3. Guy GP Jr, Thomas CC, Thompson T, Watson M, Massetti GM, Richardson LC, Centers for Disease Control and Prevention. Vital signs: melanoma incidence and mortality trends and projections — United States, 1982–2030. *MMWR Morb Mortal Wkly Rep*. 2015;64(21):591-596.
4. Community Preventive Services Task Force. The community guide: what works to promote health. The Guide to Community Preventive Services website. Avaliable at: http://www.thecommunityguide.org/index.html. Accessed October 4, 2017.
5. National Cancer Institute. Research tested intervention programs. Avaliable at: https://rtips.cancer.gov/rtips/index.do. Accessed January 29, 2018.

https://doi.org/10.1016/j.jaad.2018.10.044

Melanoma subsequent to natalizumab exposure: A report from the RADAR (Research on Adverse Drug events And Reports) program

To the Editor: Although natalizumab is approved for treating multiple sclerosis,[1] reports have raised concern about malignant melanoma (MM) after natalizumab exposure.[2,3] The aim of this study was to determine if an association was detectable for MM after natalizumab exposure in patients with multiple sclerosis.

Using RADAR methodology,[4] we searched the following databases: FDA Adverse Event Reporting System (FAERS), EudraVigilance (European Medicines Agency), and the Northwestern Medicine Enterprise Data Warehouse (NMEDW).

The FAERS search (January 2004-June 2014) comprised terms related to MM combined with natalizumab. The proportional reporting ratio (PRR) was then calculated to determine if a safety signal (defined as >3 events, chi-squared result >4, and PRR >2) was detectable.[5] We extracted data (January 2004-December 2015) from the NMEDW, a large, urban, Midwestern US population (>4 million patients, including a National Cancer Institute–designated comprehensive cancer center) for multiple sclerosis patients exposed to natalizumab who had a diagnosis for MM >3 months after initial exposure (International Classification of Diseases 9th Revision [172.0-172.9]; International Classification of Diseases 10th Revision [C43.0-C43.9]). The EudraVigilance database was searched (December 2001-November 2016) for terms related to MM combined with natalizumab.

A signal was detected in the FAERS database (PRR 2.42, 95% confidence interval 2.10-2.8) from 205 reports of MM subsequent to natalizumab exposure. In the NMEDW, of 5097 multiple sclerosis patients, 192 were exposed to natalizumab with 3 (1.6%) subsequently receiving a MM diagnosis (a significant association, Fisher's exact test, $P < .0001$). The EudraVigilance database comprised 78 reports of MM after natalizumab exposure.

These findings substantiate a recent study that linked natalizumab exposure to MM through FAERS analysis.[2] Natalizumab-exposed patients had a younger median age at MM diagnosis compared with the general (non–natalizumab-exposed) US population.[2] Mechanisms underlying the association for MM with natalizumab are incompletely understood; however, it seems that the drug's inhibitory effects on α_4-integrins might relate to MM evolution because melanoma cells expressing $\alpha_4\beta_1$ have increased homotypic intercellular adhesion and decreased ability to invade the extracellular matrix.[3] Inhibition of integrins with natalizumab might increase invasive potential. Of importance, these findings suggest that MM occurrence after natalizumab exposure might be biologically dissimilar to MM de novo.

Limitations include possible reporting bias within FAERS and possible redundancy in the EudraVigilance and FAERS databases. Moreover, signals detected from reporting in FAERS constitute reporting ratios and cannot be interpreted as incidence rates or risk ratios.[5] Furthermore, NMEDW database's small sample prevented additional analyses for potential confounding factors. Because determination of PRR requires the total number of adverse events reported for the drug of interest, number of adverse events of interest for the drug of interest, total number of all other adverse events, and the total number of all other drugs,[5] PRR could not be calculated with EudraVigilance data.

These findings demonstrate a detectable safety signal within FAERS and a statistically significant association for MM after natalizumab exposure in NMEDW; the EudraVigilance data was not inconsistent with these findings, with 78 reports being found. Of note, the full prescribing information for natalizumab does not refer to melanoma,[1] but enhanced monitoring of exposed patients seems warranted, especially for those at high risk for melanoma.

Ryan C. Kelm, BS,[a] Erika L. Hagstrom, MD,[a] Regine J. Mathieu, BS,[a] Kelsey A. Orrell, MB, BCh, BAO,[a] Linda Serrano, MD,[a] Kelly A. Mueller, BS,[a] Anne E. Laumann, MBChB, MRCP (UK),[a] Dennis P. West, PhD,[a,b] and Beatrice Nardone, MD, PhD[a]

From the Department of Dermatology,[a] and Robert H. Lurie Comprehensive Cancer Center,[b] Northwestern University, Chicago, Illinois

Funding sources: Northwestern Medicine Enterprise Data Warehouse is supported by the National Institutes of Health's National Center for Advancing Translational Sciences (grant number UL1TR001422).

