PHASE 1/2 STUDY OF TOPICAL SOR007 FOR CUTANEOUS METASTASES

Julie E. Lang[1], Sant Chawla[2], Jenny Chang[3], Gere diZerega[4], Rose Marie Cavanna-Mast[4], Christopher Savoie[4], Mario Lacouture[5]
[1]USC Norris Comprehensive Cancer Center, Los Angeles, CA. [2]Sarcoma Oncology Research Center, Santa Monica, CA. [3]Houston Methodist Cancer Center, Houston, TX. [4]US Biotest, Inc. for NanOlogy, LLC and [5]Memorial Sloan-Kettering Cancer Center, New York, New York.

Background

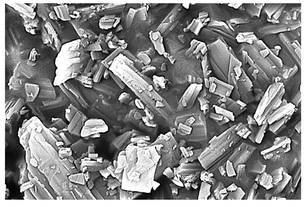
Cutaneous metastases occur in up to 10% of cancer patients (excluding melanoma) (Spratt 2014; Alcaraz 2014). Cutaneous metastases can cause considerable morbidity, leading to infection, bleeding, disfigurement and pain. The negative impacts to quality of life (QOL) for this population with advanced disease can be devastating (Spratt 2014).

Despite the prevalence and impact of cutaneous metastases, a standard of care remains elusive. Systemic chemotherapy has negligible impact on most cutaneous metastases (Fernandez-Anton Martinez 2013; Spratt 2014). Additional therapies for cutaneous metastases include electrochemotherapy (ECT), photodynamic therapy (PDT), intralesional therapy (ILT), and topical therapy (TT) but do not demonstrate great response rates (Spratt 2014; Cabula 2015). Therefore, there is a significant unmet need for an effective, less invasive therapy for cutaneous metastases in patients struggling with advanced primary cancer.

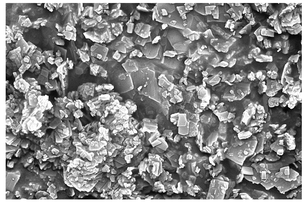
Paclitaxel is approved by FDA for several cancers known to cause skin metastases. This, in conjunction with paclitaxel's cytotoxic mechanism of action, provides the basis for the investigation of submicron particle paclitaxel (formulated as SOR007) for the topical treatment of cutaneous metastases. Based on nonclinical studies of SOR007, it is believed that the submicron particle will achieve a depot effect, providing a continuous dose of paclitaxel to the diseased skin over time with limited systemic exposure.

Specific Aims

- To determine preliminary safety and tolerability of topical SOR007
- To determine preliminary efficacy of topical SOR007 based on RECIST criteria, photograph documentation of lesion size in longest diameter, and objective clinical response
- To study potential reduction in pain at the treatment area
- To describe the pharmacokinetics of topical SOR007 ointment



Unprocessed paclitaxel



Submicron particle Paclitaxel (SOR007)

Trial Design

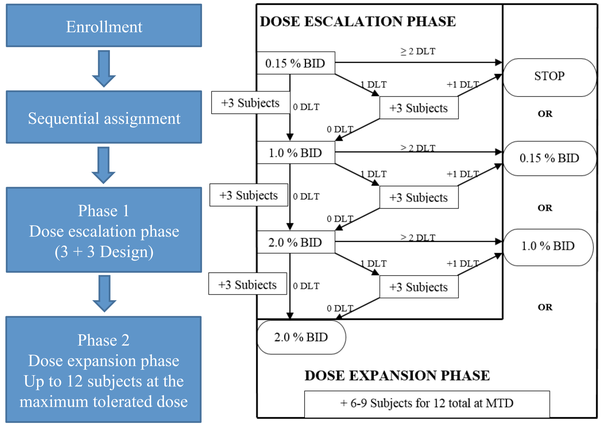


Figure 2. Dose Escalation Algorithm MTD – Maximally tolerated dose; DLT -dose limiting toxicity

ClinicalTrials.gov Identifier: NCT03101358

Primary Endpoints

- Safety and tolerability, as demonstrated by adverse events, changes in laboratory assessments, physical examination findings, and vital signs.

Secondary Endpoints

- Efficacy will be determined by the difference in the total area of eligible lesion(s) in the treatment area between baseline and Day 43 using a calibrated grid measurement system (ImageJ freeware) provided by the National Institutes of Health (NIH). Eligible lesions will be determined at baseline by the RECIST (Vn 1.1) definition of measurable tumors (≥ 10mm in its longest diameter)
- Objective Clinical Response (Complete Clinical Response (CR) + Partial Response (PR)) is defined as the percentage of patients who achieve complete clinical response or partial response 14 days after last treatment. Best overall response is defined as the best response recorded from the start of study treatment until the end of treatment.
- Reduction in pain at the treatment area will be measured by the Numeric Rating Scale (NRS-11) from baseline to Day 43
- Systemic Exposure as determined by: Time at which peak plasma concentration is observed (Tmax), Peak plasma concentration (Cmax), Area under the plasma concentration versus time curve (AUC)

