which have the greatest potential for metastasis. The results of this study suggest that a simple assessment of pain intensity will aid in the clinical diagnosis of SCC and lead to earlier appropriately aggressive treatment of these lesions.

Our subanalysis of the histologic features of these cancers revealed a correlation with perineural invasion and pain. Perineural invasion was identified in 3 cases (2 cases of SCC and 1 case of BCC). While all cases with perineural invasion were painful, the small sample size limits the generalizability of this finding.

Kyle C. Mills, MD
Shawn G. Kwatra, MD
Ashley N. Feneran, DO
Daniel J. Pearce, MD
Phillip M. Williford, MD
Ralph B. D’Agostino Jr, PhD
Gil Yosipovitch, MD

Accepted for Publication: July 7, 2012.

Author Affiliations: Departments of Pathology (Dr Mills), Dermatology (Mr Kwatra, Ms Feneran, and Drs Pearce, Williford, and Yosipovitch), Biostatistical Sciences (Dr D’Agostino), and Neurobiology and Anatomy (Dr Yosipovitch) and the Comprehensive Cancer Center of Wake Forest School of Medicine (Drs D’Agostino and Yosipovitch), Wake Forest University School of Medicine, Winston-Salem, North Carolina.

Correspondence: Dr Yosipovitch, Department of Dermatology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1071 (gyosipov@wfubmc.edu).

Author Contributions: Dr Mills, Mr Kwatra, and Drs D’Agostino and Yosipovitch 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: Mills, Pearce, D’Agostino, and Yosipovitch. Acquisition of data: Mills, Kwatra, Feneran, Pearce, Williford, and Yosipovitch. Analysis and interpretation of data: Mills, Kwatra, Feneran, D’Agostino, and Yosipovitch. Drafting of the manuscript: Mills, Kwatra, Feneran, D’Agostino, and Yosipovitch. Critical revision of the manuscript for important intellectual content: Mills, Kwatra, Pearce, Williford, D’Agostino, and Yosipovitch. Statistical analysis: D’Agostino. Administrative, technical, and material support: Kwatra, Pearce, Williford, and Yosipovitch. Study supervision: Mills, Pearce, and Yosipovitch.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We are indebted to the Wake Forest University School of Medicine Comprehensive Cancer Center for assistance with data organization.


Efficacy and Safety of Tumor Necrosis Factor Inhibitors in Acute Generalized Pustular Psoriasis

Acute generalized pustular psoriasis (GPP) is a rare, life-threatening form of psoriasis; therefore, rapidly effective treatment is needed. Etanercept was beneficial in GPP, but the benefit of infliximab or adalimumab was less frequently reported. The purpose of the present study was to evaluate the efficacy and safety of tumor necrosis factor (TNF) inhibitors in a series of patients with GPP.

Methods. A national, multicenter, retrospective study was conducted among patients who were seen in French university hospital dermatology departments and who received TNF inhibitors for GPP flaring within the postlabeling period. The study received approval from the institutional review board (Comité d’Évaluation de l’Éthique des projets de Recherche Biomédicale, Paris Nord, No. 12-017).

Patients included in the study had abrupt onset of generalized inflammatory erythema with successive waves of diffuse sterile pustules with subsequent desquamation accompanied by marked asthenia, high-grade fever, and hyperleukocytosis. They also had documented
evaluation of psoriasis severity including specified percentages of body surface area covered by pustules and erythema both before and after treatment.

Since a given patient might have received several TNF inhibitors, each TNF regimen was considered as soon as it was started during a GPP flare.

**Results.** Of the 11 patients entered into the study, 2 had inherited genetic mutations characteristic for deficiency in interleukin (IL)-36 receptor antagonist, an antagonist of cytokines belonging to the IL-1 family. The immediate efficacy of TNF inhibitors in controlling acute GPP attacks was evaluated in 16 flares (infliximab, 10; adalimumab, 3; and etanercept, 3). In the 10 patients who received infliximab, clinical remission was obtained in 8 flares (80%), with a median time for pustule clearance of 2 days (range, 1-8 days). For adalimumab, remission was achieved in 12 mo (no). The efficacy of TNF inhibitors as maintenance therapy, ie, in the prevention of subsequent GPP attacks, was evaluated in 10 flares (7 different patients). Two of 3 patients treated with infliximab were free of attacks within 6 and 22 months. Three of 4 patients treated with etanercept were free of disease flares for 3, 6, and 12 months. All 3 adalimumab-treated patients were consistently free of GPP (follow-up times, 10, 17, and 18 months) (Table). Adverse events in patients were limited to those treated with infliximab (6 of 19 patients, 32%) (Table).

