attended the tumor board conference at 7:30am and went to the research meeting at 9:00am. The rest of the day, I worked on printing out patient visit notes and organizing patient information.

Wednesday August 17, 2005

This morning, I went to medical oncology and sat in with the medical assistants. I learned how they schedule patients and how patient flow works over there. Later that afternoon, I worked on printing and organizing pictures. I made two follow-up phone calls and looked up patient appointments for tomorrow.

Thursday August 18, 2005

I went to Mineral Wells this morning to recruit more patients for the study. I met with 4 patients, 3 of which were interested in joining the study. I consented all three of them and took pictures & obtained sample hairs. Later that afternoon I went to the library to work on my literature search for the thesis. I also worked a little bit more on epi-info.

Friday August 19, 2005

I went to Weatherford today and visited patients with Dr. Page until about 2:00pm

Monday August 22, 2005

I made many follow-up phone calls today and left a message for most of my patients. I then stayed in the office and worked on my journal and data entry. I also looked up patients' schedules for the following day.

Tuesday August 23, 2005

In the morning, I attended the tumor board conference and the research meeting. I later met with a patient in the chemotherapy area and took pictures along with obtaining sample eyebrow hairs. I also called a patient back from yesterday in order to confirm an appointment.

Wednesday August 24, 2005

From 9:00am until 1:00pm I shadowed Lisa Holland a nurse practitioner at the clinic in downtown. During the afternoon, I made a follow-up phone call to a patient and made an appointment to meet with her tomorrow in Weatherford. I then called and spoke with two other patients. I met with a new patient and talked to her about the study. I then called Dr. Goode concerning the eye-drops and informed him that I will need more bottles soon. He told me to call him back in a week and he will see what he can do.

Thursday August 25, 2005

I went to Weatherford in the morning to meet with a patient. She was here because she ran out of drops so I went to give her another bottle. I also gave her more log sheets. Later this afternoon, I worked on organizing patient charts.

Friday August 26, 2005

I was supposed to go to weatherford today, to meet with a patient but she ended up rescheduling. I made a few follow-up phone calls and checked patients' appointment schedules.

Monday August 29, 2005

I went to the Weatherford clinic today to meet with a patient for her follow-up visit. I stayed there until 12:00pm and then went to the library to do more research.

Tuesday August 30, 2005

I went to the downtown clinic for the tumor board conference and research meeting in the morning. I could not attend the entire research meeting because I had to go meet with a patient for her follow-up visit. I took her pictures and obtained samples. I later went to school and took pictures of some of the hair samples through a microscope.

Wednesday August 31, 2005

I went to the Weatherford clinic today in the morning to visit with a patient for a follow-up visit. I was supposed to go to the clinic in Huguley and shadow a nurse practitioner, Helena, but was not able to make it there because I had to see my patient. I then made some follow-up phone calls to some patients from the downtown clinic.

Thursday September 1, 2005

I was out of the office today but I made some follow up phone calls in order to confirm appointment times for patients who go to the clinic in Mineral Wells. Later, I also worked on researching for the thesis.

Friday September 2, 2005

I went to Weatherford and met with a patient for a follow-up visit. I took her pictures and obtained sample hairs. I also called Dr. Goode back to find out about the eye-drops and he again told me to call him back in a couple of days. I then went to go develop the pictures that I took with the microscope and measured the thickness of the hair samples through the pictures.

Monday September 5, 2005

I worked on my thesis background information. I also worked on looking for illustrations and graphs.

Tuesday September 6, 2005

I attended the tumor board conference this morning at 7:30am. Following the conference I sat in the research meeting at 9:00am. I then spoke with a patient as a follow-up call and made sure she was doing okay. Later, I worked on my journal and entering more data into epi-info.

Wednesday September 7, 2005

I went to the clinic in Weatherford at 8:30am to meet with 4 patients for their follow-up visits. I met with all four of them and took pictures and sample hairs for all of them. Later that afternoon, I made some follow-up

phone calls and called Dr. Goode again. His secretary informed me that I can come by and pick up the eye-drops. I then printed out more pictures and organized them in the album.

