Study Identifies Health Goals of Psoriasis Patients

BY ERIK GOLDMAN
Contributing Writer

PHILADELPHIA — Willingness-to-pay studies, widely used in managed care and health policy studies to assess patient priorities, can tell dermatologists a lot about what psoriasis patients really want from their therapies, Matthew Delfino Jr. said at the annual meeting of the Society for Investigative Dermatology.

Mr. Delfino, a medical student at Harvard Medical School, Boston, has been working with the department of dermatology at Brigham and Women's Hospital to bring the skills and methodologies he learned during his business administration training to the management of skin disease.

"Willingness-to-pay [WTP] studies elicit both stated preferences, as well as unstated preferences. Higher willingness to pay is associated with stronger desire or preference for relief or improvement in a particular aspect of life," he explained.

The concept is simple: Investigators interview patients and ask them a series of questions along the lines of "Assuming a hypothetical ideally effective therapy, how much would you be willing to pay out of pocket for complete elimination of the impact or impairment of psoriasis on this particular domain of your life?"

It is akin to asking someone how much he or she would be willing to pay for an umbrella. If it is raining, and the individual's perceived need is pressing, he or she will likely be willing to pay more than if the sun is shining. "Greater impact on quality of life correlates with greater willingness to pay," Mr. Delfino explained.

Working with dermatologists at the hospital, he designed a WTP question panel that could evaluate patients' willingness to pay for alleviation of psoriasis-related impairment in eight life domains: intimacy, sleep, physical comfort, social comfort, emotional health, ability to work or participate in volunteer efforts, ability to maintain self-care, and ability to concentrate.

They recruited 40 patients with a history of psoriasis for participation in face-to-face interviews. The subjects had a mean age of 51.5 years; 83% were white and 48% were female; 60% were college educated, and 55% had annual incomes of more than $45,000.

In addition to the WTP questions, patients were also asked to rate their overall health and their psoriasis-related health on a 1- to 10-point visual analog scale.

In general, the patients were healthy, or at least they perceived themselves to be. As a group, they had an overall health score of 7.25. On psoriasis-related issues, they had a mean score of 5.4, indicating that they rated their dermatologic health considerably lower than their total health.

In terms of WTP responses, the four most important life domains for these patients were physical comfort, social comfort, emotional health, and ability to maintain self-care. The mean amount patients would be willing to pay for total elimination of physical symptoms was $2,000, with a range from $500 (the bottom price quartile) to $5,500 (the 75th quartile). Similarly, for total emotional health, the patients would be willing to pay a mean of $2,000, with a range of $250-$5,000.

At the other end of the priority spectrum, ability to sleep and ability to concentrate seem to be little affected by psoriasis. Patients were willing to pay a mean of $625 (range $50-$5,000) for total relief of sleep problems and $875 (range $25-$3,850) for elimination of any concentration problems associated with psoriasis.

These priorities were generally consistent across gender, age, and socioeconomic parameters. In fact, the investigators were surprised that education level and income had no measurable impact on the patients' WTP responses. Mr. Delfino noted that men were slightly more likely than women to report psoriasis-associated sleep problems, but there were no gender-associated differences in WTP for relief of sleep-related issues.

In general, the patients' priorities, as indicated by their WTP responses, correlated well with their perceived psoriasis-related and total health scores.

As a methodology, WTP assessment does have its limitations. "You are, in effect, 'monetizing' health outcomes, which can be very tricky," Mr. Delfino acknowledged. Further, studies like this rely almost exclusively on patient self-evaluation, which is always somewhat questionable. That said, the WTP approach is general-

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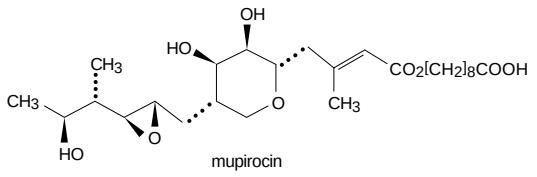
DESCRIPTION
Each gram of Centany (mupirocin ointment), 2% contains 20 mg mupirocin in a soft white ointment base consisting of castor oil, oleyl alcohol, hard fat (Softisan® 378) and propylene glycol monostearate. Mupirocin is a naturally occurring antibiotic. The chemical name is (E)-(2*S*,3*R*,4*R*,5*S*)-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-β-methyl-2 *H*-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid. The molecular formula of mupirocin is $C_{26}H_{44}O_9$ and the molecular weight is 500.63. The chemical structure is:



mupirocin

CLINICAL PHARMACOLOGY
Following the application of Centany (mupirocin ointment), 2% to a 400 cm² area on the back of 23 healthy volunteers once daily for 7 days, the mean (range) cumulative urinary excretion of monic acid over 24 hrs following the last administration was 1.25% (0.2% to 3.0%) of the administered dose of mupirocin. The monic acid concentration in urine collected at specified intervals for 24 hrs on Day 7 ranged from <0.050 to 0.637 µg/mL.

