

## YALE UNIVERSITY HUMAN INVESTIGATION COMMITTEE

Application to Involve Human Subjects in Biomedical Research 100 FR1 (2013-1)

Please refer to the HIC website for application instructions and information required to complete this application. The Instructions are available at	HIC OFFICE USE ONLY	
http://www.yale.edu/hrpp/forms- templates/biomedical.html Submit the original application and one (1) copy of all materials including relevant sections of the grant which funds this project (if applicable) to	DATE STAMPED-RECEIVED	PROTOCOL NUMBER
the HIC.		

## SECTION I: ADMINISTRATIVE INFORMATION

Title of Research Project: Top	ical Tofacitinib f	for the Treatm	ent of Alop	ecia Areata and Its Variants
Principal Investigator:	Principal Investigator: Yale Academic Appointment:			
Brett King, MD, PhD		Assistant Pr	rofessor of D	ermatology
Department: Dermatology				
Campus Address: 333 Cedar St	treet, LMP 5040,	New Haven, C	T 06520	
Campus Phone: (203) 785-4092	2 <b>Fax:</b> (203)	785-7637	Pager: NA	E-mail: brett.king@yale.edu
Protocol Correspondent Name	e & Address (if d	ifferent than PI	):	
Campus Phone:	Fax:	E-mail:		
Yale Cancer Center CTO Prot	tocol Correspond	lent Name & A	Address (if a	pplicable):
Campus Phone:	Fax:	E-mail:		
Business Manager:				
Campus Phone :	Fax :	E-mail		
<b>Faculty Advisor:</b> (required if PI resident, fellow or other trainee)	is a student, NA	Yale Acade	emic Appoir	ntment:
Campus Address:				
Campus Phone:	Fax:	Pager:	E-mail:	

Investigator Interests:

Does the principal investigator, or do any research personnel who are responsible for the design, conduct or reporting of this project or any of their family members (spouse or dependent child) have an incentive or interest, financial or otherwise, that may affect the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? Note: The Principal Investigator (Project Director), upon consideration of the individual's role and degree of independence in carrying out the work, will determine who is responsible for the design, conduct, or reporting of the research.

See Disclosures and Management of Personal Interests in Human Research http://www.yale.edu/hrpp/policies/index.html#COI

o Yes 🛛 🕅 No

Do you or does anyone on the research team who is determined by you to be responsible for the design, conduct or reporting of this research have any patent (sole right to make, use or sell an invention) or copyright (exclusive rights to an original work) interests related to this research protocol?

o Yes 🛛 🕅 No

If yes to either question above, list names of the investigator or responsible person:

The Yale University Principal Investigator, all Yale University co-investigators, and all Yale University individuals who are responsible for the design, conduct or reporting of research must have a current financial disclosure form on file with the University's Conflict of Interest Office. Yale New Haven Hospital personnel who are listed as con-investigators on a protocol with a Yale University Principal Investigator must also have a current financial disclosure form on file with the University's Conflict of Interest Office. If this has not been done, the individual(s) should follow this link to the COI Office Website to complete the form: <u>http://www.yale.edu/coi/</u>

NOTE: The requirement for maintaining a current disclosure form on file with the University's Conflict of Interest Office extends primarily to Yale University and Yale-New Haven Hospital personnel. Whether or not they are required to maintain a disclosure form with the University's Conflict of Interest Office, all investigators and individuals deemed otherwise responsible by the PI who are listed on the protocol are required to disclose to the PI any interests that are specific to this protocol.

#### SECTION II: GENERAL INFORMATION

1. **Performing Organizations:** Identify the hospital, in-patient or outpatient facility, school or other agency that will serve as the location of the research. Choose all that apply:

a. Internal Location[s] of the Study:	
Magnetic Resonance Research Center	Yale University PET Center
(MR-TAC)	YCCI/Church Street Research Unit (CSRU)
Yale Cancer Center/Clinical Trials Office (CT	ΓΟ) [YCCI/Hospital Research Unit (HRU)]
Vale Cancer Center/Smilow	YCCI/Keck Laboratories

Page 2 of 26

	Yale-New	Haven	Hospital	—Saint
--	----------	-------	----------	--------

Yale-New Haven Hospital

Raphael Campus

Cancer Data Repository/Tumor Registry Specify Other Yal

e Location: Yale Dermatology-Middlebury	e Location:	Yale Dermatology-Middlebury
---	-------------	-----------------------------

b.	External	Location	S	:

- APT Foundation, Inc.
- Connecticut Mental Health Center
- Other Locations, Specify:

Haskins Laboratories John B. Pierce Laboratory, Inc. Clinical Neuroscience Research Unit (CNRU) Veterans Affairs Hospital, West Haven International Research Site (Specify location(s)):

 $\times N/A$ 

# c. Additional Required Documents (check all that apply):

*YCCI-Scientific and Safety Committee (YCCI-SSC)	Approval Date:
*Pediatric Protocol Review Committee (PPRC)	Approval Date:
*YCC Protocol Review Committee (YRC-PRC)	Approval Date:
*Dept. of Veterans Affairs, West Haven VA HSS	Approval Date:
*Radioactive Drug Research Committee (RDRC)	Approval Date:
VNHH-Radiation Safety Committee (YNHH-RSC)	Approval Date:
Magnetic Resonance Research Center PRC (MRRC-PRC)	Approval Date:
YSM/YNHH Cancer Data Repository (CaDR)	Approval Date:

Dept. of Lab Medicine request for services or specimens form

Imaging on YNHH Diagnostic Radiology equipment request form (YDRCTO request) found at http://radiology.yale.edu/research/ClinTrials.aspx)

\*Approval from these committees is required before final HIC approval is granted. See instructions for documents required for initial submission and approval of the protocol. Allow sufficient time for these requests. Check with the oversight body for their time requirements.