Thursday September 8, 2005

I went to Mineral Wells and met with one of the patients there. The other two will be seen next week. I stayed there until about 11:00am. In the afternoon, I came back to the downtown clinic and printed out patient notes to put in their charts. I also made more copies of the daily medication log sheets. I then went by Dr. Goode's office to pick up the box of eye-drops.

Friday September 9, 2005

All day today, I worked on writing my thesis.

Monday September 10, 2005

I went to the library today because I did not have any patients to see. I worked on learning more about epi-info and also entered more data into the program. I also looked up more articles on prostaglandin analogues.

Tuesday September 11, 2005

I attended the tumor board conference at 7:30am. Following that, I went to the research meeting. I then caught up on my journal and organized some pictures.

Wednesday September 12, 2005

I met with a new patient today at the downtown clinic. I explained to her about the study and she seemed interested. I also made some follow-up

phone calls. I then called the two patients at Mineral Wells to confirm their appointments for tomorrow.

Thursday September 15, 2005

I went to Mineral Wells today and met with both of my patients at 11:00am and at 2:00pm. I was there mostly all day and made two follow-up phone calls while I was there. I also updated some patient information. I was informed today that one of my patients on the study was taken off the study by Joyce. The patient was experiencing red eyes and was sensitive all around the eye. She was also experiencing a headache on the side of the treated eye. I tried to call the patient but got no answer.

Friday September 16, 2005

I worked on organizing pictures and eyebrow hair samples. I also worked a little on my thesis.

Monday September 19, 2005

I went to Weatherford today to meet a patient in order to take pictures. I then made some follow-up phone calls and updated patient information.

Tuesday September 20, 2005

Attended the tumor board conference at 7:30am and then sat in on the research meeting at 9:00am. I then met with two patients for their follow-up visits at the downtown clinic.

Wednesday September 21, 2005

All day today, I worked on organizing information for the thesis and putting all the research in order.

Thursday September 22, 2005

I went to visit a patient for a follow-up visit at the downtown clinic. I took her pictures and gave her another bottle of the eye-drops. I then made some follow-up phone calls. The rest of the afternoon, I printed out pictures and organized them into the album.

Friday September 23, 2005

I went to the library and started writing up my thesis. I reviewed some more articles and worked on my background and materials and methods sections.

Monday September 26, 2005

I called up a patient and tried to locate her because her phone number had changed. I then looked up her schedule to see when she was supposed to come in to the office. The rest of the day, I worked on my thesis and reformatted the protocol. I then did more research on hair and hair growth.

Tuesday September 27, 2005

I went to the tumor board conference and the research meeting this morning. I then met with one of my patients for a follow-up visit. The rest of the afternoon, I went to the library and worked on my thesis.

Wednesday September 28, 2005

I went to Weatherford this morning to visit with a patient for her follow-up visit. I then called up two patients for their follow-up phone calls and to check with them about their schedules. I finally got a hold of the

patient who experienced and adverse event. She stated that her eye had cleared up and that it took two weeks to completely clear up. I went back to the downtown clinic and spoke with Jennifer about maybe shadowing Dr. Buchanan during surgeries. I then printed out all of my pictures and stayed late in order to finish printing. I also made a chart to keep track of the eye-drops count and worked on epi-info.

Thursday September 29, 2005

I went to Mineral Wells this morning to meet a patient for her follow-up visit. I then looked up a patients schedule for tomorrow. I then went back to the clinic in downtown and caught up on my journal. I also printed out a manual for epi-info and printed out all patient notes in order to update charts.

Friday September 30, 2005

I went to Weatherford this morning for a follow-up visit with a patient. I met with her and printed out her exam notes. I then called up a few patients to reschedule their appointments. Then, I went back to the clinic in downtown and made a patient questionnaire. Later that afternoon, I attended the clinical research internship meeting at 3:00pm.

Monday October 3, 2005

I went to Weatherford this morning for a follow-up visit with a patient. While taking her picture, I saw some growth on her treated eye and was able to tell a difference between the two eyebrow sites! I then informed Dr. Page about it and he told me that in a cancer study with about 14

patients, one is statistically significant to move forward. Later in the afternoon, I went to the library and worked on my thesis.

