The Use of Digital Health Technology to Measure Nocturnal Scratch and Sleep in Atopic Dermatitis: Response to Abrocitinib

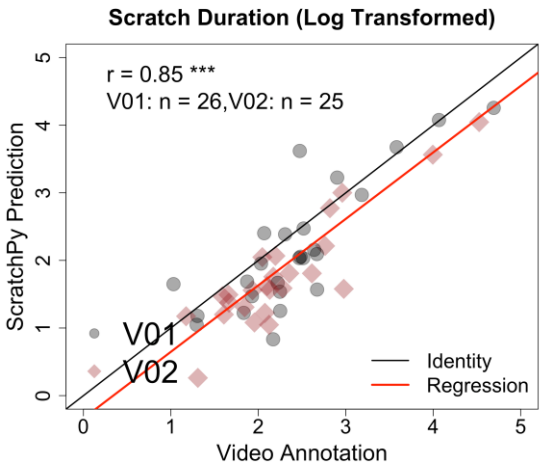
Yao Zhang[1] , Junrui Di[1] , Yiorgos Christakis[2] , Nikhil Mahadevan[3] , Jonathan Bruno[2] , and Carrie A. Northcott[2]

1 Biostatistics, Early Clinical Development (ECD), Pfizer, Cambridge, MA.
2 Digital Medicine and Translational Imaging (DMTI), ECD, Pfizer, Cambridge, MA.
3 University of Texas at Austin.

ClinicalTrials.gov Identifier: NCT03720470

Introduction

- Atopic Dermatitis (AD) is a common skin condition that affects **greater than 15% of adults** and **~20% of children** in high-income countries
- AD lesions are commonly red, excoriated, and oozing patches, and are often accompanied **by intense, unrelenting pruritus and subsequent scratching. Scratching has also been demonstrated to be increased at night due to multiple factors**. Several of these factors are intertwined in leading to sleep disruptions. All of which results in reduced quality of life for the patient. However, it is currently challenging to measure nocturnal scratching and sleep in AD patients.
- AD is often said to be an "itch (that leads to scratching), and ultimately results in rashes," creating a vicious cycle. While itch and scratching are related – one can be itchy and not scratch and scratch and not be itchy!
- Previous validation studies demonstrated that wearable sensors (accelerometry) plus algorithms quantitatively reflect nocturnal scratch and sleep measures in **a quantitative continual manner; moreover, scratch and sleep measures obtained from AD subjects correlate with "gold standards" of these measures (Figure-right; Scratch algorithm (ScratchPy)** determined scratching correlated **to video scratch annotations).**



Objective: To evaluate the effect of abrocitinib on the frequency and duration of nocturnal scratching and sleep disruption in patients with moderate to severe AD using digital health technology, wearable accelerometry devices, over the assessment period.

- Laughter MR, et al. The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990-1997. British Journal of Dermatology, 2020
- Mahadevan, N, et al. Development of digital measures for nighttime scratch and sleep using wrist-worn wearable devices. NJP Digit Med. 2021.

This study was sponsored by Pfizer Inc.

Material and Methods: Nocturnal Scratch and Sleep using Accelerometry

- The nocturnal scratch and sleep endpoints were exploratory and optional in the study:
  "A Phase 3 Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Parallel Group, Multi-Center Study Investigating the Efficacy and Safety of PF-04965842 and Dupilumab in Comparison With Placebo in Adult Subjects on Background Topical Therapy, With Moderate to Severe Atopic Dermatitis "
- The study assessed the efficacy and safety of abrocitinib 100 mg or 200 mg QD and dupilumab (as per label) compared with placebo in adult subjects (≥18 years of age) on background topical therapy, with moderate to severe AD.