2. Probable Duration of Project: State the expected duration of the project, including all follow-up and data analysis activities. 12 months

3.	Research Type/Phase: (Check all that apply)
	a. Study Type
	Single Center Study
	Multi-Center Study
	Does the Yale PI serve as the PI of the multi-site study? Yes No
	Coordinating Center/Data Management
	Other:
	b. Study Phase N/A
	Pilot Phase I Phase II Phase III Phase IV
	Other (Specify):

Page 3 of 26

- 4. Area of Research: (Check all that apply) Note that these are overlapping definitions and more than one category may apply to your research protocol. Definitions for the following can be found in the instructions section 4c:
- Clinical Research: Patient-Oriented
- Clinical Research: Epidemiologic and Behavioral
- Translational Research #1 ("Bench-to-Bedside")
- Translational Research #2 ("Bedside-to-Community")
- 5. Is this study a clinical trial? Yes 🖂 🛛 No 🗌

NOTE the current ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events" If yes, where is it registered?

Clinical Trials.gov registry  $\boxtimes$ Other (*Specify*)

## Registration of clinical trials at their initiation is required by the FDA, NIH and by the ICMJE.

If this study is registered on clinicaltrials.gov, there is new language in the consent form and compound authorization that should be used.

For more information on registering clinical trials, including whether your trial must be registered, see the YCCI webpage, <u>http://ycci.yale.edu/researchers/ors/registerstudy.aspx</u> or contact YCCI at 203.785.3482)

6. Does the Clinical Trials Agreement (CTA) require compliance with ICH GCP (E6)? Yes ⊠ No □

7. Will this study have a billable service? A Billable Service is <u>defined</u> as a service or procedure that will be ordered, performed or result in charging in EPIC for individuals who are enrolled in a clinical research study, <u>regardless</u> if the charge is intended to be paid by the subject/their insurance or the research study.

Yes 🛛 No

If you answered "yes", this study will need to be set up in OnCore Support <u>http://medicine.yale.edu/ymg/systems/ppm/index.aspx</u>

8. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes No X\_ If Yes, please answer questions a through c and note instructions below. If No, proceed to Section III.

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform?

Page 4 of 26

 Clinical Research: Outcomes and Health Services
 Interdisciplinary Research
 Community-Based Research b. Will you be using any new equipment or equipment that you have not used in the past for this procedure?

c. Will a novel approach using existing equipment be applied?

If you answered "no" to question 7a, or "yes" to question 7b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

#### SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

1. **Funding Source:** Indicate all of the funding source(s) for this study. Check all boxes that apply. Provide information regarding the external funding source. This information should include identification of the agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the M/C# and Agency name (if grantfunded). If the funding source associated with a protocol is "pending" at the time of the protocol submission to the HIC (as is the case for most NIH submissions), the PI should note "Pending" in the appropriate section of the protocol application, provide the M/C# and Agency name (if grant-funded) and further note that University (departmental) funds support the research (until such time that an award is made).

PI	Title of Grant	Name of Funding Source	Funding	Funding Mechanism
Brett King, MD, PhD	NA	departmental	<ul> <li>Federal</li> <li>State</li> <li>Non</li> <li>Profit</li> <li>Industry</li> <li>Other</li> <li>For Profit</li> <li>Other</li> <li>none</li> </ul>	Grant-M# Contract# Contract Pending Investigator/Department Initiated Sponsor Initiated Other, Specify: Yale

IRB Review fees are charged for projects funded by Industry or Other For-Profit Sponsors. Provide the Name and Address of the Sponsor Representative to whom the invoice should be sent. *Note: the PI's home department will be billed if this information is not provided.* 

#### Send IRB Review Fee Invoice To:

Name: Company: Address:

Page 5 of 26

Principal	Brett King, MD, PhD	Yale University School of Medicine	
Investigator			
Role: co-	Brittany Craiglow, MD	Yale University School of Medicine	
investigator			
Role: study	Lucy Liu	Yale University School of Medicine	
personnel			
Role:			
Role:			
Role:			

- 2. Research Team: List all members of the research team. Indicate under the affiliation column whether the investigators or study personnel are part of the Yale faculty or staff, or part of the faculty or staff from a collaborating institution, or are not formally affiliated with any institution. ALL members of the research team MUST complete Human Subject Protection Training (HSPT) and Health Insurance Portability and Accountability Act (HIPAA) Training before they may be listed on the protocol. See NOTE below. NOTE:
- 3. The HIC will remove from the protocol any personnel who have not completed required training. A personnel protocol amendment will need to be submitted when training is completed.

#### SECTION IV:

## PRINCIPAL INVESTIGATOR/FACULTY ADVISOR/ DEPARTMENT CHAIR AGREEMENT

As the principal investigator of this research project, I certify that:

- The information provided in this application is complete and accurate.
- I assume full responsibility for the protection of human subjects and the proper conduct of the research.
- Subject safety will be of paramount concern, and every effort will be made to protect subjects' rights and welfare.
- The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
- All members of the research team will be kept apprised of research goals.
- I will obtain approval for this research study and any subsequent revisions prior to my initiating the study or any change and I will obtain continuing approval of this study prior to the expiration date of any approval period.
- I will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or have acquired the appropriate approval from the Dean's Office or Office of the Provost, or the Human Subject Protection Administrator at Yale-New Haven Hospital, or have a faculty advisor.
- I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities.