Tuesday October 4, 2005

I attended the tumor board this morning at 7:30am where they discussed typical scanning vs. melanoma scanning. I then attended the research meeting at 9:00am. I spoke with three patients for their 2 week follow-up. I then went to school to work on my thesis.

Wednesday October 5, 2005

I worked on writing up chapter two of my thesis at school. I also spoke with Dr. Agrawal about using the microscope in his lab. Additionally, I made a few follow-up phone calls.

Thursday October 6, 2005

I worked on the thesis in the library. I also transferred all of the hair samples from the album to petri dishes.

Friday October 7, 2005

I went to Weatherford to meet with a patient at Radiology Associates in Weatherford. I first stopped at the clinic to get a bottle of the drops to give to the patient. I then met up with her for her follow-up visit. I explained to her about the study again including the time period because she did not seem to understand it the first time.

Monday October 10, 2005

Today I worked on my thesis all day. I worked on writing the background information and making charts for the patient demographic information.

Tuesday October 11, 2005

Today I worked on my thesis again all day. I worked on organizing the statistics and obtaining charts through excel.

Wednesday October 12, 2005

Today I worked on the background information for my thesis. I also worked on learning how to use SPSS in order to make graphs for my results. I then made some follow-up phone calls to two patients. One of those patients is supposed to be moving to San Antonio and did not know when she can meet with me next. We decided that if she was still here in two weeks then I'll see her and she will call me as soon as she finds anything out.

Thursday October 13, 2005

Today I went to the clinic in downtown to meet a patient for her follow-up visit. I then made some follow-up phone calls to about 3 patients. Then I went to the library to work on my thesis.

Friday October 14, 2005

I made one follow-up phone call today. I then worked on my thesis background all day. I also went to go talk to Carolyn in the graduate office about my defense date.

Monday October 15, 2005

I worked on my thesis all day today and also caught up on writing my journal.

Tuesday October 16, 2005

Today I attended the research meeting at 9:00am. I then met with two patients for their follow-up visits. After lunch, I went to school to get my defense date sheet signed by all my committee members. I then worked on my thesis.

Wednesday October 17, 2005

I worked on re-formatting my journal and caught up on writing it. I then worked on the thesis title page and appendix. Then I wrote a little more on the background and added in illustrations. I also looked up a patient appointment schedule. I then wrote in appointment times and follow-up phone call days for all patients.

Thursday October 18, 2005

I went to the Mineral Wells clinic this morning for a follow-up treatment visit for a patient. It was her last treatment visit so I also had her fill out the patient questionnaire. I then visited some patients along with Dr. Page. Then I went to the library at school to work on my thesis. I looked up 3 more articles and scanned in all my illustrations.

Friday October 19, 2005

I will be working on completing my thesis from now on and continue going to the clinic for follow-up patient visits.

APPENDIX A

PROTOCOL SYNOPSIS

Title	An Open-Label Pilot Study Evaluating the Effects of Travoprost on Eyebrow Regrowth among Patients Undergoing Chemotherapy for Cancer Treatments
Principle Investigator **Student Co-Investigator**	Ray Page D.O., Ph.D. Nausheen Habib, B.S.
Study Objective	The primary objective of this study is to evaluate the ability of Travoprost to increase eyebrow hair thickness, and density on cancer patients undergoing cytotoxic chemotherapy and/or who have already completed chemotherapy.
Study Design	This study is a pilot study in patients who have gone through or are currently going through chemotherapy. Patients, who have lost their eyebrows or are in the process of losing their eyebrows while undergoing cytotoxic chemotherapy prior to the screening visit, will be screened for study inclusions. Patients, who have met all inclusion/exclusion criteria, will be enrolled into the study. Patients will be enrolled in a 14 week study. Patients will be evaluated at screening (baseline), and at weeks 4, 8, and 12. A post treatment follow-up visit will occur 14 days after the last dose of study medication. Total study participation time will be approximately 14 weeks, including screening, treatment, and follow-up.
Subject Selection	Approximately 14 male and female adult patients (over the age of 18 years) with uncomplicated reactions to chemotherapy will be enrolled in this study. Patients must also meet all of the inclusion and exclusion criteria. **Inclusion Criteria:** • Capable of providing informed consent. • Men and women of non-childbearing potential above the age of 18 years. Women of child-bearing potential (WCBP) must have a negative urine pregnancy test at Baseline and must agree to use adequate measures of contraception [oral contraceptives, contraception patch, birth control injections, intrauterine device (IUD), or double barrier method] to avoid pregnancy during the study. • Patients undergoing chemotherapy or who have recently (i.e., no longer than 6 months prior to screening visit) undergone chemotherapy in order to treat cancer; and who have lost their eyebrows as a side-effect of cytotoxic chemotherapy.

