
ABSTRACTS

Lanny Garth Close, MD, *Section Editor*

NEOPLASMS, MALIGNANT

Comparison of the Efficacy and Safety of Miconazole 50-Mg Mucoadhesive Buccal Tablets with Miconazole 500-Mg Gel in the Treatment of

Oropharyngeal Candidiasis: A Prospective, Randomized, Single-Blind, Multicenter, Comparative, Phase III Trial in Patients Treated with Radiotherapy for Head and Neck Cancer.

Bensadoun RJ, Daoud J, El Gueddari B, Bastit L, Gourmet R, Rosikon A, Allavena C, Ceruse P, Calais G, Attali P, *Cancer* 2008;112:204–211.

Oropharyngeal candidiasis (OPC) is the most common oral fungal infection in patients with cancer, with a mean incidence between 30% and 70%. The prevalence in patients treated for head and neck cancers is even higher, owing to therapy-induced mucositis as well as markedly reduced salivary secretion. Often, because of the recalcitrant nature of this infection, physicians treat patients with systemic therapy early in their course. This also helps reduce problems with compliance. However, with such a widespread prevalence, there is growing

concern of breeding resistant organisms with the use of systemic therapy. Additionally, use of systemic therapy increases the risk of liver toxicity and drug–drug interactions.

The authors of this paper compared the use of a once-daily miconazole mucoadhesive buccal tablet (MBT) to the standard regimen of 4-times-daily miconazole oral gel (MOG). Their primary endpoint was clinical success at day 14, with secondary endpoints of clinical success at day 7, clinical cure, improvement of clinical symptoms, mycologic cure, recurrence rate, and safety.

A total of 282 patients who were treated with radiation for head and neck cancers, with clinical signs and symptoms of OPC, were eligible for this multicenter, single blind, randomized study. OPC had to be confirmed by culture. These patients were then randomized to receive either the once-daily miconazole Lauriad 50-mg MBT or MOG 125-mg 4 times daily; both regimens lasted 14 days. The patients were then followed at days 0, 7, 14, 30, and 60. At each visit, the extent of oral candidiasis was quantified, based upon number of lesions, severity of symptoms, and cultures.

After 14 days of treatment, the success rate in the MBT group was essentially equal to the success rate in the MOG group ($p < .0001$, 56% vs 49%). In fact, the results indicated a strong trend toward superiority in favor of MBT.

Clinically, patient symptoms were improved in 70.3% and 76.5% of the subjects in the MBT and MOG groups, respectively. In terms of recurrence of infection after complete resolution, 19% and 12.5% of patients had recurrence 14 days after treatment in the MBT versus MOG, respectively. After 45 days, the numbers were 21.5% and 17%, respectively. Average time to recurrence was 18.75 days and 20.60 days, respectively. The safety profile was equivalent for both forms of medication, with an incidence of serious adverse events (SAEs) of 0.7% in the MBT group and 4.7% in the MOG group.

The authors concluded that miconazole 50 mg MBT is an efficacious and safe alternative to systemic antifungal agents and that it compared favorably to the miconazole 500 mg gel administered 4 times a day. They saw clinical success in >55% of patients, and compared that to other studies showing 53% efficacy with oral fluconazole.

Further, the authors commented that there was no relationship between clinical cure and mycologic cure, an expected finding in a population with a high rate of candida at baseline. In fact, mycologic cure is not the goal of treatment.

The authors noted that the medication was easily tolerated, had a 10-fold lower dose than the topical gel, and was a once-daily dose. They concluded that

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miconazole MBT may facilitate compliance with the Infectious Disease Society of America's recommendations to treat OPC with topical agents.

Jason G. Newman, MD

Salvage Therapy in Relapsed Squamous Cell Carcinoma of the Oral Cavity: How and When?

Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, Lin CH, Chen IH, Huang SF, Cheng AJ, Yen TC, *Cancer* 2008;112:94–103.

This article evaluates several factors associated with relapse of oral cavity cancer and suggests settings in which salvage therapy may be the most effective. The authors retrospectively reviewed charts from 1996 to 2005 and identified 955 patients with oral cavity squamous cell carcinoma (OSCC). Of those, they found 272 patients (28.5%) with first relapse. Of the 272 patients, 212 were considered salvageable. A cutoff of 10 months was chosen as the basis for designating “early” versus “late” recurrence, based upon 5-year disease-specific survival (DSS) and overall survival (OS). There were 161 early-relapse patients and 111 late-relapse patients. Of the patients who had a relapse, 133 had a local recurrence, 139 had neck recurrences, and 87 patients had metastatic recurrences develop.

