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Long Term Outcomes for Basal Cell Carcinoma Treated with Vismodegib Extended Alternate Day Dosing

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Background/Objectives: Management of locally advanced basal cell carcinoma (BCC) has change dramatically since the introduction of vismodegib, a hedgehog pathway inhibitor. While response rates to vismodegib exceeds 30%, nearly 100% of patients on standard dosing experience side effects with many patients discontinuing therapy as a result. Alternative dosing regimens have been proposed to increase the therapeutic longevity of vismodegib and we report a novel extended alternate day (EAD) dosing for this medication.

Methods: IRB approved retrospective chart review including all locally advanced BCC patients treated by Dr. Ratner with vismodegib between 1/2015 and 5/2018. All clinical data, including patient and tumor characteristics, patient outcomes, vismodegib dosing schedule and tumor response was extracted from the electronic medical record, compiled and analyzed in Microsoft Excel. All dosing listed indicates vismodegib 150 mg taken either daily (FDA approved) or on a variable alternate day schedule.

Results: Nine total patients were identified, one treated with daily dosing and 8 treated with EAD dosing. Mean patient age was 84 years with a mean duration of vismodegib therapy of 255 days. Six patients went on

every other day dosing for a mean of 125 days, every third day dosing for 94 days and up to weekly dosing depending on patient and tumor response. Three patients underwent Mohs micrographic surgery (MMS) while on EAD dosing and 4 remained on therapy at the end of the study period. None of the patients on EAD dosing discontinued due to side effects and all maintained tumor response (mean 50% reduction in length and width) to medication during the follow up period.

Discussion: Extended alternate day therapy provided effective tumor control over a mean of 8.5 months for seven of the nine patients. All patients on EAD dosing experienced a decrease in tumor size, with none exhibiting tumor progression on EAD dosing. While a smaller sample size, this is a significant improvement over previously reported outcomes for vismodegib therapy. One patient who discontinued his every five-day vismodegib dosing due to hospitalization did have tumor regrowth, but after resuming therapy with EAD dosing, experienced a continued reduction in tumor size. Four of nine patients under went MMS after starting EAD dosing indicating that this schedule may be an effective in those who are unable to tolerate standard vismodegib dosing as a neoadjuvant to MMS.

Conclusion: EAD dosing provided a titratable, well tolerated regimen for vismodegib therapy that maintained efficacy over eight months or more. Clinicians should consider EAD dosing for patients who respond to vismodegib but are unable to tolerate its side effects. Further study will help determine whether EAD dosing might extend vismodegib's utility, providing an option of lower dose, long-term suppressive therapy for BCC patients unable to tolerate surgery or radiation.