	• Patients must be willing to adhere to the study visit schedule and other protocol requirements. **Exclusion Criteria:** • Patients who, in the 2 weeks prior to study screening, have had any changes to their concomitant medication(s) (i.e., new medication or change in dosage) that might affect reaction to treatment. • Patients who currently have glaucoma and are being treated with bimatoprost, latanoprost and/or travoprost • Patients who have undergone intraocular surgery, laser trabeculoplasty, or laser iridotomy. • Patients who have a history of uveitis within 12 months prior to the beginning of treatment or during the treatment period; and those with changes in the ophthalmic treatment regimen within 6 months prior to the beginning of treatment • Pregnant or lactating women, as well as women of childbearing potential who are not using an acceptable method(s) of contraception. • Any concomitant illnesses, laboratory abnormalities, or other findings that place the patient at unacceptable risk, in the opinion of the Investigator. • Patients who cannot communicate with the Investigator or who are unlikely to cooperate with the requirements for the study. • Use of any of the treatment medication within 30 days prior to the screening visit.
Study Procedure	A review of all inclusion/exclusion criteria to verify that the patient qualifies for the study will be conducted at the screening visit. All patients who meet the inclusion/exclusion criteria and who have given consent will go through the treatment period where they will receive two drops of travoprost twice a day. Travoprost will be applied topically and unilaterally at the site of eyebrow growth. Patient's second eye will be used as control. The duration of the study will be approximately 14 weeks, which includes the screening period, treatment period, and follow-up visits. 5 scheduled visits which will include one baseline visit at day 0, and four treatment visits at the end of weeks 4, 8, 12, and 14.

Additionally 3 follow-up phone calls will be made every 2 weeks throughout the treatment period.

During each study visit, including the follow-up visit, the patient will participate in the following screening and study procedures: read and sign consent form (screening visit only), obtain a complete medical history (screening visit only), documentation of all medications taken 8 weeks prior to the screening visit (i.e. prescription medication, over-the-counter drugs, herbal preparations, and vitamins), physical exam including measurements of vital signs (blood pressure, pulse, temperature, and respiratory rate) and weight, urine pregnancy test (screening visit and final treatment period), review of any adverse events, obtain a sample eyebrow hair (if available), photographs will be taken of each eyebrow, collection of medication log.

Statistical Analysis

Criteria for Evaluation:

To quantify an increase in eyebrow density, a photograph of each eyebrow site (control and experimental) will be presented to 3 independent reviewers. Each individual reviewer will evaluate the photograph and assigning a number (0-4) to each photograph according to a standardized scale. The three numbers from each evaluator will then be averaged and assigned to the photograph as the increase in eyebrow density. Each photograph will be taken according to the standardized set procedures. Growth in eyebrow hair thickness will be evaluated through a microscopic analysis of a sample from the patient. A 50% increase in hair thickness and/or eyebrow density will be considered statistically significant.

Subject Selection

The study will enroll enough patients in order to see a 50% increase in hair thickness and/or eyebrow density. In order to calculate the appropriate number of patients, the following assumptions will be made:

1. A two-sided t-test
2. 80% power at a 95% confidence interval

Taking these assumptions into consideration, a total patient population of 15 patients will be enrolled into the study. The patients own eye will serve as control, therefore the drug will be applied to 15 eyebrow sites and the other 15 sites will serve as control. This will give a total number of sites being studies to equal 30.