(Sutt	Kmz	Brett King	9/22/15	
PI Name (I	PRINT) and S	Signature	Date	

<ul> <li>Department Chair's Assurance Statement</li> <li>Do you know of any real or apparent institutional conflict of interest (e.g., Yale ownership of a sponsoring company, patents, licensure) associated with this research project?</li> <li>□ Yes (provide a description of that interest in a separate letter addressed to the HIC.)</li> <li>○ No</li> </ul>
As Chair, do you have any real or apparent protocol-specific conflict of interest between yourself and the sponsor of the research project, or its competitor or any interest in any intervention and/or method tested in the project that might compromise this research project?
I assure the HIC that the principal investigator and all members of the research team are qualified by education, training, licensure and/or experience to assume participation in the conduct of this research trial. I also assure that the principal investigator has departmental support and sufficient resources to conduct this trial appropriately.
Chair Name (PRINT) and Signature     Richard Edelson     10/2/15
Department
<b>YNHH Human Subjects Protection Administrator Assurance Statement</b> <i>Required when the study is conducted solely at YNHH by YNHH health care providers.</i>
<ul> <li>As Human Subject Protection Administrator (HSPA) for YNHH, I certify that:</li> <li>I have read a copy of the protocol and approve it being conducted at YNHH.</li> <li>I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.</li> <li>The principal investigator of this study is qualified to serve as P.I. and has the support of the hospital for this research project.</li> </ul>
YNHH HSPA Name (PRINT) and Signature     Date

# SECTION V: RESEARCH PLAN

1. Statement of Purpose: State the scientific aim(s) of the study, or the hypotheses to be tested.

To investigate the use of topical tofacitinib to promote hair regrowth in patients with alopecia areata, alopecia totalis, and alopecia universalis.

2. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

Alopecia areata (AA) is a condition characterized by recurrent localized hair loss, usually involving the scalp, though other hair-bearing sites may be affected. Two variants of AA, alopecia totalis (AT) and alopecia universalis (AU), are characterized by complete loss of scalp hair and complete loss of all body hair, respectively. The prevalence of AA is 0.1-0.2%; its variants occur less often. The treatment of AA includes steroid injections into the skin at sites of involvement as well as topical steroids. When these therapies fail there are few, if any, reliable treatment options.

In a murine model of alopecia areata, a Type I cytotoxic pathway has been demonstrated to be responsible for the disease state, with NKG2D-expressing CD8+ cytolytic T-lymphocytes identified as both necessary and sufficient for induction of disease<sup>1</sup>. Upregulation of IL-15 in the outer root sheath of the hair follicle activates cytolytic T-lymphocytes, which in turn produce IFN, leading to activation of the hair follicle and upregulation of IL-15, NKG2D ligands, and MHC molecules, all of which target the hair follicle for attack. Systemic treatment with the JAK inhibitors tofacitinib (a JAK 1/3 inhibitor) and ruxolitinib (a JAK 1/2 inhibitor) prevents the onset of AA in grafted AA mice, and topical treatment reverses AA in these mice. JAK 1/3 signaling mediates IL-15 activation of T-lymphocytes, explaining the success of these therapies.

Based on the details above, we treated a single patient with alopecia universalis (and psoriasis) with oral tofacitinib, and he experienced complete hair regrowth<sup>2</sup>. Subsequently, we carried out a clinical trial investigating oral tofacitinib for the treatment of AA and its variants in 30 patients (Yale HIC # 1407014260 / ClinicalTrials.gov NCT02197455), for which data analysis is currently underway. This trial was replicated at Stanford University in 36 patients (NCT02312882). In our clinical practice we have now treated over 100 patients with oral tofacitinib. In addition, we have successfully treated a patient with compounded topical ruxolitinib, and she experienced hair regrowth (accepted for publication). Although rare, there are risks for serious adverse effects with systemic therapy that might be avoided if topical therapy were an option. Given this, the use of topical tofacitinib should be evaluated.

**3. Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

This will be an open label clinical trial. We plan to treat 10 adults with AA (with at least 2 patches of alopecia involving the scalp), AT or AU with tofacitinib ointment for a maximum of 6 months. During treatment, patients will be evaluated every 4 weeks and effectiveness of the medication will be measured by changes in hair growth. Laboratory evaluation will be performed before and during treatment in order to monitor for adverse effects of the medication.

Study data will be gathered at outpatient clinic visits. Participants enrolled in the study will receive up to 90 grams of tofacitinib 2% ointment monthly. In participants with AA, topical

tofacitinib will be applied to up to half of the alopecic patches (no more than 4 patches). In participants with AT or AU, tofacitinib 2% ointment will be applied to half of the scalp. Topical tofacitinib will be applied twice daily. Patients will wash their hands prior to and following application of the ointment. Patients demonstrating hair regrowth in the tofacitinib application sites will subsequently apply tofacitinib ointment to all involved sites when evidence of regrowth is observed at the initial sites of application. Treatment will be discontinued when either full regrowth has occurred in areas of application or at 6 months of treatment, whichever comes first. If a clinically significant adverse effect (lab abnormality or patient-reported adverse effect) is encountered, then the application frequency will be decreased to once daily. In the case of a serious adverse effect, tofacitinib ointment will be immediately discontinued.

