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**Contact Information:** Nicole Urman, nurman@stanford.edu, Department of Dermatology, Stanford, CA 94305

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**Introduction**

There is a great need for non-surgical therapies for patients with frequent basal cell cancers (BCCs) as the repeated surgeries can lead to severe morbidity and functional impairment. We conducted a systematic computational drug repositioning screen which identified histone deacetylase (HDAC) inhibitors as a potential therapy for BCC. We showed that HDAC inhibitors can suppress Hedgehog signaling and growth of BCC cells and murine BCC allografts, though optimal therapeutic effect was limited by systemic toxicity. Here, we report interim results of an open-label clinical trial of the topical HDAC inhibitor, remetinostat, as a neoadjuvant treatment for BCC. Remetinostat is designed to be metabolically labile so that topical application produces effective local HDAC inhibition in tumors while minimizing systemic HDAC inhibition and toxicity.

**Trial Design**

- Enrolled subjects had at least 1 BCC of any subtype between 5 and 25mm in size.
- Participants applied remetinostat gel 1% 3 times/day under bandage occlusion to BCC(s) for 6 weeks prior to undergoing surgical excision.
- The primary outcome was overall response rate (ORR) measured by at least a 30 percent decrease in tumor area.
- Secondary objectives include suppression of GLI1 mRNA expression and the safety and tolerability of remetinostat.

**Enrollment and Interim Results**

- 3 participants (15 tumors) removed for compliance < 70%. 1 participant currently in trial.

**Adverse Events:**

- Patients develop grade 1-2 eczematous reaction +/- pain at application sites
- Anecdotally associated with use of occlusive dressings, tumor shrinkage/clearance
- Can obscure edges of tumor
- 2 of 14 subjects had their study drug temporarily discontinued (for 1-3 days) due to AEs
- Improves within ~2-4 weeks of discontinuing medication

**Results - qPCR**

- Participants could choose to opt in to having pre- and post-treatment biopsies taken and analyzed via qPCR for PTCH and GLI1 mRNA.
- GLI1 mRNA level changes, post-treatment: 8-fold, 4-fold, 5-fold decreases, 5-fold increase

**Conclusions**

- The ORR, at least a 30% decrease in longest diameter, was 64% (9/14).
- The average decrease in tumor area is 70% (n=14), while the average decrease in longest diameter is 62% (n=14). 43% (6/14) of tumors were fully cleared.
- Grade 2 eczematous local site reactions occurred in 71% (10/14) tumors treated with topical remetinostat.
- No systemic toxicities have been observed.
- Barriers to effective treatment include refrigeration of remetinostat gel and 3x/day application with occlusion for 6 weeks.
- Initial results suggest that remetinostat gel offers a potentially effective, non-surgical intervention for treatment of localized BCCs.

**References**

- Mirza, A. et al, Cell, 2019
- Mirza, A. et al, JCI Insight, 2017