Risk/Benefit Assessment	The potential risks of using travoprost eye drops directly in the eye include ocular hyperemia, decreased visual acuity, eye discomfort, pain in the eye, foreign body sensation, pruritus, abnormal and blurred vision, inflammation of the eyelids and cornea, cataract, cell conjunctivitis, dry eyes, iris discoloration, photophobia, subconjunctival hemorrhage, and tearing. Other rare nonocular effects include: angina, anxiety, arthritis, back pain, slow heartbeat, bronchitis, chest pain, cold syndrome and depression. Since the eye drops will be topically applied to the eyebrows and not directly in the patient's eyes, there are minimal risks involved with this study. Given that the risks involved have been minimized, the significant benefits of this study outweigh the risks involved.
Research Sites	**Medical Center Clinic** 800 West Magnolia Fort Worth, TX 76104 Phone (817) 759-7000 **Weatherford Clinic** 907 Foster Lane Weatherford, TX 76086 Phone (817) 596-0637 **Huguley Clinic** 11805 S. Freeway, Ste 201 Burleson, TX 76028 Phone (817) 551-5312 **Mineral Wells Clinic** 400 S.W. 25th Avenue Mineral Wells, TX 76067 Phone (940) 325-0627

APPENDIX B

Disclosure and Consent
Medical Treatment and Procedures

You have the right, as a patient, to be informed about your condition and the recommended medical or diagnostic procedure to be used so that you make the decision whether or not to undergo the treatment/ procedure after knowing the risks and hazards involved. This disclosure is not meant to scare or alarm you; it is simply an effort to make you better informed so you may give or withhold your consent to the treatment/procedure.

I voluntarily request my physician, and such associates, technical assistants and other health care providers as they may deem necessary, to treat my condition which has been explained to me as: (Loss of eyebrow hairs due to cytotoxic chemotherapy):

I understand that the following medical and/or diagnostic procedures are planned for me and I voluntarily consent and authorize these procedures: Travoprost treatment for eyebrow hair regrowth after undergoing chemotherapy. (Investigational use of an approved drug)

I understand that my physician may discover other or different conditions that require additional or different procedures than those planned. I authorize my physician, and such associates, technical assistants, and other health care providers to perform such other procedures that are advisable in their professional judgment.

I understand that no warranty or guarantee has been made to me as to result or cure. Just as there may be risks and hazards in continuing my present condition without treatment, there are also risks and hazards related to the performance of the medical and/or diagnostic procedures planned for me. I realize that the following effects risks and hazards may potentially occur and/or increase if the medication is applied directly into my eyes: increased amount of blood in the eye chamber, decreased eye pressure decreased visual acuity, eye discomfort, itching, abnormal or blurred vision, inflammation of the eyelids and/or cornea, cataract, dry eyes, iris discoloration, light sensitivity, subconjunctival hemorrhage, eye disorder, and tearing. Other rare effects also include chest pain, anxiety, arthritis, back pain, slow heartbeat, bronchitis, cold syndrome, depression, indigestion, gastrointestinal disorder, headache, high cholesterol, high blood pressure, infection, pain, prostate disorder, sinusitis, urinary incontinence and urinary tract infection.

I have been given an opportunity to ask questions about my condition, alternative forms of treatment, risks of non-treatment, the procedures to be used, and the risks and hazards involved, and I believe that I have sufficient information to give this consent.

I certify this form has been fully explained to me, that I have read it or have had it read to me, that the blank spaces have been filled in, and that I understand its contents.

Date:_____ Time: _____

_____ _____

Patient or legally responsible person Witness

Patient Name:

APPENDIX C

TRAVOPROST INFORMATION PACKET

TITLE: AN OPEN-LABEL PILOT STUDY EVALUATING THE EFFECTS OF TRAVOPROST ON EYEBROW REGROWTH AMONG PATIENTS UNDERGOING CHEMOTHERAPY FOR CANCER TREATMENTS

SPONSOR: University of North Texas Health Science Center
3500 Camp Bowie Blvd
Fort Worth, TX 76107
(817) 735-2000

PRINCIPAL INVESTIGATOR: Ray Page D.O., Ph.D.
STUDENT CO-INVESTIGATOR: Nausheen Habib, B.S.

This document describes the purpose, procedures, benefits, risks, and safety measures of the study. It also explains other treatment methods available for you and your right to remove yourself from the study at any time. No assurances can be made as to the results of this study.