Screening labs will include *QuantiFERON®* TB gold or PPD, fasting lipid panel, complete metabolic panel, and complete blood count with differential. Females of childbearing potential will require a negative pregnancy test prior to initiating treatment. While on treatment, participants will be evaluated every 4 weeks. Physical exam of the skin with special attention to presence or absence of hair growth, photographs of the skin, as well as a complete review of systems (headache, dizziness, fever, cough, shortness of breath, nausea, vomiting, diarrhea) will be performed at each visit. Severity of Alopecia Tool (SALT) will be used to score alopecia severity prior to and at the end of treatment, and the change in SALT score will be measured. Visits will take place at Yale Dermatology – Middlebury or Yale Dermatology Associates. Patients will be evaluated monthly for a maximum of 6 months. As above, patients who experience complete hair growth prior to 6 months will discontinue therapy at the visit when full hair growth has occurred. Labs will be monitored at 1 month and at completion of therapy, which for most patients will be after 6 months of treatment, and will include fasting lipid panel, complete blood count with differential, and complete metabolic panel. This will require 2-3 vials or approximately 6-12 mL of blood at each blood draw).

# 3. Genetic Testing N/A 🖂

## A. Describe

- i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned
- ii. the plan for the collection of material or the conditions under which material will be received
- iii. the types of information about the donor/individual contributors that will be entered into a database
- iv. the methods to uphold confidentiality
- B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects?
- C. Is widespread sharing of materials planned?
- D. When and under what conditions will materials be stripped of all identifiers?
- E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials?

- i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)?
- F. Describe the provisions for protection of participant privacy
- G. Describe the methods for the security of storage and sharing of materials
- 4. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

A total of 10 participants, 18 years of age or older will be enrolled. Participants must have a diagnosis of AA, AT or AU.

5. Subject classification: Check off all classifications of subjects that will be <u>specifically</u> recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

Children	Healthy	Fetal material, placenta, or dead fetus
Non-English Speaking	Prisoners	Economically disadvantaged persons
Decisionally Impaired	Employees	Pregnant women and/or fetuses
Vale Students	Females of ch	ildbearing potential

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects? 
Yes No (If yes, see Instructions section VII #4 for further requirements)

6. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

Patients will be included in the study if all of the following conditions are met:

- Age  $\geq$  18-years old
- Diagnosis of AA with at least 2 patches of alopecia involving the scalp, AT or AU
- Stable hair loss present for 6 months or longer
- No treatment for alopecia areata in the past 1 month
- No evidence of spontaneous hair regrowth

Patients will be excluded from the study if any of the following conditions are met:

- Age <18 years old
- Patients have received treatment known to affect alopecia areata within 1 month of enrolling in the study
- Patients whose current episode of AT or AU is more than 5 years
- Patients with a history of malignancy (except history of successfully treated basal cell or squamous cell carcinoma of the skin)
- Patients known to be HIV or hepatitis B or C positive

## Page 10 of 26

- Patients with positive tuberculin skin test or positive QuantiFERON® TB test
- Patients with leukopenia or anemia
- Patients with renal or hepatic impairment
- Patients taking immunosuppressive medications, including but not limited to prednisone, methotrexate, mycophenolate mofetil, azathioprine, tacrolimus, cyclosporine, or TNF-α inhibitors
- Women who are pregnant or nursing
- 7. How will **eligibility** be determined, and by whom?

Eligibility will be determined by the PI, Brett King, MD, PhD and/or co-investigator Brittany Craiglow, MD. Patients will be evaluated in person at a regular clinic appointment to determine if they meet inclusion criteria.

8. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The risks associated with oral tofacitinib are listed below:

- Infections, including severe and opportunistic infections
- Viral reactivation
- Neutropenia
- Lymphopenia
- Anemia
- Malignancy
- Lymphoma
- Gastrointestinal perforation
- Headache
- Diarrhea
- Increased liver transaminases
- Increased creatinine
- Increased cholesterol

The above risks are very unlikely likely to occur with topical administration given what is known about transepidermal absorption and minimal surface area of application in this trial. Therefore, the only reasonably foreseeable risk is irritation at the site of application. There are no other known risks to the study.

9. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

Screening visit will allow for exclusion of patients who do not meet inclusion criteria. Maximum time on treatment will be 6 months. Patients will undergo clinical evaluation every month during treatment and labs will be monitored at 1 and 6 months of treatment. Surface area of application will be limited to the scalp.

- 10. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.) For more information, see the Instructions, page 24.
  - a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal risk
  - b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
  - c. Copy, paste, and then tailor an appropriate Data and Safety Monitoring Plan from <u>http://www.yale.edu/hrpp/forms-templates/biomedical.html</u> for
    - i. Minimal risk
    - ii. Greater than minimal/moderate risk
    - iii. High risk

## Minimal Risk DSMP

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews monthly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator (monitor) or the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project as they are reviewed by the principal investigator. The protocol's research monitor, co-investigators and Pfizer will be informed of adverse events within 5 days of the event becoming known to the principal investigator.

11. Statistical Considerations: Describe the statistical analyses that support the study design.

This will be a pilot study that will be primarily observational in nature, and statistics will be purely descriptive. Pre-and post-treatment SALT scores will be compared for individual patients, and the mean change in score values from baseline will be described. Clinical photographs will be used to demonstrate presence or absence of hair regrowth.

# SECTION VI: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, state N/A and delete the rest of the section.

# A. DRUGS, BIOLOGICS and RADIOTRACERS

1. **Identification of Drug, Biologic or Radiotracer:** What is (are) the **name(s)** of the drug(s) biologic(s) or radiotracer(s) being used? Identify whether FDA approval has been granted and for what indication(s).