Microbiology: Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*. Its spectrum of activity includes gram-positive bacteria. It is also active, *in vitro* only, against certain gram-negative bacteria. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to this unique mode of action, mupirocin does not demonstrate cross-resistance with other classes of antimicrobial agents.

When mupirocin resistance occurs, it results from the production of a modified isoleucyl-tRNA synthetase or the acquisition, by genetic transfer, of a plasmid mediating a new isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC > 500 mcg/mL) has been reported in increasing numbers of isolates of *Staphylococcus aureus* and with higher frequency in coagulase-negative staphylococci. Methicillin resistance and mupirocin resistance commonly occur together in *Staphylococcus aureus* and coagulase-negative staphylococci.

Mupirocin is bactericidal at concentrations achieved by topical administration. However, the minimum bactericidal concentration (MBC) against relevant pathogens is generally eight-fold to thirty-fold higher than the minimum inhibitory concentration (MIC). In addition, mupirocin is highly protein bound (>97%), and the effect of wound secretions on the MICs of mupirocin has not been determined.

Mupirocin has been shown to be active against susceptible strains of *Staphylococcus aureus* and *Streptococcus pyogenes*, both *in vitro* and in clinical studies. (See **INDICATIONS AND USAGE.**)

INDICATIONS AND USAGE
Centany (mupirocin ointment), 2% is indicated for the topical treatment of impetigo due to: *Staphylococcus aureus* and *Streptococcus pyogenes*.

CONTRAINDICATIONS
This drug is contraindicated in individuals with a history of sensitivity reactions to any of its components.

WARNINGS
Centany (mupirocin ointment), 2% is not for ophthalmic use.

PRECAUTIONS
If a reaction suggesting sensitivity or chemical irritation should occur with the use of Centany (mupirocin ointment), 2%, treatment should be discontinued and appropriate alternative therapy for the infection instituted.

As with other antibacterial products, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Centany (mupirocin ointment), 2% is not formulated for use on mucosal surfaces. Centany (mupirocin ointment), 2% is not intended for nasal use.

Information for Patients: Use this medication only as directed by your healthcare provider. It is for external use only. Avoid contact with the eyes. The medication should be stopped and your healthcare practitioner contacted if irritation, severe itching or rash occurs. If impetigo has not improved in 3 to 5 days, contact your healthcare practitioner.

Drug Interactions: The effect of the concurrent application of Centany (mupirocin ointment), 2% and other drug products is unknown.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals to evaluate carcinogenic potential of mupirocin have not been conducted.

Results of the following studies performed with mupirocin calcium or mupirocin sodium *in vitro* and *in vivo* did not indicate a potential for genotoxicity: rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, *Salmonella* reversion test (Ames), *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse lymphoma assay, and bone marrow micronuclei assay in mice.

Reproduction studies were performed in male and female rats with mupirocin administered subcutaneously at doses up to 14 times the human topical dose (approximately 60 mg mupirocin/day) on a mg/m² basis and revealed neither evidence of impaired fertility nor impaired reproductive performance attributable to mupirocin.

Pregnancy
Teratogenic Effects.
Pregnancy Category B: Reproduction studies have been performed in rats and rabbits with mupirocin administered subcutaneously at doses up to 22 and 43 times, respectively, the human topical dose (approximately 60 mg mupirocin per day) on a mg/m² basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Centany (mupirocin ointment), 2% is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of Centany (mupirocin ointment), 2% have been established in the age range of 2 months to 16 years. Use of Centany (mupirocin ointment), 2% in these age groups is supported by evidence from adequate and well-controlled studies of Centany (mupirocin ointment), 2% in impetigo in pediatric patients studied as a part of the pivotal clinical trials. (See **CLINICAL STUDIES.**)

ADVERSE REACTIONS
The following local adverse reactions have been reported in connection with the use of Centany (mupirocin ointment), 2%; application site reactions and pruritus, each in 1% of patients; contact dermatitis and furunculosis, each in 0.7% of patients; and exfoliative dermatitis and rash, each in 0.3% of patients.