Inclusion Criteria

- Male and female patients ≥ 18 years of age
- Malignancies resulting in cutaneous metastasis
- Cutaneous metastases diagnosis confirmed prior to consent
- ECOG Grade 0 - 2, with minimum life expectancy of at least 3 months
- At least one baseline eligible lesion (i.e, ≥ 10mm diameter in the longest diameter)
- Willing to refrain from using other lotions, creams, etc. during the treatment period
- Subjects with adequate organ and bone marrow function
- Last dose of any systemic non-taxane cytotoxic chemotherapy completed at least one day prior to Day 1. Last dose of any systemic taxane cytotoxic chemotherapy completed at least 4 weeks prior to Day 1
- Willing to use appropriate birth control for patients of child-bearing potential
- Abstinence of any physical contact near the treatment area during and up to 2 weeks after the treatment phase

Exclusion Criteria

- Open or ulcerated wound(s) extending through the dermis within the treatment area;
- Colorectal, hepatocellular, gallbladder, cholangiocarcinoma, neuroendocrine, melanomas, hematological and central nervous system (CNS) malignancies
- Active viral hepatitis A, B, or C or preexisting or acute liver disease
- Treatment with the following within the 4 weeks prior to the screening visit: radiotherapy, intralesional therapy; laser therapy surgery (other than biopsy) to the target area, local hyperthermia, levulinic acid, 5-fluorouracil, high potency corticosteroids (including systemic steroids), retinoids, diclofenac, hyaluronic acid, imiquimod
- Elective surgery for treatment of the cutaneous metastases during the study and up to 4 weeks after the treatment period. Cutaneous metastases are required to remain in-situ and measurable for up to 2 weeks after last treatment to achieve study objectives
- Known allergic reactions, irritations or sensitivity to the active ingredients or other components of SOR007
- Symptoms of a clinically significant illness that may place the subject at risk by trial participation or influence the outcome of the trial in the four weeks before first treatment and during the trial
- Participation in the treatment phase of another clinical trial within the four weeks prior to treatment in this clinical trial
- Investigator's opinion of subject's probable noncompliance or inability to understand the trial and/or give adequate informed consent
- Evidence of current chronic alcohol or drug abuse
- Pregnancy and/or lactating

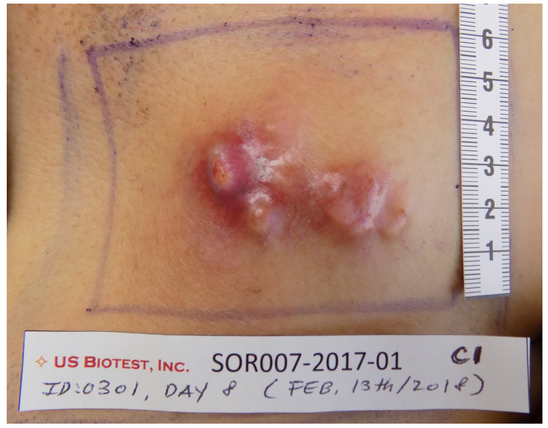


Figure 1. Example of cutaneous metastasis

Statistical Methods

The results of this trial will be based on descriptive statistics only. No formal statistical inference (i.e. "p-values") will be applied.

Contact Information

Rose Marie Cavanna-Mast, rosemarie.cavanna@usbiotest.com
Gere diZerega, gere.dizerega@usbiotest.com
Julie E Lang, MD Julie.Lang@med.usc.edu

References

- Alcaraz I, Cerroni L, Rutten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. Am J Dermatopathol. 2012; 34; 347-393.
- Cabula C, Campana LG, Grilz G, Galuppo S, Bussone R, De Meo L, Bonadies A, Curatolo P, De Laurentiis M, Renne M, Valpione S, Fabrizio T, Solari N, Guida M, Santoriello A, D'Aiuto M, Agresti R. Electrochemotherapy in the treatment of cutaneous metastases from breast cancer: a multicenter cohort analysis. Ann Surg Oncol. 2015; 22; S442-S450.
- Campana LG, Testori A, Curatolo P, Quaglino P, Mocellin S, Framarini M, Borgognoni L, Ascierto PA, Mozillo N, Guida M, Bucher S, Rotunno R, Marenco F, De Salvo GL, De Paoli A, Rossi CR, Bonadies A. Treatment efficacy with electrochemotherapy: a multi-institutional prospective observational study on 376 patients with superficial tumors. Eur J Surg Oncol. 2016; 42(12); 1914-1923.
- Fernández-Antón Martínez, Parra-Blanco V, Avilés Izquierdo JA, Suárez Fernández RM. Cutaneous metastases of internal tumors. Actas Dermosifiliogr. 2013; 104(10); 841-853.
- Sideras K, Zahasky KM, Kaur JS. Response of cutaneous metastases from breast cancer to capecitabine. Clinical Medicine: Oncology. 2008; 2; 415-418.
- Spratt DE, Gordon Spratt EA, Wu S, DeRosa A, Lee NY, Lacouture ME, Barker CA. Efficacy of skin-directed therapy for cutaneous metastases from advanced cancer: a meta-analysis. Journal of Clinical Oncology. 2014; 32(28); 3144-3155.