Topical tofacitinib ointment has been studied for the treatment of psoriasis and atopic dermatitis (phase II trials) but is not currently FDA-approved. The oral form of tofacitinib citrate is FDA-approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to, or who are intolerant of, methotrexate.

All protocols which utilize a drug, biologic or radiotracer **not** approved by, but regulated by, the FDA, or a radiotracer regulated by the RDRC, must provide the following information:

a. What is the Investigational New Drug (IND) number assigned by the FDA? 203214

b. Who holds the IND? Pfizer

c. All protocols which utilize a radiotracer not approved by, but regulated by the FDA must provide the IND number:

Alternatively, use of the investigational radiotracer may be under RDRC/RSC oversight: (check if appropriate)\_\_\_\_\_

For all investigational radiotracers, attach a copy of the RDRC/RSC application (for radioisotopes used in the PET Center, PET Center personnel may complete this step) Go to <u>http://rsc.med.yale.edu/login.asp?url=myApps.asp</u>. When you have logged in, complete the application and attach a copy to this submission.

Alternatively, an **exemption from IND filing requirements** may be sought for a clinical investigation of a drug product that is lawfully marketed in the United States. If there is no IND and an exemption is being sought, review the following categories and complete the category that applies *(and delete the inapplicable categories)*:

## Exempt Category 1

The clinical investigation of a drug product that is lawfully marketed in the United States can be exempt from IND regulations if all of the following are yes:

- i. The intention of the investigation is NOT to report to the FDA as a well-controlled study in support of a new indication for use or to be used to support any other significant change in the labeling for the drug.  $\Box$  Yes  $\Box$  No
- ii. The drug that is undergoing investigation is lawfully marketed as a prescription drug product, and the intention of the investigation is NOT to support a significant change in the advertising for the product.  $\Box$  Yes  $\Box$  No
- iii. The investigation does NOT involve a route of administration or dosage level or use in populations or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product. Yes No
- iv. The investigation will be conducted in compliance with the requirements for institutional (HIC) review and with the requirements for informed consent of the FDA regulations (21 CFR Part 50 and 21 CFR Part 56). Yes No
- v. The investigation will be conducted in compliance with the requirements regarding promotion and charging for investigational drugs. Yes No
- 2. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this drug is being administered to humans, include relevant data on animal models.

Oral tofacitinib was approved by the FDA in 2012 for the treatment of moderate to severe rheumatoid arthritis (RA) who have had an inadequate response to, or who are intolerant of, methotrexate. It is likely to be approved by the FDA in the next 4-8 weeks for the treatment of psoriasis. Its use is currently being studied in a variety of other inflammatory diseases, including psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, Crohn's disease, and ulcerative colitis (clinicaltrials.gov).

Topical tofacitinib 2% ointment has been demonstrated to be well-tolerated and effective for the treatment of plaque psoriasis.<sup>3</sup> It has also been studied in a phase II trial for atopic dermatitis (results not yet published).

The following table presents the risks as summarized in the package insert for **oral** XELJANZ. As mentioned above, the risks are likely to be far lower or nonexistent with topical administration because of minimal transepidermal absorption and the limited surface area of application being proposed in this study. As stated in Pfizer's investigator brochure, based on in vitro data, systemic bioavailability is predicted to be low ( $\leq$ 3%) following topical dosing relative to the oral route of administration.

**Table 1:** Adverse Effects with the use of oral tofacitinib citrate. The following data includes two phase 2 and five phase 3 doubleblind, controlled, multicenter trials. In these trials, patients were randomized to doses of XELJANZ 5 mg twice daily (292 patients) and 10 mg twice daily (306 patients) monotherapy, XELJANZ 5 mg twice daily (1044 patients) and 10 mg twice daily (1043 patients) in combination with DMARDs (including methotrexate) and placebo (809 patients). All seven protocols included provisions for patients taking placebo to receive treatment with XELJANZ at Month 3 or Month 6 either by patient response (based on uncontrolled disease activity) or by design, so that adverse events cannot always be unambiguously attributed to a given treatment. Comparisons between placebo and XELJANZ were based on the first 3 months of exposure, and comparisons between XELJANZ 5 mg twice daily and XELJANZ 10 mg twice daily were based on the first 12 months of exposure.

Adverse effect	Tofacitinib citrate:	Tofacitinib citrate:	Placebo	Notes:
	5 mg twice daily	10 mg twice daily		
Percentage of patients with any adverse effect requiring discontinuation of therapy.	4%	4%	3%	Any adverse reaction during the 0-3 months exposure in the double-blind, placebo-controlled trials.
Overall infection:	20%	22%	18%	Most common reported infections were URI, nasopharyngitis and UTI with a rate of 4%, 3% and 2%, respectively.
Serious infection: 0-3 months of therapy.	11 patients (1.7 events per 100 patient-years)	11 patients (1.7 events per 100 patient-years)	1 patient (0.5 events per 100 patient-years)	Most common serious infections included pneumonia, cellulitis, herpes zoster and UTI. The rate difference between treatment groups (and the corresponding 95% confidence interval) was 1.1 (-0.4, 2.5) events per 100 patient-years for the combined 5 mg twice daily and 10 mg twice daily tofacitinib group minus placebo.
Serious infection: 0-12 months of therapy.	34 patients (2.7 events per 100 patient-years)	33 patients (2.7 events per 100 patient-years)	N/A	Most common serious infections included pneumonia, cellulitis, herpes zoster and UTI. The rate difference between tofacitinib doses (and the corresponding 95% confidence interval) was -0.1 (-1.3, 1.2) events per 100 patient-years for 10 mg twice daily tofacitinib minus 5 mg twice daily tofacitinib.
<b>Tuberculosis:</b> 0-3 months of therapy	0	0	0	During the 0 to 3 months exposure, tuberculosis was not reported in patients who received placebo, 5 mg twice daily of tofacitinib, or 10 mg twice daily of tofacitinib.