DOSAGE AND ADMINISTRATION
A small amount of Centany (mupirocin ointment), 2% should be applied to the affected area three times daily. The area treated may be covered with a gauze dressing if desired. Patients not showing a clinical response within 3 to 5 days should be re-evaluated.

CLINICAL STUDIES
The efficacy of topical Centany (mupirocin ointment), 2% in impetigo was tested in one study. Patients with impetigo were randomized to receive either Centany (mupirocin ointment, 2%) or Bactroban® Ointment (mupirocin ointment, 2%) t.i.d. for 7 days. Clinical efficacy rates at the follow-up visit (one week after end of therapy) in the evaluable populations (adults and pediatric patients included) were 94% for Centany (mupirocin ointment, 2%) (n=233) and 95% for Bactroban® Ointment (mupirocin ointment, 2%) (n=242). Pathogen eradication rates at follow-up for both medications were 98%.

Pediatrics
There were 413 pediatric patients aged 2 months to 15 years in the clinical study described above. Clinical efficacy rates at follow-up in the evaluable populations were 93% for Centany (mupirocin ointment, 2%) (n=199) and 95% for Bactroban® Ointment (mupirocin ointment, 2%) (n=214).

HOW SUPPLIED
Centany (mupirocin ointment), 2% is supplied in 15 gram (NDC 0062-1610-01) and 30 gram (NDC 0062-1610-03) tubes.
Store at controlled room temperature 20° to 25°C (68° to 77°F).

OrthoNeutrogena

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WHO Moves to Standardize Clinical Trial Info

BY KERRI WACHTER
Senior Writer

The World Health Organization has launched a major initiative to standardize the way that information on clinical trials is made available to the public.

In an attempt to address growing public concerns about the transparency of medical research involving human participants, WHO is recommending 20 key details that all clinical trial registries should include.

"Registration of all clinical trials and full disclosure of key information at the time of registration are fundamental to ensuring transparency in medical research and fulfilling ethical responsibilities to patients and study participants," Dr. Timothy Evans, assistant director-general of the WHO, said in a written statement.

WHO's International Clinical Trials Registry Platform is not itself a registry but provides standards for all clinical trial registries. These standards require information about sources of monetary or material support, primary and secondary sponsors, contacts for public and scientific queries, countries of recruitment, health conditions or problems studied, interventions, key inclusion and exclusion criteria, study design, date of first enrollment, target sample size, recruitment status, and primary and secondary outcomes. The voluntary initiative is part of a growing movement toward greater accessibility to clinical trial information, prompted in part by high-profile cases involving the suppression of data by pharmaceutical companies.

The initiative is part of a growing movement for more accessibility to clinical trial data, prompted in part by prominent cases involving suppression of such data.

In the European Union, all clinical trials conducted in member states are required to be registered in the EudraCT database, supervised by the European Medicines Agency. In the United States, www.ClinicalTrials.gov (developed and run by the National Institutes of Health) enrolls publicly and privately funded clinical trials worldwide. However, there are several hundred other national and private clinical trial registries around the world. The Registry Platform seeks to bring participating registries together in a global network to provide a single point of access to the information stored in them, according to a WHO statement.

The WHO has acknowledged the need to balance increased transparency with the protection of competitive advantage. It may come down to a question of the timing of disclosure. In comments submitted to a WHO formal consultation on disclosure timing policy in April, the Pharmaceutical Research and Manufacturers of America noted "there may be infrequent instances where companies may regard certain data elements as sensitive for competitive reasons and wish to delay public disclosure." In particular, the organization said that companies may wish to delay the disclosure of the official scientific title of the study, specific mechanism or molecular identifiers of the intervention, target sample size, primary outcome, and key secondary outcomes.

The WHO Registry Platform is expected to launch a web-based search portal later this year that would allow interested individuals to search among participating registries for clinical trials taking place or completed throughout the world.

