Background

Cutaneous Metastases (CM) are progressive malignant skin lesions of advanced solid tumors and are usually associated with pain, pruritus, edema, discharge, and malaise, or additional morbidity like secondary infections, all negatively affecting quality of life. Lesion-directed therapies including advanced wound care, topical agents, cryosurgery, electrodessication, and intralesional therapies have been limited by insufficient efficacy, inconvenience, or toxicity. 1 In this open-label trial, submicron particle paclitaxel in an arbocel base (SOR007) was evaluated for topical treatment of CM from breast cancer (n=21), leiomyosarcoma (n=5) and Paget’s disease (n=3). Previous preclinical and clinical studies with topical SOR007 demonstrated penetration of paclitaxel into the dermis with minimal local skin reactions and negligible systemic absorption.

Methods & Results

Inclusion Criteria

- Signed informed consent
- Age 18 years
- Maligancy resulting in cutaneous metastases (CM) of at least one eligible lesion
- Diagnosis confirmed prior to consent by a qualified investigator
- Tumor response (OTR), (BOR) and (CR) was achieved at least 60 days after the last subject in each cohort of three, completed 15 days of SOR007 applications, or after Visit 4 to determine if dose escalation and/or, add to the current study dose, or expand the previous dose. This trial was repeated for each escalated dose until all dose levels were evaluated. No dose limitations (SCTD) were included in any subject at the 25% concentration to carry-over to dose escalation.

Exclusion Criteria

- Open / uncontrolled systemic or topical therapies during the dose-escalation phase, subjects self-collected on harvesting filters into precipitation chamber
- Colorectal, hepatocellular, gallbladder, thyroid, cutaneous, neuroendocrine, dermatological, hematological, and CNS malignancy
- Active liver hepatitis A, B, or C or liver disease
- Hypersensitivity to paclitaxel
- Allergic skin reaction to arboce or components of the SOR007 ointment
- Significant (≥10mm) lesion (≥10mm in diameter) on pretreatment baseline photograph

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Graph 1. % Change by Subject

Graph 2. % Change by Lesion

Table 1. Safety

Analysis of adverse events (AE) was completed at the end of study. There were 106 AEs observed: 36 (1.5%) were serious adverse events (SAE) considered related to the SOR007 application. No deaths occurred during the study. Two subjects were not assessed due to early termination. Tumor response (OTR), (BOR) and (CR) was achieved in 18% of the subjects after visit 4. Disproportionate increase in surface area to diameter ratio was noted. There was preliminary evidence of decreased lesion progression and reduction in total lesion area in most CM subjects. There were also preliminary signs of partial to complete pain relief for approximately half of each Group A and Group B subjects. Other adverse events included pain at the treatment site, petechiae, and pruritus. There was a non-significant trend towards improvement in pain scores and CTCAE (National Cancer Institute) grade II to III. Conclusions

SOR007 was determined to be safe and well-tolerated when applied to CM lesions with no significant local reactions or evidence of systemic toxicity. Systemic paclitaxel absorption was negligible. There was preliminary evidence of decreased lesion progression and reduction in total lesion area in most CM subjects. There was a reduction in lesion area at the 2.0% dose and lesion area stabilized between 2.0% and 3.0% at 28 days post-treatment. The study followed a standard 3+3 dose-escalation phase to determine dose efficacy. There were no significant local reactions or systemic toxicity. Evaluation of pain and CTCAE (National Cancer Institute) grade II to III.

References