Tuberculosis: 0-12 months of therapy	0	6 (0.5 events per 100 patient-years)	N/A	The rate difference between tofacitinib doses (and the corresponding 95% confidence interval) was 0.5 (0.1, 0.9) events per 100 patient-years for 10 mg twice daily tofacitinib minus 5 mg twice daily tofacitinib. Cases of disseminated tuberculosis were also reported. The median tofacitinib exposure prior to diagnosis of tuberculosis was 10 months (range from 152 to 960 days).
<b>Opportunistic infections</b> (excluding tuberculosis): 0-3 months of therapy	0	0	0	In the seven controlled trials, during the 0 to 3 months exposure, opportunistic infections were not reported in patients who received placebo, 5 mg twice daily of tofacitinib, or 10 mg twice daily of tofacitinib.
<b>Opportunistic infections</b> (excluding tuberculosis): 0-12 months of therapy	4 (0.3 events per 100 patient-years)	4 (0.3 events per 100 patient-years)	N/A	The rate difference between tofacitinib doses (and the corresponding 95% confidence interval) was 0 (-0.5, 0.5) events per 100 patient-years for 10 mg twice daily tofacitinib minus 5 mg twice daily tofacitinib.
Malignancy: 0-3 months of therapy.	2 patients (0.3 events per 100 patient-years)	2 patients (0.3 events per 100 patient-years)	0	Most common types of malignancy were lung and breast cancer, followed by gastric, colorectal, renal cell, prostate cancer, lymphoma and malignant melanoma. The rate difference between treatment groups (and the corresponding 95% confidence interval) was 0.3 (-0.1, 0.7) events per 100 patient-years for the combined 5 mg and 10 mg twice daily tofacitinib group minus placebo.
Malignancy: 0-12 months of therapy	5 patients (0.4 events per 100 patient-years)	7 patients (0.6 events per 100 patient-years)	N/A	One of these malignancies was a case of lymphoma that occurred during the 0 to 12 month period in a patient treated with tofacitinib 10 mg twice daily. The rate difference between tofacitinib doses (and the corresponding 95% confidence interval) was 0.2 (-0.4, 0.7) events per 100 patient-years for 10 mg twice daily tofacitinib minus 5 mg twice daily tofacitinib.

Lymphopenia: confirmed decreases in absolute lymphocyte counts below 500 cells/mm <sup>3</sup> .	0.04%	0.04%	N/A	Confirmed lymphocyte counts less than 500 cells/mm3 were associated with an increased incidence of treated and serious infections.
<b>Neutropenia:</b> ANC below 1,000 cells/mm <sup>3</sup> .	0.07%	0.07%	N/A	There were no ANC below 500 cells/mm <sup>3</sup> observed in any treatment group. There was no clear relationship between neutropenia and the occurrence of serious infections.
Liver enzyme elevations: percentage of patients with ALT elevations >3x ULN on DMARD trials.	1.3%	1.2%	1.0%	No elevations of liver enzymes were seen in controlled monotherapy with tofacitinib.
Liver enzyme elevations: percentage of patients with AST elevations >3x ULN on DMARD trials.	0.5%	0.4%	0.6%	No elevations of liver enzymes were seen in controlled monotherapy with tofacitinib.
Lipid elevations: Mean LDL cholesterol	Increased by 15%	Increased by 19%	N/A	Dose-related elevations in lipid parameters (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) were observed at one month of exposure and remained stable thereafter.
Lipid elevations: Mean HDL cholesterol	Increased by 10%	Increased by 12%	N/A	Dose-related elevations in lipid parameters (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) were observed at one month of exposure and remained stable thereafter.
Lipid elevations: Mean LDL/HDL ratios	Unchanged	Unchanged	N/A	
Serum creatinine elevations:	Mean increase in serum creatinine was < 0.1 mg/dL	Mean increase in serum creatinine was < 0.1 mg/dL		Dose-related elevations in serum creatinine were observed with tofacitinib treatment.
				Up to 2% of patients were discontinued from tofacitinib treatment due to the protocol-specified discontinuation criterion of an increase in creatinine by more than 50% of baseline. The clinical significance of the observed serum creatinine elevations is unknown.

ANC: absolute neutrophil count, DMARD: disease-modifying anti-rheumatic drug, ULN: upper limit of normal, URI: upper respiratory infection, UTI: urinary tract infection

## Page 17 of 26

- 3. Source: a) Identify the source of the drug or biologic to be used.
  - Pfizer Pharmaceuticals
  - b) Is the drug provided free of charge to subjects?  $\boxtimes$  Yes  $\square$  No
    - If yes, by whom? Pfizer
- 4. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, and for parenteral products, method of sterilization and method of testing sterility and pyrogenicity.

Check applicable Investigational Drug Service utilized:

- YNHH IDS
  - **CMHC Pharmacy**

Yale Cancer Center West Haven VA None N/A

**PET Center** Other:

Note: If the YNHH IDS (or comparable service at CMHC or WHVA) will not be utilized, explain in detail how the PI will oversee these aspects of drug accountability, storage, and preparation.