Conflicts of interest: None disclosed.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Correspondence to: Beatrice Nardone, MD, PhD, 676 N St. Clair St, Ste 1600, Chicago, IL 60611

E-mail: b-nardone@northwestern.edu

REFERENCES

1. Tysabri prescribing information v. 08/2017.
2. Sabol RA, Noxon V, Sartor O, et al. Melanoma complicating treatment with natalizumab for multiple sclerosis: a report from the Southern Network on Adverse Reactions (SONAR). *Cancer Med*. 2017;6:1541-1551.
3. Mullen JT, Vartanian TK, Atkins MB. Melanoma complicating treatment with natalizumab for multiple sclerosis. *N Engl J Med*. 2008;358:647-648.
4. McKoy JM, Fisher MJ, Courtney DM, et al. Results from the first decade of research conducted by the Research on Adverse Drug events And Reports (RADAR) project. *Drug Saf*. 2013;36:335-347.
5. Sakaeda T, Tamon A, Kadoyama K, Okuno Y. Data mining of the public version of the FDA Adverse Event Reporting System. *Int J Med Sci*. 2013;10:796-803.

https://doi.org/10.1016/j.jaad.2018.10.052

The effect of antimicrobial washes on antibacterial resistance in hidradenitis suppurativa lesions

To the Editor: Hidradenitis suppurativa (HS) is a chronic relapsing inflammatory skin condition that results in painful nodules, abscesses, and sinus tracts typically in intertriginous body sites.[1] Topical and oral antibiotics are the first-line treatment for HS[2,3]; however, there is concern regarding antibiotic resistance in target and nontarget bacteria, as well as regarding the growth of opportunistic pathogens.[4] Some clinical practice guidelines for HS recommend concomitant antimicrobial washes, including chlorhexidine, bleach baths, and benzoyl peroxide for reducing inflammation and antibacterial resistance rates.[2,3] Importantly, for acne, studies have found that combining benzoyl peroxide with standard antibiotics can significantly reduce the antibacterial resistance in those lesions.[5] In this study, we sought to examine the association between antibiotic resistance in HS lesions and antimicrobial washes.

Table I. Descriptive characteristics of patients and bacterial cultures

Characteristic	Value
Patients (N = 80)	
Age, y	
Mean (SD)	35.5 (14.4)
Sex, n (%)	
Female	59 (73.8%)
Male	21 (26.3%)
Cultures and washes (N = 121 cultures)	
Body site of culture, n (%)	
Axilla	49 (40.5%)
Buttocks and groin	34 (28.1%)
Trunk	13 (10.7%)
Head and neck	12 (9.9%)
Thigh	10 (8.3%)
Arm	2 (1.7%)
Not specified	1 (0.8%)
Use of antibiotics* and/or wash, n (%)	
No antibiotics or wash	50 (41.3%)
Antibiotics + wash	35 (28.9%)
Antibiotics alone	25 (20.7%)
Wash alone	11 (9.1%)
Type of antimicrobial wash, n (%)	
No wash	75 (62.0%)
Chlorhexidine	17 (14.1%)
Dilute bleach bath	8 (6.6%)
Benzoyl peroxide	4 (3.3%)
≥2 washes	17 (14.1%)

SD, Standard deviation.
*Oral or topical antibiotics.

We conducted a cross-sectional analysis of 80 patients with HS who had a total of 121 HS lesional cultures; the 80 patients were from 2 academic medical centers in Pennsylvania and California. Information on demographics, culture results with the isolated species and associated antibiotic susceptibilities, use of oral and/or topical antibiotics within 1 month before or concurrent with culture, and use of an antimicrobial wash within 1 month before or concurrent with culture was collected and analyzed.

Patient and HS lesional culture characteristics are outlined in Table I. The most common sites of culture were the axillae, buttocks, and groin. Many of the cultures (41.3%) were performed in the absence of oral or topical antibiotic or antimicrobial wash use. Chlorhexidine was the most commonly used antimicrobial wash, but dilute bleach baths, benzoyl peroxide washes, or combinations of all 3 antimicrobial washes were also documented. Table II demonstrates the variation among groups that received antibiotic treatment only, antimicrobial washes only, both, or neither and the associated