If you are not completely truthful with your study doctor/nurse about your health history, you may harm yourself by participating in this study.

PURPOSE OF STUDY:

You are being asked to participate in a study evaluating the effects of Travoprost eye drops on eyebrow regrowth.

Travoprost is a FDA approved drug currently used in the treatment of glaucoma and ocular hypertension. Hair growth (i.e., eyelashes, eyebrows, and upper cheek region), being a common side-effect of using travoprost, is being measured in patients who are loosing their eyebrow hair due to chemotherapy treatments.

NUMBER OF PARTICIPANTS:

About 14 male and female patients will be participating in this study.

LENGTH OF THE STUDY:

The study will be approximately 14 weeks including the screening visit, treatment period, follow-up phone calls, and follow-up visits. When the target number of subjects have entered the treatment phase of the study, any extra enrollment will be closed. Therefore, it is possible that you were in the screening phase, ready to enter the treatment phase, and be discontinued without your consent if the target number of patients have already been enrolled into the treatment phase of the study.

STUDY PROCEDURES:

If you agree to participate in the study, you will be asked to read and sign the consent form before any study procedures can be started. If you qualify for the study, you will receive the study medication and medication log. In addition to the following visits, a 2 week follow-up phone call will be done throughout the study period.

The following tests and procedures will be performed at the Screening Visit/Baseline Visit (Day 0): The screening period may last up to 7 days after the initial screening visit has been completed.

1. A complete medical history will be obtained.

2. All medications in the last 4 weeks, including any over-the-counter drugs, herbal medications, and vitamins used in the prior 4 weeks will be documented.

3. A brief physical exam, including vital signs (i.e., blood pressure, respiratory rate, pulse, temperature) and weight.

4. A urine pregnancy test will be conducted where necessary.

5. A hair sample from each eyebrow will be obtained (if available) in order to measure length, and thickness. A photograph of each eyebrow will also be taken in order to measure eyebrow density.

6. Review of all inclusion/exclusion criteria to verify that the you qualify for the study.

7. If you meet all the criteria, you will receive study medication and the medication log and begin treatment. Treatment may begin up to 7 days after the initial screening visit.

The following tests and procedures will be performed during the Treatment Visits (Weeks 4 and 8):

1. Measurements of vital signs (i.e., blood pressure, respiratory rate, pulse, temperature) and weight will be obtained and documented.

2. A review of your current medications will be conducted.

3. You will be asked about adverse events. Any worsening illnesses will be recorded as adverse events.

4. You will be asked about study medication dosing, and the patient medication log will be reviewed.

5. A hair sample from each eyebrow will be obtained (if available) in order to measure length, and thickness. A photograph of each eyebrow will also be taken in order to measure eyebrow density.

The following tests and procedures will be performed at the Final Study Visit (Week 12):

1. Measurements of vital signs (i.e., blood pressure, respiratory rate, pulse, temperature) and weight will be obtained and documented.

2. A review of your current medications will be conducted.

3. You will be asked about adverse events. Any worsening illnesses will be recorded as adverse events.

4. You will be asked about study medication dosing, and the patient medication log will be reviewed.

5. A hair sample from each eyebrow will be obtained (if available) in order to measure length, and thickness. A photograph of each eyebrow will also be taken in order to measure eyebrow density.

The following tests and procedures will be performed at the Follow-up Visit (Week 14):

1. Measurements of vital signs (i.e., blood pressure, respiratory rate, pulse, temperature) and weight will be obtained and documented.

2. A review of your current medications will be conducted.

3. You will be asked about adverse events. Any worsening illnesses will be recorded as adverse events.

4. A hair sample from each eyebrow will be obtained (if available) in order to measure length, and thickness. A photograph of each eyebrow will also be taken in order to measure eyebrow density.

RISKS INVOLVED:

The following risks may potentially occur and/or increase if the study medication is accidentally applied directly into the eye of the patient.