# 5. Use of Placebo: 🛛 Not applicable to this research project

If use of a placebo is planned, provide a justification which addresses the following:

- a. Describe the safety and efficacy of other available therapies. If there are no other available therapies, state this.
- b. State the maximum total length of time a participant may receive placebo while on the study.
- c. Address the greatest potential harm that may come to a participant as a result of receiving placebo.
- d. Describe the procedures that are in place to safeguard participants receiving placebo.

# 6. Use of Controlled Substances:

Will this research project involve the use of controlled substances in human subjects? Yes No See HIC Application Instructions to view controlled substance listings.

If yes, is the use of the controlled substance considered:

Therapeutic: The use of the controlled substance, within the context of the research, has the potential to benefit the research participant.

Non-Therapeutic: Note, the use of a controlled substance in a non-therapeutic research study involving human subjects may require that the investigator obtain a Laboratory Research License. Examples include controlled substances used for basic imaging, observation or biochemical studies or other non-therapeutic purposes. See Instructions for further information.

7. Continuation of Drug Therapy After Study Closure 🛛 Not applicable to this project

Are subjects provided the opportunity to continue to receive the study drug(s) after the study has ended?

Yes If yes, describe the conditions under which continued access to study drug(s) may apply as well as conditions for termination of such access.

Patients who experience hair regrowth that is not durable after study completion may elect to restart the medication.

 $\boxtimes$  No If no, explain why this is acceptable.

The drug will be provided by Pfizer for the duration of the study only.

#### **B. DEVICES**

N/A

## SECTION VII: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

#### 1. Targeted Enrollment: Give the number of subjects:

a. targeted for enrollment at Yale for this protocol: 10

b. If this is a multi-site study, give the total number of subjects targeted across all sites\_\_\_\_

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

Flyers	Internet/Web Postings	Radio
Posters	Mass E-mail Solicitation	Telephone
Letter	Departmental/Center Website	Television
Medical Record Review	Departmental/Center Research Boards	Newspaper
Departmental/Center Newsletters	Web-Based Clinical Trial Registries	
VCCI Recruitment database	Clinicaltrials.gov Registry (do not send	materials to
HIC)		

Other (describe): outpatient clinic (see Recruitment Procedures below)

#### 3. Recruitment Procedures:

- a. Describe how potential subjects will be identified.
  - Dr. King and Dr. Craiglow see 5-10 new patients and 10-20 established patients with AA, AT or AU every month their clinics at Yale Dermatology
- b. Describe how potential subjects are contacted.

At the time of their routine appointment with Dr. King or Dr. Craiglow patients will be told of the study.

c. Who is recruiting potential subjects?

Patients will be recruited from the clinical practice of Dr. Brett King and Dr. Brittany Craiglow.

## 4. Screening Procedures

- a. Will email or telephone correspondence be used to screen potential subjects for eligibility prior to the potential subject coming to the research office? Ves No
- b. If yes, identify below all health information to be collected as part of screening and check off any of the following HIPAA identifiers to be collected and retained by the research team during this screening process.

# HEALTH INFORMATION TO BE COLLECTED:

HIPAA identifiers:

All geographic subdivisions smaller than a State, including: street address, city, county, precinct,
zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to
the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by
combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the
initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is
changed to 000.
Telephone numbers
Fax numbers

- E-mail addresses
- Social Security numbers
- Medical record numbers
- Health plan beneficiary numbers

Account numbers

All elements of dates (except year) for dates related to an individual, including: birth date, admission date, discharge date, date of death, all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

Certificate/license numbers

Vehicle identifiers and serial numbers, including license plate numbers

Device identifiers and serial numbers

Web Universal Resource Locators (URLs)

Internet Protocol (IP) address numbers

Biometric identifiers, including finger and voice prints

Full face photographic images and any comparable images

Any other unique identifying numbers, characteristics, or codes

## 5. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

Yes, all subjects

 $\boxtimes$  Yes, some of the subjects. Some patients may be existing patients, while others will be new patients.

No

If yes, describe the nature of this relationship.

Doctor-patient relationship (established patients in our clinics).

6. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one: For entire study: \_\_\_\_\_ For recruitment purposes only: \_\_\_\_\_

- i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data;
- ii. If requesting a waiver of signed authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data;

By signing this protocol application, the investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

7. **Required HIPAA Authorization:** If the research involves the creation, use or disclosure of protected health information (PHI), separate subject authorization is required under the HIPAA Privacy Rule. Indicate which of the following forms are being provided:

Compound Consent and Authorization form

HIPAA Research Authorization Form

8. Consent Personnel: List the names of all members of the research team who will be obtaining consent/assent.

Brett King, MD, PhD; Brittany Craiglow, MD

 Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

The patient will be offered participation in the study during an outpatient visit to either Dr. Brett King or Dr. Brittany Craiglow. The project description, known risks of the research drug, etc. are detailed in the consent form and will be discussed with potential study participants.

10. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

Study subjects will be considered to have capacity to provide informed consent if they provide comprehensible and sensible answers to the following questions:

- (1) Tell me what will happen if you agree to partake in this study?
- (2) Can you leave this study once it begins?

Page 21 of 26

- (3) What should you do if you want to stop being in this study?
- 11. Documentation of Consent/Assent: The attached consent form will be used to obtain consent.
- 12. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. Translated copies of all consent materials must be submitted for approval prior to use.

None will be included in this study.

**13.** Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

Not Requesting a consent waiver

Requesting a waiver of signed consent

**Requesting a full waiver of consent** 

**A**. <u>Waiver of signed consent</u>: (Verbal consent from subjects will be obtained. **If PHI is collected, information in this section must match Section VII, Question 6**)

#### Requesting a waiver of signed consent for <u>Recruitment/Screening</u> only

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research? Yes No

b. Does a breach of confidentiality constitute the principal risk to subjects?

