A Multi-Center, Randomized, Double-Blind, Vehicle-Controlled Phase II Study to Evaluate the Efficacy, Tolerability and Safety of Topical Povidone-Iodine in Cancer-Therapy Associated Paronychia

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BACKGROUND

Taxanes, Epidermal Growth Factor Receptor Inhibitors (EGFRIs), mitogen-activated protein kinase enzyme (MEK) inhibitors and mammalian target of rapamycin (mTOR) inhibitors are the main classes of drugs known to cause cancer-therapy associated paronychia (CAP).

CAP presents with numerous physical findings including erythema, edema, purulent or serosanguinous discharge, onycholysis, subungual and/or periungual granulation tissue.

Current management strategies include minimizing trauma, decreasing periungual inflammation, preventing secondary infection, eliminating excessive granulation tissue, topical anti-inflammatory agents, topical or oral antibiotic/antimycotic agents to treat secondary infection, electrocautery, silver nitrate, nail avulsion and surgical I&D.

There is no standard of care for treatment; dose modification or discontinuation may result.

METHODS

Povidone-iodine (PVP-I):

- Aqueous solution is a nontoxic, commonly used topical broad spectrum anti-microbial
- Activity against bacteria, yeast, fungi, protozoa, molds, viruses
- Resistance-free/ MOA non-specific
- Formulated for increased penetration

Patients randomized into 3 treatment arms: 1% PVP-I solution, 2% PVP-I solution or vehicle-control solution applied twice-a-day to the nail plate, periungual and subungual spaces.

Study Duration: 8 weeks

Study Visits (3): day 1; two to four weeks; six to eight weeks

Paronychia Severity Grading (PSG) Scale modified from CTCAE version 4.03 was developed for increased sensitivity (**Table 1**).

Endpoints: 1. Primary: To evaluate the efficacy of twice daily 1% or 2% PVP-I topical solution versus vehicle-control in adult patients with CAP as evidenced by a 2 grade reduction (or reduction to zero if grade 1 at baseline) on the six-point PSG scale.
2 . Secondary objectives assessed the impact on quality of life (QoL) and safety.

Table 1

Grade 0	No signs or symptoms of paronychia
Grade 1	Erythema of periungual skin
Grade 2	Erythema, edema of periungual skin
Grade 3	Erythema, edema, discharge from periungual skin
Grade 4	Erythema, edema, discharge, periungual granulation tissue
Grade 5	Erythema, edema, discharge, subungual granulation tissue

RESULTS

There were 102 patients across 14 centers randomized to study; 35 patients in the 1% PVP-I group, 34 patients in the 2% PVP-I group and 33 patients into the vehicle-control group. Breakdown by baseline CTCAE grade and therapy classification provided in **Table 2**.

Primary Efficacy Endpoint:

- 2% PVP-I group, 88 of 167 (52.7%, P=0.0063) affected nails from 34 patients enrolled met the primary endpoint versus vehicle-control. **Figures 1 and 2** represent a reduction from Grade 3 to Grade 0 on the PSG scale.
- 1% PVP-I group, 83 of 205 (40.5%, P=0.6059) affected nails from 35 patients enrolled met the primary endpoint versus vehicle-control.

Secondary Efficacy Endpoint:

- QoL: Nineteen of 29 patients (65.5%) in the 2% PVP-I arm reported moderately or very painful nails at baseline that decreased to 15 patients (51.7%) at visit 2 and five patients (17.2%) at visit 3.
- Safety: No patients required dose reductions, interventions or discontinued the trial due to treatment related adverse events in any of the treatment arms.

Table 2

	1% PVP-I	2% PVP-I	Vehicle-Control	Overall
CTCAE Grade of Nails with Paronychia at Baseline, n (%)				
Grade 1	55 (26.8%)	53 (35.6%)	42 (24.9%)	150 (27.8%)
Grade 2	136 (66.3%)	97 (58%)	96 (56.8%)	328 (60.6%)
Grade 3	14 (6.8%)	18 (10.8%)	31 (18.3%)	63 (11.6%)
Tumor therapy, Number of nails				
Taxanes	148	110	129	387
MEK/mTOR inhibitors	13	1	0	14
EGFRIs	4	15	2	21
Combination of classes	40	41	38	119

CONCLUSIONS

The six-point PSG scale developed for this trial can be successfully utilized.
Treatment with 2% PVP-I topical solution showed clinically and statistically superior efficacy compared with vehicle-control solution, improved QoL and an excellent safety profile.

Phase III clinical trial in preparation.