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The high rate of placebo response in hidradenitis suppurativa clinical trials: Recommendations for future clinical trials

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The authors recently published a systematic review showing a robust placebo response in randomized clinical trials (RCTs) for hidradenitis suppurativa (HS), especially for physical signs. Three additional international/US-based RCTs for moderate-severe HS patients have been reported that did not meet the primary end point and demonstrated high placebo responses (n = 66-179). Four active doses of IFX-1 (IV anti—human complement factor C5a monoclonal antibody; InflaRx) were compared with placebo. IFX-1 treatment achieved a maximum HS Clinical Response (HiSCR) rate of 51.5% while placebo resulted in HiSCR of 47.1%. An RCT investigated MEDI8968 (subcutaneous interleukin-1 receptor 1 inhibitor, AstraZeneca). 23.6% of participants were responders in the active arm (PGA score of 0, 1 or 2 at week 12) compared with 18.5% of those receiving placebo. The study was terminated early. The third RCT compared CJM112 (subcutaneous anti—IL-17A monoclonal antibody; Novartis) versus placebo. Of those receiving active treatment, 32% were responders (decrease in HS-PGA of at least 2 points), while 12.5% of those receiving placebo met this definition. In order to accommodate the large and variable placebo response in HS, the following should be considered: recruit HS patients from well established HS practices, stratify recruitment and randomization across all spectrums of disease activity, employ a trial duration which will account for the natural history of the disease, agree upon a verified set of primary and secondary outcomes; and employ diagnostic imaging techniques to mitigate subjectivity in assessing outcomes. Furthermore, publishing negative outcomes should be encouraged in order to learn from all HS RCTs.

Commercial disclosure: None identified.

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Homeless patients receive different care for common skin diagnoses: An intradermatologist analysis

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Homeless individuals have significant skin disease attributable to environmental exposures, lack of access to medical resources, and inconsistent health care. However, disparities in how clinicians manage common dermatologic conditions in homeless patients relative to other patients has yet to be explored. We performed a retrospective review of patients seen from 2011 to 2017 at a referral-based dermatology clinic for the homeless. Patients diagnosed with common skin conditions, including actinic keratosis (AK; n = 157), dermatitis (n = 58), warts (n = 38), or acne (n = 27), were age-, sex-, diagnosis-, and provider-matched 1:5 to non-homeless patients seen at the University of Utah's dermatology clinics. Acne patients who were homeless were prescribed fewer medications compared with non-homeless patients ($P = .02$), particularly oral medications (48.1% in homeless patients vs 71.6% in non-homeless patients; $P = .02$). Homeless patients with dermatitis received fewer high-potency topical steroids (19% vs 42.2%; $P = .001$) and were less likely to receive biopsies (0% vs 10.8%; $P = .009$). Comparing patients diagnosed with warts, genital warts were more commonly diagnosed in homeless patients (42.1% vs 3.4%; $P < .001$). Homeless patients with non-genital warts were less likely to receive a prescription (4.5% vs 30.4%; $P = .01$). Regarding follow-up, homeless patients were less likely to be recommended a follow-up visit compared with non-homeless patients diagnosed with acne or AKs (44.4% vs 74.0%; $P = .003$ and 36.8% vs 86.9%; $P < .001$, respectively). These findings reveal intra-dermatologist treatment variations in patients by homeless status and highlights the need for standardized treatment guidelines regardless of patient sub-population for these common skin diseases.

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Allergic contact dermatitis in patients with atopic dermatitis: A 10-year retrospective review

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Allergic contact dermatitis (ACD) is prevalent in 20% of patients with atopic dermatitis (AD). We performed a retrospective chart review of patients patch tested at the Massachusetts General Hospital from 2007 to 2016 to investigated the rate of ACD among patients with AD and those without AD. We further stratified by adult or pediatric (<18 years). Statistical analyses were carried out by contingency tables using χ^2 and Fisher exact tests. A total of 2373 patients were patch tested: 695 (29.3%) in AD group and 1678 (70.7%) in non-AD group. One or more positive reactions were observed in 424 (61.0%) patients in AD group compared with 1003 (59.8%) patients in non-AD group. When stratified by age, there was no significant difference in ACD prevalence in the patients with AD and without AD. Nickel, Fragrance Mix 1, and Balsam of Peru were the top allergens in both groups. Six allergens were statistically different between AD and non-AD groups. Patients with AD had an increased sensitization to lanolin (amerchol-L101), quaternium-15, glyceryl monothioglycolate and dialkyl thiourea compared with non-AD patients. Patients with AD were noted to have decreased sensitization to neomycin and cinnamic aldehyde. Patients with AD were equally likely to develop contact sensitization as non-AD patients, regardless of age. Exposures to personal care products, such as lanolin containing moisturizers, in patients with AD may play a role in sensitization to specific allergens. Clinicians should consider patch testing patients with AD who report worsening of dermatitis or AD that does not respond to usual treatment.

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Inverse regulation of Notch4 and Wnt5a in melanoma

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Background: Notch and Wnt signaling pathways have been frequently reported to play an important role in the initiation, progression, and metastasis of melanoma, yet there remains a lack of research concerning the crosstalk and regulation of Notch4-Wnt5a. Wnt5a has been well documented to promote melanoma invasion and metastasis by inducing an epithelial-mesenchymal transition. Recent literature describes a tumor suppressive function of Notch4 via initiation of a mesenchymal-epithelial—like transition. Here, we demonstrate inverse reciprocal regulation between Notch4 and Wnt5a in melanoma.

Methods: Notch4 and Wnt5a were overexpressed in melanoma cell lines to evaluate the interactions between these pathways. Publicly available RNA microarray data from both highly and poorly invasive melanoma cell lines were analyzed for Notch4, Wnt5a, and β-catenin expression. IHC staining of human melanoma samples was performed to evaluate expression of these proteins in vivo.

Results and Conclusions: Overexpression of Notch4 suppresses non-canonical Wnt5a on the protein level, while stabilizing the canonical Wnt effector β-catenin. Wnt5a overexpression suppresses Notch4 protein levels, suggesting a reciprocal regulatory mechanism. Wnt5a expression is significantly increased in highly invasive cell lines, whereas expression of Notch4 and β-catenin is significantly increased in poorly invasive cell lines. A strong staining for Notch4 in 69% and Wnt5a in 94% of metastases was found with distinct staining patterns of areas with high Notch4 or Wnt5a or combined expression, suggesting a complex and adaptable regulatory mechanism. Our results warrant further investigation into the mechanisms by which the Notch4-Wnt5a axis contributes to phenotypic-switching and metastasis in melanoma.

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