Yes No

## OR

c. Does the research activity pose greater than minimal risk?

☐ Yes *If you answered yes, stop. A waiver cannot be granted.* Please note: Recruitment/screening is generally a minimal risk research activity

#### AND

d. Does the research include any activities that would require signed consent in a non-research context? 
Yes No

<b>Requesting a waiver of signed consent for the <u>E</u></b>	ntire Study (Note that an information
sheet may be required.)	

If requesting a waiver of signed consent, please address the following:

a. Would the signed consent form be the only record linking the subject and the research? Yes No

b. Does a breach of confidentiality constitute the principal risk to subjects?

Yes No

## OR

#### AND

B. Full waiver of consent: (No consent from subjects will be obtained for the activity.)

#### Requesting a waiver of consent for <u>Recruitment/Screening</u> only

a. Does the research activity pose greater than minimal risk to subjects?

Yes *If you answered yes, stop. A waiver cannot be granted.* Please note:

Recruitment/screening is generally a minimal risk research activity

b. Will the waiver adversely affect subjects' rights and welfare? Yes No

c. Why would the research be impracticable to conduct without the waiver?

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

# **Requesting a full waiver of consent for the <u>Entire Study</u> (Note: If PHI is collected, information here must match Section VII, question 6.)**

If requesting a full waiver of consent, please address the following:

a. Does the research pose greater than minimal risk to subjects?

Yes If you answered yes, stop. A waiver cannot be granted.

b. Will the waiver adversely affect subjects' rights and welfare? Yes No

c. Why would the research be impracticable to conduct without the waiver?

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

## SECTION VIII: PROTECTION OF RESEARCH SUBJECTS

#### Confidentiality & Security of Data:

a. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

Name, age, gender, race, age of onset of alopecia areata and subsequent natural history (including episodes of regrowth and recurrence), prior therapies, comorbid conditions, percent scalp involvement of hair loss at initial presentation and follow-up visits (as measured via Severity of Alopecia Tool – SALT score), involvement of eyebrows, eyelashes and body hair, treatment including dose and duration, response to treatment, adverse effects

b. How will the research data be collected, recorded and stored? Laptop 1 with patient data in an Excel spreadsheet with a code identifier for each patient. The code identifiers will be stored separately on a different laptop computer. The laptops are encrypted with Yale security software.

- c. How will the digital data be stored? CD DVD Flash Drive Portable Hard Drive Secured Server Laptop Computer Desktop Computer Other
- d. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?
  Study participants will be identified with a code number. Codes will be maintained in a separate file. All data will be kept in password-protected files on an encrypted Yale laptop. Do all portable devices contain encryption software? Xes No
  If no, see http://hipaa.yale.edu/guidance/policy.html
- e. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

Code identifiers will be destroyed by Dr. Brett King by deleting the file so that the data is deidentified. The de-identified data will be kept for two years.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), SSC, etc.)? (please distinguish between PHI and de-identified data)

Dr. Brett King, Dr. Brittany Craiglow, Lucy Liu, YSM3, Yale Human Investigation Committee, Pfizer, Food and Drug Administration

g. If appropriate, has a <u>Certificate of Confidentiality</u> been obtained? No

h. Are any of the study procedures likely to yield information subject to mandatory reporting requirements? (e.g. HIV testing – reporting of communicable diseases; parent interview - incidents of child abuse, elderly abuse, etc.). Please verify to whom such instances will need to be reported.

Yes; participants will be screened for TB, HIV and hepatitis B and C. Those found positive will be notified in person and will be reported to Connecticut's Department of Public Health per mandatory reporting requirements.

# SECTION IX: POTENTIAL BENEFITS

**Potential Benefits:** Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

The benefits include regrowth of hair. The results of this study may serve as a proof-of-concept for the use of topical tofacitinib or other JAK inhibitors in the treatment of AA and its variants.

#### SECTION X: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?

Alternatives include any and all therapeutic interventions offered them by their dermatologist (determined by their dermatologist prior to study enrollment) including but not limited to the following:

- Immunosuppressive therapy (e.g. prednisone, cyclosporine)
- Intralesional corticosteroids
- Topical contact sensitization therapy (e.g. anthralin, squaric acid dibutylester)
- Topical corticosteroids
- No treatment
- 2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

No payment for participation will be made.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

There will be no cost to patients to participate in the study.

- 4. In Case of Injury: This section is required for any research involving more than minimal risk.
  - a. Will medical treatment be available if research-related injury occurs? Yes.
  - b. Where and from whom may treatment be obtained? From appropriate staff at YNHH.
  - c. Are there any limits to the treatment being provided? No.
  - d. Who will pay for this treatment? The patient or the patient's insurance company.

e. How will the medical treatment be accessed by subjects? Treatment may be provided in the YNHH outpatient dermatology office or the emergency room if more urgent treatment is necessary.

## **References:**

1. Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is

## Page 25 of 26

reversed by JAK inhibition. Nature medicine. Sep 2014;20(9):1043-1049.

2. Craiglow BG, King BA. Killing two birds with one stone: oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. *J Invest Dermatol*. Dec 2014;134(12):2988-2990.

3. Ports WC, Khan S, Lan S, et al. A randomized phase 2a efficacy and safety trial of the topical Janus kinase inhibitor tofacitinib in the treatment of chronic plaque psoriasis. *Br J Dermatol.* Jul 2013;169(1):137-145.