The authors compared patients in the early versus late categories and found that patients with early recurrences were of a significantly younger age and demonstrated prevalence of moderate and poorly differentiated cancer, pathologic N2b lymph node status, extracapsular spread, pathologic stage IV disease, neck recurrence, and distant metastasis. There was a statistically significant higher rate of local recurrence in patients with late relapsed OSCC. A late relapse was associated with a better overall survival than a relapse that occurred within the first 10 months.

When the authors used multivariate analysis to predict early relapse, they found that stage III or IV disease, tumor depth greater than 10 mm, poor differentiation, and the presence of distant metastasis significantly affected 5-year DSS and OS before salvage therapy. For patients with late relapse, multivariate analysis identified poor differentiation, distant metastasis, pT3 and pT4 disease, extracapsular spread, and neck recurrence as variables that significantly affected 5-year DSS and OS prior to salvage therapy.

In evaluating outcomes after salvage therapy, the patients were divided into 3 groups based upon type of salvage: surgical salvage (with or without radiation therapy [RT], chemotherapy, or concurrent chemoradiotherapy [CCRT]); salvage RT/CCRT; and palliative therapy. In patients with early relapse, a significant benefit was noted for salvage therapy in terms of both 5-year OS and DSS. No difference was noted between patients treated with surgery (with or without RT/CCRT) and those treated with salvage RT/CCRT. In patients with late-relapse OSCC, a significant benefit was noted for salvage therapy as well. However, in this group, surgery (with or without RT/CCRT) had a statistically significant improved outcome compared with RT/CCRT for both 5-year DSS and OS.

Based upon the data that they collected, the authors highlight several findings. First, early-relapse patients seem to benefit from either surgery (with or without RT/CCRT), or RT/CCRT alone. These early recurrences seem to be associated with more aggressive tumor biology. This compared to late-stage relapses, which seem to benefit from surgical salvage (with or without RT/CCRT) more than RT/CCRT alone. Overall, early-relapse OSCC patients had worse outcomes than did their counterparts with late relapses. In the early-relapse patients, patients with primary tumor depth less than

10 mm should be considered for salvage therapy, according to the authors.

This paper helps create parameters for treating patients with relapse of OSCC. The authors do an effective job of analyzing not only the variables that account for early versus late recurrence but also the variables that may help predict benefit from aggressive treatment in the salvage setting.

Jason G. Newman, MD

Outcomes After Radiotherapy for Squamous Cell Carcinoma of the Eyelid.

Petsuksiri J, Frank SJ, Garden AS, Ang KK, Morrison WH, Chao KSC, Rosenthal DI, Schwartz DL, Ahamad A, Esmaeli B, *Cancer* 2008;112:111–118.

Squamous cell carcinoma of the eyelid is a relatively rare occurrence. When it occurs, surgery is the established primary treatment. However, functional and cosmetic reconstruction is of paramount importance in order to gain good rehabilitation. Radiotherapy has been reported as the primary treatment in a limited number of series.

The authors of this manuscript report on 39 patients with 42 eyelid carcinomas treated over a 55-year period. Thirty-two tumors were treated primarily, whereas 10 were given postoperative radiotherapy. The median tumor size was approximately 1.4 cm, with most occurring in the lower lid and the rest occurring in the medial, upper, and lateral canthus. Indications for primary radiotherapy included medical comorbidities as well as concern that reconstruction would not be optimal. Over the time course of the study, treatment changed from superficial orthovoltage x-rays to electrons and finally to photons. The 5-year local control rate for all patients was 88%. There were no isolated lymph node failures in the patients who received radiation alone. The 5-year disease-free survival was

90% of the primary and 69% of the postoperative radiotherapy groups.

Well-documented ophthalmologic examinations were available in half ($n = 20$) of the patients. Sixteen percent of patients had grade 2 ophthalmologic complications, as

follows: 1 epiphoria, 1 asymptomatic cataract, and 1 neovascular glaucoma. Twenty-six percent of patients developed grade 1 complications, including epiphoria and keratitis. The findings of this study agree with those of previous studies that support the concept that

primary radiotherapy should be considered as a treatment in patients who refuse surgery, patients who are poor surgical candidates, or patients with significant comorbidities.

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