RESEARCH LETTER

Aprepitant for the Treatment of Pruritus in Sézary Syndrome: A Randomized Crossover Clinical Trial

Pruritus may impair quality of life in patients with Sézary syndrome, the leukemic variant of cutaneous T-cell lymphomas. Management of pruritus is challenging and often unsatisfactory. Retrospective reports have found aprepitant, a neurokinin 1 receptor antagonist approved for the treatment of chemotherapy-induced or postoperative emesis, to show some efficacy in managing pruritus in patients with cutaneous T-cell lymphomas.1-5

We conducted a randomized, double-blind, placebo-controlled crossover study in patients with Sézary syndrome to test the hypothesis that treatment with the neurokinin 1 receptor antagonist aprepitant would decrease pruritus.

Methods | Patients seen in the Vanderbilt University Cutaneous Lymphoma clinic meeting the International Society for Cutaneous Lymphomas-European Organisation for Research and Treatment of Cancer criteria6 for Sézary syndrome were eligible. Patients with Sézary syndrome with uncontrolled pruritus and a baseline visual analog scale for pruritus of greater than 40 mm were eligible. Participants were also required to be on a stable medication regimen for Sézary syndrome and a stable antipruritic medication regimen for 3 months prior to the study. Written informed consent was obtained and the protocol was approved by the Vanderbilt Institutional Review Board and carried out according to the Declaration of Helsinki. The study protocol is available in the Supplement. Placebo or aprepitant (125 mg on day 1, followed by 80 mg on days 2-7) was ingested daily for 7 days followed by a 1-week washout period before taking the other treatment. The primary outcome measure was severity of pruritus measured using a visual analog scale of 0 to 100 mm (worst pruritus imaginable). The secondary outcome measure was quality of life using the Dermatology Life Quality Index instrument.

Mixed-effect models were used to analyze the data with a random subject effect and with treatment (aprepitant vs placebo) and time as fixed effects; baseline pruritus by visual analog scale was included as a covariate. Paired comparisons at specific time points or between time points were made using a Wilcoxon signed-rank test. Hypotheses were tested at the level of α = .05.

Results | Five patients were randomized to therapy and completed the study. The Table provides characteristics of the patients. All of the patients had been treated with more than 1 medication, and all were undergoing photopheresis.

Discussion | To our knowledge, we report herein the results of the first randomized, double-blind, placebo-controlled

Table. Characteristics of 5 Patients With Sézary Syndrome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>62.4 (12.8)</td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
</tr>
<tr>
<td>Race, European descent, No.</td>
<td>5</td>
</tr>
<tr>
<td>Time since diagnosis, mean (SD), mo</td>
<td>31.4 (28.2)</td>
</tr>
<tr>
<td>Treatment, No.</td>
<td></td>
</tr>
<tr>
<td>Photopheresis</td>
<td>5</td>
</tr>
<tr>
<td>Bexarotene</td>
<td>3</td>
</tr>
<tr>
<td>Antihistamine</td>
<td>3</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>4</td>
</tr>
<tr>
<td>Histone deacetylase inhibitor</td>
<td>2</td>
</tr>
<tr>
<td>Triamcinolone cream</td>
<td>3</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure. Self-reported Visual Analog Scale (VAS) Assessment of Pruritus at Baseline Screening and on Each Day of Study Medication Use

A score of 100 mm indicated the worst pruritus imaginable, and a score of 0 indicated no pruritus. Orange circles indicate the aprepitant study arm; blue circles indicate the placebo study arm. Error bars indicate standard error of the mean. There was a significant difference at day 5 of P < .001 vs baseline.

There were no differences in quality-of-life measures between the 2 interventions. Pruritus did not change over 7 days of treatment in the placebo arm but increased significantly during the aprepitant treatment (Figure). In multivariable analysis, baseline pruritus (every 10 unit increment, 7.20; 95% CI, 5.98-8.44; P < .001) and treatment (10.63; 95% CI, 3.49-17.77; P = .004) had a significant effect on pruritus over the 7-day treatment period.

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A crossover study of aprepitant for the treatment of pruritus in patients with Sézary syndrome. The data do not support the efficacy of aprepitant as an antipruritic agent in patients with Sézary syndrome. This is in contrast to at least 7 case series that have reported an improvement in symptoms in a total of 17 patients with Sézary syndrome or mycosis fungoides.1-5

This study has limitations. Although the study was randomized, blinded, and placebo controlled, the sample size was small including only 5 patients. Because pruritus can vary in patients with Sézary syndrome due to changes in disease activity and external factors such as ambient temperature and humidity, we cannot exclude the impact of these factors on the scoring of pruritus by visual analog scale. We dosed aprepitant daily for 1 week, and we cannot exclude the possibility that the results would have been different if we had used intermittent dosing.

In conclusion, in patients with Sézary syndrome, aprepitant treatment may not improve pruritus as reported in previous retrospective observational studies. The unexpected observation of worsened pruritus in patients receiving aprepitant vs placebo warrants larger prospective studies with a similar design to confirm our findings.

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Author Contributions: Drs Zic and Brown had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Zic, Straka, McGirt, Yu, Brown.

Acquisition, analysis, or interpretation of data: Zic, Nian, Yu, Brown.

Drafting of the manuscript: Zic, Brown.

Critical revision of the manuscript for important intellectual content: Zic, Straka, McGirt, Nian, Brown.

Statistical analysis: Nian, Yu, Brown.

Administrative, technical, or material support: Zic, McGirt.

Study supervision: Zic, Brown.

Conflict of Interest Disclosures: None reported.

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Program Director and Resident Perspectives on New Parent Leave in Dermatology Residency

New parent leave (NPL) has been defined as leave from work for all parents after welcoming a child regardless of how they became parents (including giving birth to a child, adoption, surrogacy, or fostering). New parent leave is essential for the well-being of the infant and family. Of note, the United States and Papua New Guinea are the only 2 nations in the world that do not have statutory paid leave.1

A study reported that 64.1% of dermatology residents are women, most of childbearing age.2 A recent survey found that female dermatologists were most likely to have a child during residency (51%) compared with during other stages of their training and career.3 Residents have a finite time to learn their medical specialty and are subject to rules of the American Board of Dermatology (ABD)4 and varying institution-specific policies for absences during their training. The goal of our work was to investigate how NPL is currently handled in dermatology residency programs and how the policies are perceived by program directors (PDs) and residents.

Methods | The resident and PD surveys about NPL were sent via the Association of Professors of Dermatology email listserv, which includes the PD and chairs of 91 discrete residency programs, who then forwarded the resident survey link to members of their residency program; responses were collected from October 16, 2017, to March 13, 2018. The resident response rate could not be calculated owing to this distribution method. Survey answers were deidentified and analyzed using Excel (Microsoft Corp). This study was granted exempt status by the University of California, San Francisco Institutional Review Board. Participation was optional, and participants had to provide informed consent before accessing the survey.

Results | Of the 91 programs surveyed, 54 PDs (59.3%) and 139 residents responded. The PDs reported that their residency programs consisted of 261 women (65.3%) and 245 men (34.7%).