Stomatitis prevention during everolimus/exemestane treatment for metastatic breast cancer: a phase 2 study of steroid-based mouthwash

Hope S. Rugo,1 Mark S. Chambers,2 Jennifer Litton,2 Ingrid Mayer,3 Jaqueline Rogerio,4 Lisa DeMars,4 Jose Geronimo,4 Ghulam Warsi,4 Timothy F. Meiller5

1UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA
2The University of Texas MD Anderson Cancer Center, Houston, TX, USA
3Vanderbilt University, Nashville, TN, USA
4Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
5University of Maryland Medical System, Baltimore, MD, USA

2434/2500 Characters (including spaces)

Background: Stomatitis—inflammation of mucous membranes lining the mouth—has been observed in approximately 44-86% of everolimus-treated patients and tends to develop within the first month of therapy. Steroid mouthwashes have been successfully used to treat stomatitis in other patient populations, and anecdotal clinician reports indicate that use of a steroid-based mouthwash can prevent and treat stomatitis in patients with advanced breast cancer being treated with everolimus. However, no clinical trial data are available.

Methods: This phase 2, single-arm study will evaluate efficacy of 0.5 mg/5 mL dexamethasone oral solution in preventing stomatitis during treatment of HR+/HER2– breast cancer with everolimus 10 mg/day plus exemestane 25 mg/day. A baseline oral assessment will be conducted, and patients will be provided instructions on self-monitoring for stomatitis. All patients will be instructed to perform routine oral care. Eligible patients will receive a steroid-based mouthwash (alcohol-free 0.5 mg/5 mL dexamethasone solution). Patients will be instructed to perform the mouthwash regimen 4 times/day and swish the mouthwash in their mouth for a minimum of 120 seconds before rinsing. Patients will be instructed to abstain from eating or drinking for at least 1 hour after using the mouthwash. The mouthwash regimen will begin on the first day of everolimus administration after dosing and will continue 2 months, with an additional 2 months at the physician’s discretion. Primary end point is incidence of stomatitis (grade ≥2) at 2 months; secondary end points include average number of times a day the mouthwash regimen was performed and time to resolution of stomatitis (grade ≥2).
**Results:** Assuming a 13% absolute reduction in the rate of grade ≥2 stomatitis from the historical control rate of 33% and one-sided type 1 error = 0.05 and power = 80%, 73 evaluable patients are necessary. To account for 25% of the total patient population being nonevaluable, 97 patients will be enrolled for this study. The definition of grade ≥2 stomatitis will be strictly defined using physical examination, Normalcy of Diet Subscale, and patient-reported visual analog scale scores, to ensure objective and consistent grading.

**Conclusion:** This study is expected to reveal specific treatment strategies to prevent everolimus-associated stomatitis or ameliorate the severity.

Funded by Novartis Pharmaceuticals Corporation.