Real-World Evaluation of the Effect of Jublia on Nail Polish

Study Protocol and Statistical Analysis Plan

NCT03022916

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Introduction:

Onychomycosis is commonly encountered dermatologic disease that has been traditionally very difficult to eradicate. Distal lateral subungual onychomycosis (DLSO) is the most common variety of onychomycosis. DLSO can lead to significant patient morbidity through nail thickening, nail discoloration, and pain. These symptoms can have a significant negative impact of patient's quality of life, and improvement is often appreciated upon successful treatment of the disease.

Traditional therapies for DLSO included oral antifungal medications, many of which can be associated with drug-drug interactions and hepatotoxicity. These side effects can limit the applicability of oral antifungals for treating DLSO. New, safer, topical therapies have been developed for the treatment of DLSO such as topical efinaconazole 10% solution (Jublia), which was recently approved by the FDA. Jublia has been shown in clinical trials to be efficacious for the treatment of DLSO and is well tolerated by patients.

Jublia was studied in clinical trials on subject with clean, dry nails that were free of any polish. Many women wear toe nail polish, particularly in the summer time, and thus wearing polish is potentially a major limitation of Jublia for the treatment of DLSO. A recent publication by Zeichnern using cadaver nails suggests that Jublia application has a negative effect on nail polish texture. As this has not been our clinical experience, we believe this topic requires further evaluation in a real world setting. We propose to examine how Jublia affects various nail polishes tested on the toes of healthy volunteers.

PRE-CLINICAL OBSERVATIONS

We have noted the following:

- Per the publication by Zeichnern, Jublia penetrates the nail with polish. The polishes tested were Essie, Revlon and Dior. Patients often prefer less expensive polish for home pedicures.

- The current approved package insert instructs patients to brush the medication on the nail plate with the applicator brush. Jublia immediately degrades/damages the

nail polish when the brush applicator touches the polished nail on 1 polish layer with no top coat. The polish color transfers to the brush applicator.

- When Jublia is dropped on to the nail plate with 1 polish layer with no top coat, the polish degrades within 1-2 days requiring polish reapplication.
- When Jublia is dropped on to the nail plate with 1-2 layers of color and a conventional top coat, the polish degrades in 2-7 days requiring polish reapplication.
- Darker nail polish appeared to smudge or show damage more readily than lighter polish colors.
- When Jublia is dropped on to the nail plate with 1 base coat, 2 layers of color and one top coat, the color remained stable for 14 days. The brands used for this observation were China Glaze base/top coat and OPI polish.

RESEARCH QUESTIONS

We pose to evaluate the following treatment scenarios utilizing the surface tension application technique.

- How many days can one color layer and a top coat without base coat be maintained (2 layers of lacquer)?
- How many days can no base coat, two color layers and a top coat be maintained (3 layers of lacquer)?
- How many days can one base coat, two color layers and a top coat be maintained (4 layers of lacquer)?
- Are other base and/or top coats, besides China Glaze brand, successful in extending polish appearance with daily Jublia application?

- Does color shade influence the polish appearance with daily Jublia application?
- What brands of color polish work best?
- Which type of polish works best?

OBJECTIVES

Primary objective is to evaluate the quality of nail polishes after application of Jublia. This will be evaluated visually by photographing toe nails after single application of Jublia as well as after sequential daily applications of Jublia.

Two drug store brands (Essie, Revlon), 3 beauty supply store/spa brands (Orley, China Glaze, OPI) and 2 department store brands will be evaluated (Dior, Estee Lauder). A light and dark shade will be chosen for each brand. The brand specific top and base coat will be used.

Brand	Light Color	Dark Color	Top Coat	Base Coat
Essie	X	X	X	X
Revlon	X	X	X	X
OPI	X	X	X	X
Orley	X	X	X	X
China Glaze	X	X	X	X
Estee Lauder	X	X	X	X
Dior	X	X	X	X

Primary Objective Measurements:

The great toe nail will be photographed sequentially after application of a variety of nail polish with a single application of Jublia and after sequential daily applications of Jublia. The contralateral great toe will also be painted with polish and will serve as the control in each subject.

DESIGN

Number of Subjects: 5

Number of Polish Cycles: approximately 50 cycles

5 eligible subjects will be included to participate in about 10 cycles each for a total of approximately 50 cycles.

Outline:

This is an open-label, real-world evaluation of the effect of Jublia on different nail polish and different nail polish application techniques. Each subject will use one great toe as a target toe and the contralateral great toe as a control toe. Names, brands, and colors of polishes will be recorded. As this is a real-world study, drug store, beauty supply store brands, and department store brands will be used. Professional pedicures will not be evaluated. Jublia will be applied once daily. The goal is to apply Jublia to the nail for 14 days with none or acceptable wear on the polish appearance.

A cycle will include:

1. Apply one color coat and one top coat. Allow to completely dry.

2. Drop the Jublia on the treatment toe and allow the mediation to disperse across the nail plate. The brush should not touch the nail plate. Use the brush applicator to brush the medication to the hyponychium. Allow to completely dry.

3. Photographs (M-F) will be taken until the cosmetic appearance of the nail polish is adversely affected.

4. Apply two color coats and one top coat. Allow to completely dry.

5. Drop the Jublia on the treatment toe and allow the mediation to disperse across the nail plate. The brush should not touch the nail plate. Use the brush applicator to brush the medication to the hyponychium. Allow to completely dry.

6. Photographs (M-F) will be taken until the cosmetic appearance of the nail polish is adversely affected.

7. Apply one base coat, two color coats and one top coat. Allow to completely dry.

8. Drop the Jublia on the treatment toe and allow the mediation to disperse across the nail plate. The brush should not touch the nail plate. Use the brush applicator to brush the medication to the hyponychium. Allow to completely dry.

9. Photographs (M-F) will be taken until the cosmetic appearance of the nail polish is adversely affected.

If the subject feels the nail polish has degraded or become damaged, the subject will be asked what qualities of the nail polish were damaged (ex: sheen, color, chipping, smudging). After a polish cycle is completed, the subjects will be allowed to participate in subsequent cycles.

All successful, completed cycles will be repeated by 2 additional subjects to demonstrate reproducibility. As time allows, additional combinations of color polish and base/top coats may be tested up to a maximum of 50 cycles.

References:

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The statistical analysis for this study compares the difference between a single coat of polish, two layers of polish, and a top coat as measured number of days to degradation, smudging, loss of luster, and tackiness. This was then check for statistically significant differences in the number of days to degradation. The interim analysis was presented in poster form, and no further analyses was conducted or planned.