Very Common Side Effects (Greater than 10%)
- Ocular hyperemia (increased amount of blood in the eye chamber)
- Decreased intraocular pressure

Common Side Effects (1-5%)
- Decreased visual acuity (clearness, sharpness)
- Eye discomfort
- Pain in the eye
- Foreign body sensation
- Pruritus (itching)

Uncommon Side Effects (0.2-5%)
- Abnormal vision
- Blurred vision
- Inflammation of the eyelids
- Cataract
- Conjunctivitis (inflammation)
- Dry eyes
- Eye disorder
- Iris discoloration
- Inflammation of the cornea
- Photophobia (light sensitivity)
- Subconjunctival hemorrhage
- Tearing

Nonocular Effects (1-5%)
- Angina pectoris (chest pain)
- Anxiety
- Arthritis
- Back pain
- Slow heartbeat

- Bronchitis
- Chest pain
- Cold syndrome
- Depression
- Indigestion
- Gastrointestinal disorder
- Headache
- High cholesterol
- High blood pressure
- Infection
- Pain
- Prostate disorder
- Sinusitis
- Urinary incontinence
- Urinary tract infection

If you see any of the above problems or any other changes in the way you feel, you should let the study doctor or study staff know as soon as possible. Side effects usually disappear after the treatment is stopped. Your study doctor can however prescribe other drugs in the meantime.

The effect Travoprost on pregnancy is unknown. Therefore, if you are pregnant, planning to become pregnant, or breastfeeding you cannot participate in the study.

Any new and important information which is found during the study and which may change your mind in continuing with this study will be shared with you.

OTHER TREATMENT OPTIONS:

Currently there are no other treatments available for loss of eyebrow hair during chemotherapy

BENEFITS TO TAKING PART IN THIS STUDY:

1. Treatment will help to increase eyebrow hair length and thickness and eyebrow density.
2. Information obtained from this study will benefit other patients undergoing chemotherapy and may add to the medical knowledge about the use of this medication.

COSTS OF PARTICIPATING:

You will not have to pay to participate in the study. The study drug, and any treatment procedures will be given to you at no charge.

PAYMENT FOR PARTICIPATING:

You will not be paid for taking part in this study.

CONFIDENTIALITY OF RECORDS:

All of your records will be kept confidential according to the law. Your study results and financial data related to the costs of your treatment may be published and/or disclosed to certain government agencies. Your identity will not be disclosed. In order to verify the data obtained from the study, representatives from Alcon Drug Company may inspect the research study records and your medical records related to the study. These groups do follow rules in order to make sure to keep your information confidential.

Release of Personal Information

Your personal health information includes information that was collected for entry in this study along with any information collected during the study. The purpose of collecting this information is to allow the study staff and doctor to study the results.

- If you decide not to release you personal health information for the study, you will not be able to take part in this study because the study staff and/or the study doctor will not be able to collect the needed information for the study drug

- The information that your study doctor will send to Alcon Drug Company will not include your name, address, or social security number. Your initials and assigned code number will be used on the information sent.

- The study doctor may send your personal health information to the Alcon Drug Company, including people who work with Alcon Drug Company to monitor the study and review the study results.

- The results of the study may be published in a medical book or journal, or presented at meeting for educational purposes. Your name or any other personal health information identifying you will not be used in those materials or presentations.

- You may ask to see and copy your health information related to the study. You may also ask the study doctor to correct any study-related information about you that you feel is

wrong. You may have to wait until the closing of the study to view your records so the reliability of the study is ensured.

If you no longer wish to share your personal health information, you may cancel your permission at any time by writing to the study staff and/or study doctor at the address below:

Ray D. Page, D.O., Ph.D.
Director of Research
Medical Oncology and Hematology
800 W. Magnolia Avenue
Fort Worth, TX 76104
Phone (817) 759-7000
Fax (817) 759-7030

If you cancel your permission after you have started this study, the study staff will no longer collect any other personal health information and you will not be able to further participate in the study. Information already collected will, however, be needed in order to properly evaluate the study results.

IF YOU HAVE ANY QUESTIONS AND PROBLEMS:

Please contact your study doctor for medical treatment if you think you are hurt as a result of this study. Any emergency medical care that was caused as a result of this study and is not covered by your insurance company will be given to you without any costs. You will still have to pay for all treatment which is not study-related.