For more information on the registry platform, visit www.who.int/ictrp/en. ■

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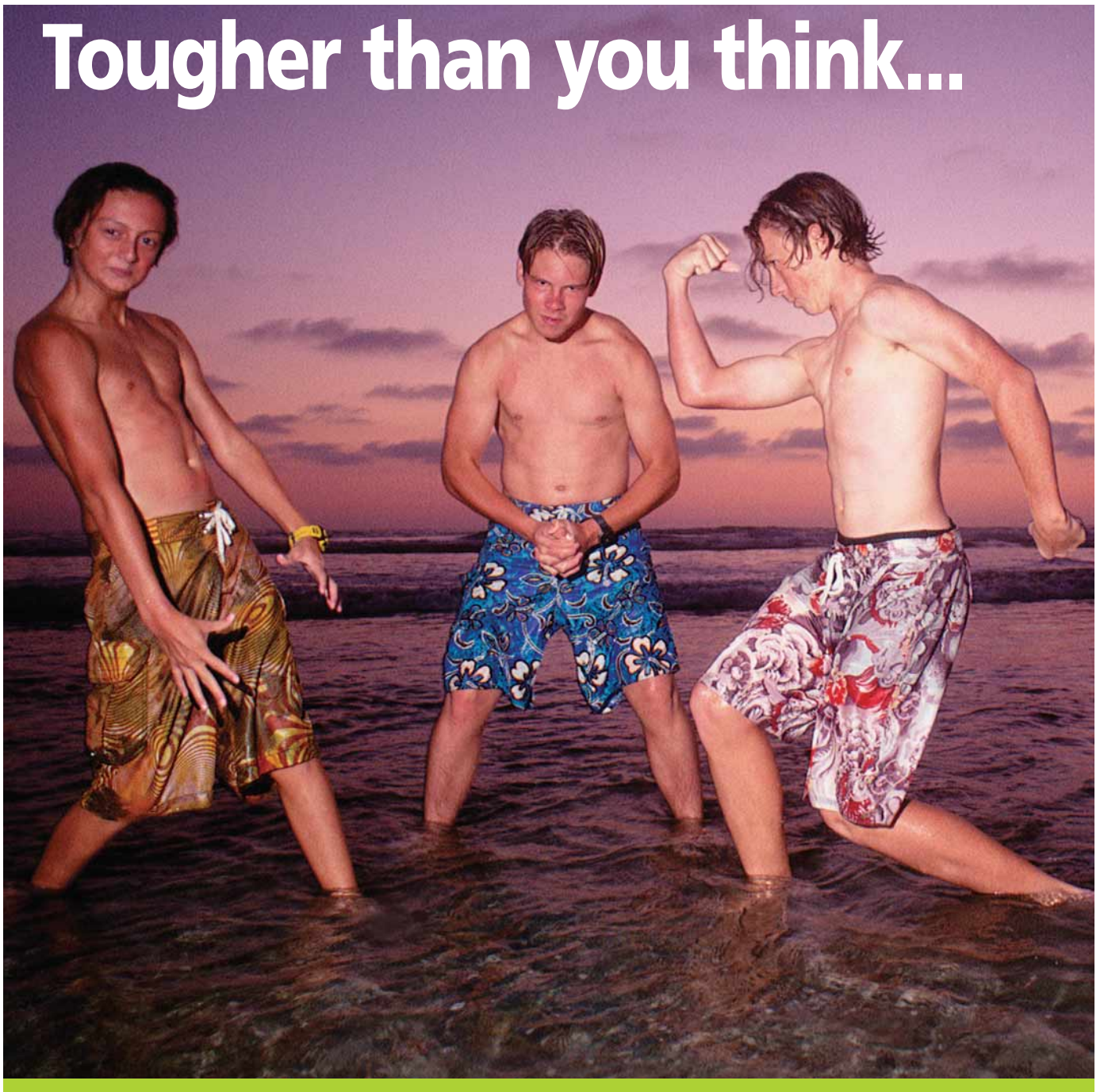
ly accepted in health policy literature, and advocates believe it can reveal important information about patients' real-world experiences, desires, and preferences that cannot be obtained through other lines of questioning.

Mr. Delfino said that the Brigham group is continuing to explore ways to apply WTP methodology in psoriasis. The next step is to go back to the medical records of patients in the study cohort and determine if there are any correlations between disease severity, duration, body surface area involvement, or other measures of psoriasis and the patients' response to the WTP questions. ■



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