**Comment.** This series of patients, the largest to our knowledge without limiting reporting only therapeutic success, emphasizes the rapid and complete control of GPP attacks in most infliximab-treated cases. These data provide additional support for the efficacy of TNF inhibitors during the acute phase of GPP and for guidelines recommending infliximab as first-line treatment in life-threatening forms of psoriasis, including GPP.

### Table. Efficacy and Safety of Anti-TNF Treatment for Generalized Pustular Psoriasis Flares

<table>
<thead>
<tr>
<th>Patient No./ Sex</th>
<th>Drug Used</th>
<th>Pustule Clearance, d</th>
<th>Efficacy on GPP Flare</th>
<th>Duration of Anti-TNF Drug Prescription</th>
<th>New GPP Flare</th>
<th>Adverse Events</th>
<th>Reason for Anti-TNF Cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F</td>
<td>INF</td>
<td>6</td>
<td>Yes</td>
<td>1 d</td>
<td>NA</td>
<td>None</td>
<td>CR</td>
</tr>
<tr>
<td>2/M</td>
<td>ADA/NR</td>
<td>&lt;28</td>
<td>Yes</td>
<td>17 mo</td>
<td>No</td>
<td>None</td>
<td>CR, patient wish</td>
</tr>
<tr>
<td>3/M</td>
<td>INF</td>
<td>3</td>
<td>Yes</td>
<td>12 mo</td>
<td>NA</td>
<td>Drug-induced lupus, mo 12</td>
<td>AE</td>
</tr>
<tr>
<td>4/F</td>
<td>INF</td>
<td>NR</td>
<td>No</td>
<td>&gt;18 mo</td>
<td>No</td>
<td>None</td>
<td>AE</td>
</tr>
<tr>
<td>5/F</td>
<td>INF</td>
<td>8</td>
<td>Yes</td>
<td>6 mo</td>
<td>No</td>
<td>None</td>
<td>Uncontrolled PV</td>
</tr>
<tr>
<td>6/F</td>
<td>ADA/NR</td>
<td>NR</td>
<td>NE</td>
<td>3 mo</td>
<td>No</td>
<td>Drug-induced hepatitis, mo 3</td>
<td>AE</td>
</tr>
<tr>
<td>7/F</td>
<td>INF</td>
<td>2</td>
<td>Yes</td>
<td>14 d</td>
<td>NR</td>
<td>Hypersensitivity: vomiting, febrile eruption, d 14</td>
<td>AE, patient wish</td>
</tr>
<tr>
<td>8/F</td>
<td>ADA/NR</td>
<td>7</td>
<td>Yes</td>
<td>10 mo</td>
<td>No</td>
<td>None</td>
<td>Lack of efficacy</td>
</tr>
<tr>
<td>9/F</td>
<td>INF</td>
<td>1</td>
<td>Yes</td>
<td>21 wk</td>
<td>Yes</td>
<td>Culture-negative pneumonia, d 3 Klebsiella pneumoniae soft-tissue abscess, d 20</td>
<td>GPP attack</td>
</tr>
<tr>
<td>10/F</td>
<td>ETA</td>
<td>NR</td>
<td>NE</td>
<td>4 mo</td>
<td>Yes</td>
<td>None</td>
<td>GPP attack</td>
</tr>
<tr>
<td>11/F</td>
<td>INF</td>
<td>2</td>
<td>Yes</td>
<td>1 d</td>
<td>NA</td>
<td>Hypersensitivity: urticaria, wk 6</td>
<td>CR</td>
</tr>
<tr>
<td></td>
<td>ADA</td>
<td>NR</td>
<td>NE</td>
<td>28</td>
<td>No</td>
<td>None</td>
<td>Regulatory reasons</td>
</tr>
</tbody>
</table>

**Abbreviations:** ADA, adalimumab; AE, adverse event; anti-TNF, treatment with tumor necrosis factor inhibitor; CR, complete remission of psoriasis; DITRA, deficiency in IL-36 receptor antagonist; ETA, etanercept; GPP, generalized pustular psoriasis; IL, interleukin; INF, infliximab; NA, not applicable; NE, not evaluated; NR, not reported; PV, psoriasis vulgaris.

a According to physician.

b The occurrence of GPP flare during maintenance anti-TNF could be evaluated only in patients for whom the initial GPP flare was controlled with anti-TNF and for whom anti-TNF was maintained.

c Patients 7 and 8 were diagnosed as having DITRA.
cytokine cascade. Nevertheless, alternative inflammatory pathways may also operate. Indeed, recent evidence for a major role of a dysregulation of pathways belonging to the IL-1 family is of special interest, identifying alternative targets for therapy.\(^4\) Since GPP is likely to be characterized by genetic and physiopathologic heterogeneity, in the future, tailored immunointervention is likely to offer optimal treatment outcomes. In the meantime, TNF inhibitors appear to provide great help in the control of the acute phase of GPP. Although results are more striking with infliximab owing to the higher number of patients, the risk-benefit ratio of the different TNF blockers should ideally be comparatively investigated in prospective multicenter studies.