Please see your study doctor about any questions or concerns that you may have about being in this research study or if you think that you may have suffered from an illness related to this study. If you have any questions later, please feel free to contact your study doctor or the study coordinator at the following phone number:

Ray D. Page, D.O., Ph.D.
Director of Research
Medical Oncology and Hematology
800 W. Magnolia Avenue
Fort Worth, TX 76104
Phone (817) 759-7000
Fax (817) 759-7030

APPENDIX D

DAILY MEDICATION LOG

Patient Initials _____

Location of treated eyebrow: _____

Study No: _____

Date	Time of drug administration	Side-effects	Additional Comments

APPENDIX E

Schedule of Study Visits

July 19, 2005 — **Screening Visit**
Collection of informed consent
Review of Inclusion/Exclusion criteria
Physical exam conducted
Eyebrow sample obtained, and pictures taken
Distribution of study medication and daily patient logs

August 2, 2005 — **Follow-up phone call**

August 16, 2005 — **Treatment Visit 1**
Measurement of vital signs
Review of adverse events
Eyebrow sample obtained, and pictures taken

August 30, 2005 — **Follow-up phone call**

September 13, 2005 — **Treatment Visit 2**
Measurement of vital signs
Review of adverse events
Eyebrow sample obtained, and pictures taken

September 27, 2005 — **Follow-up phone call**

October 11, 2005 — **Final Treatment Visit**
Measurement of vital signs
Review of adverse events
Eyebrow sample obtained, and pictures taken
Study medication and daily patient logs will be obtained

October 25, 2005 — **Follow-up Visit**
Measurement of vital signs
Review of adverse events
Eyebrow sample obtained, and pictures taken

APPENDIX F

Patient Name _____ **Study Number**_____

AN OPEN-LABELED PILOT STUDY EVALUATING THE EFFECTS OF TRAVOPROST ON EYEBROW REGROWTH AMONG PATIENTS UNDERGOING CHEMOTHERAPY FOR CANCER

PATIENT QUESTIONAIRE

1) Are you currently undergoing chemotherapy?

YES NO

2) If you answered yes, when (month/year) did you start this particular combination?

_____/_____

3) If you are not currently on chemotherapy, when (month/year) did you stop?

_____/_____

4) What type of chemotherapy are you currently on?

_____

5) When (month/year) did you start noticing the eyebrow hair loss?

_____/_____

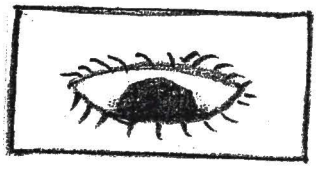
6) Have you noticed any changes in your eyebrow hairs after going on the travoprost eyebrow study? Please explain below.

_____
_____
_____
_____

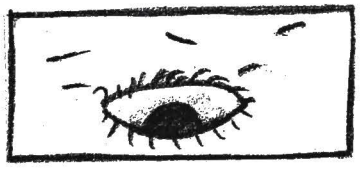
APPENDIX G

STANDARDIZED SCALE FOR EYEBROW DENSITY MEASUREMENTS

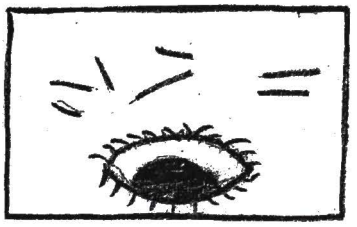
0 **No eyebrow hair**



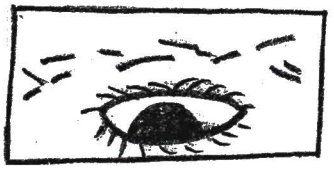
1 **Thin hairs present in few areas**



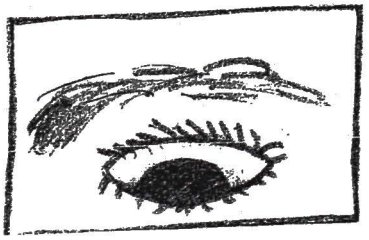
2 **A fair amount of hair scattered throughout the eyebrow line or elsewhere**



3 **A full eyebrow line with hair being sparsely dispersed; large amounts of hair elsewhere on upper eyelid**



4 **A complete, full eyebrow line and/or large amounts of hair seen elsewhere on upper eyelid; very dense**



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