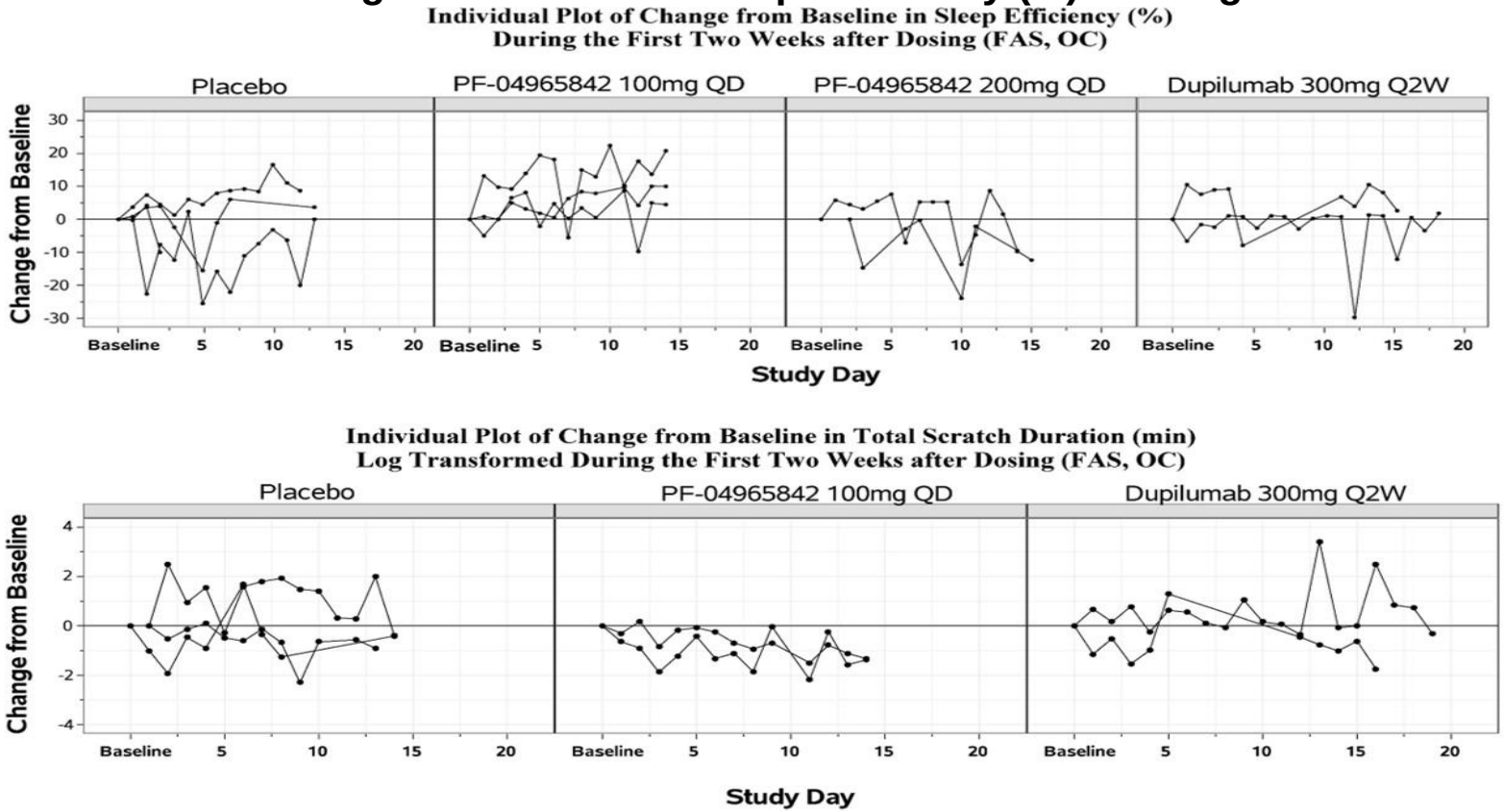
- **Nocturnal Scratch and Sleep measures:**
  - Sites from the following countries included in this sub-study: United States, Canada and Australia
  - Subjects that opted into this aspect of the study were provisioned two fully-charged and pre-configured accelerometry devices (GeneActiv; 20 Hz) to wear (one on each wrist, right and left)
  - Subjects were also informed that they may refuse or remove the devices at anytime without an impact on study participation
  - The subjects were asked to wear the devices 1 of 3 ways, and could opt out of this aspect of the study at anytime:
    - Preferred method: 1 week prior to Day 1 and then through Day 15 of treatment, continuously everyday, all day and night
    - Wear the devices for approximately 72 hours continuously during the first week of treatment and approximately 72 hours continuously during the second week of treatment
    - Wear the devices in the evenings only, beginning 3 hours before sleep through 3 hours after waking for 1 week prior to the Day 1/Baseline visit and 2 weeks following the Day 1/Baseline visit
  - Nocturnal Scratch and Sleep Endpoints: Night-time Scratch and Sleep algorithms (*Mahadevan, N, et al. Development of digital measures for nighttime scratch and sleep using wrist-worn wearable devices. NJP Digit Med. 2021.)*
  - Change from baseline (defined as the average of available measures during Day -3 to Day -1) were calculated for all post-dose measurements

Task	Prescreen	Day 1	Day 15
Configured fully charged left and right accelerometry devices provided to subject and appropriate training provided	X	X	
Site downloaded data from accelerometry devices		X	X
Site collected accelerometry devices from subject		X	X

Results:

- n=11 had data evaluable in endpoint summaries
- While limited data was obtained, it provided the opportunity to evaluate the endpoints in clinical trial conditions more fully with pharmacological interventions.
- As anticipated, placebo resulted in variable responses regarding sleep and nocturnal scratch during the two-week treatment and measurement period. In contrast, treatment with abrocitinib (PF-04955842) generally showed an increase in sleep efficiency and decrease in scratch duration and events, even with the limited number of participants.

Abrocitinib – Induced Changes Observed in Sleep Efficiency (%) and Night-time Scratch Duration (min)



Summary

- The use of digital wearables to measure nocturnal scratch and sleep provides a continuous quantitative measure of the patient's nocturnal scratch and sleep throughout a study.
- With limited data, descriptive analyses showed abrocitinib-induced changes in nocturnal scratch and sleep measures that weren't observed with placebo. Even with limited data collected, these changes appeared to have a meaningful clinical impact; as additional data are collected in future studies, we can statistically evaluate these changes.
- Continuous wear of the devices is ideal allowing for an appropriate measure of "activity baseline" and assists in taking into account potential "non-wear" times.
- Moreover, continuous measures of endpoints reveals the "day to day" variability that naturally occurs (ex. a person doesn't always go to sleep at the same time every day); therefore, these data provided the opportunity to evaluate statistical considerations to account for inter-subject day-to-day variation, e.g., taking the 3-consecutive-day average for each of the endpoints to "smooth out" the variation.
- Additional clinical studies will allow further validation to extend our knowledge about the characteristics of the proposed digital endpoints, including minimally clinically important differences (MCID).

Conclusions

- Wrist worn accelerometers and associated digital endpoints could provide quantitative knowledge regarding pharmacotherapies on the action of scratching and sleep quantity in the symptomatic AD population.
- In addition, these novel digital endpoints will enhance our understanding of AD and provide future opportunities to refine and improve therapies for other conditions.