Manuelle Viguier, MD, PhD
François Aubin, MD, PhD
Emmanuel Delaporte, MD
Cécile Pagès, MD
Carle Paul, MD, PhD
Marie Beylot-Barry, MD, PhD
Catherine Goujon, MD
Michel Rybojad, MD
Hervé Bachelez, MD, PhD
for the Groupe de Recherche sur le Psoriasis de la Société Française de Dermatologie

Accepted for Publication: June 4, 2012.

Author Affiliations: Sorbonne Paris Cité Université Paris Diderot, Assistance Publique-Hôpitaux de Paris, Service d’Dermatologie, Hôpital Saint-Louis, Paris, France (Drs Viguier, Pagès, Rybojad, and Bachelez); Université de Franche Comté, EA 3181, IFR 133, and Dermatologie, Centre Hospitalier Universitaire (CHU), Besançon, France (Dr Aubin); Université Lille 2, Dermatologie, Centre Hospitalier Régional Universitaire, Lille, France (Dr Delaporte); Université Paul Sabatier, Dermatologie, Hôpital Larrey, CHU, Toulouse, France (Dr Paul); Université Bordeaux 2, EA 2406 et Service de Dermatologie, Hôpital Haut-Lévêque, CHU, Bordeaux, France (Dr Beylot-Barry); Immunologie Clinique, Centre Hospitalier Lyon-Sud, Lyon, France (Dr Goujon); Groupe de Recherche sur le Psoriasis de la Société Française de Dermatologie, Paris (Drs Viguier, Aubin, Paul, Beylot-Barry, Goujon, Rybojad, and Bachelez); and Institut National de la Santé Et de la Recherche Médicale (INSERM) U781, Hôpital Necker-Enfants Malades, Paris (Dr Bachelez).

Correspondence: Dr Viguier, Hôpital Saint-Louis, Service de Dermatologie, 1 Avenue Claude-Vellefaux, Paris, 75475 CEDEX 10, France (manuelle.viguier@sls.aphp.fr).

Author Contributions: All authors had full access to all 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: Viguier, Aubin, and Bachelez. Acquisition of data: Viguier, Aubin, Delaporte, Pagès, Paul, Beylot-Barry, Goujon, Rybojad, and Bachelez. Analysis and interpretation of data: Viguier, Aubin, Paul, and Bachelez. Drafting of the manuscript: Viguier, Pagès, Goujon, Rybojad, and Bachelez. Critical revision of the manuscript for important intellectual content: Viguier, Aubin, Delaporte, Paul, Beylot-Barry, and Bachelez.


tistical analysis: Bachelez. Administrative, technical, and material support: Pagès, Paul, Rybojad, and Bachelez. Study supervision: Viguier, Aubin, and Bachelez.


Conflict of Interest Disclosures: The following authors are board members and/or consultants and/or received payment for development of educational presentations and/or travel/accommodation expenses: Dr Viguier (Pfizer, Abbott, MSD/Schering-Plough, Janssen); Dr Aubin (Merck Serono, MSD/Schering-Plough, Pfizer, Abbott, Janssen, Galderma, Leo Pharma, Novartis, Astellas, La Roche Posay); Dr Delaporte (Pfizer, Abbott, MSD/Schering-Plough, Janssen); Dr Paul (Abbott, Amgen, Celsene, Janssen, Leo Pharma, Novartis); Dr Beylot-Barry (Janssen, Aubin, Celsene, Leo Pharma, Novartis); Dr Rybojad (Janssen); Dr Bachelez (Abbott, Celsene, Janssen, Leo Pharma, Novartis, Pfizer, MSD/Schering-Plough).

Additional Contributions: We thank Cristina Livideau, MD, and Aude Maza, MD, for their help in collecting data.


COMMENTS AND OPINIONS

The Utility of a Portable Video Player in Wart Removal

W

We read with interest, the study by Tey et al,\(^1\) describing the usefulness of a portable video player for preschool children undergoing removal of cutaneous viral warts. The authors report significant reduction in anxiety scores with this intervention. However, actual clinical benefits seem to be modest, if at all present. There were no significant differences in treatment time, time required to persuade the child to cooperate, or the need for restraints. The authors, quoting qualitative data, mention that using the video player lessened the likelihood of prematurely stopping treatment, but the number of such stoppages is not reported, and the number of patients for whom restraints were required (a proxy measure) did not differ between groups.

The authors also make the subjective statement that children who received the intervention seemed more willing to return for treatments. Warts often require multiple treatments, and anxious children are likely to refuse treatment at follow-up sessions based on fears generated by the previous experience. Objective infor-