Predictors of Nonresponse to Dupilumab in Patients With Atopic Dermatitis: A Machine Learning Analysis of United States Health Records and Claims Data

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3rd Annual RAD Virtual Conference; December 11-13, 2021

Editorial/medical writing support under the guidance of the authors was provided by Vojislav Pejović, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med*. 2015;163:461-464).
This study was sponsored by Pfizer Inc.

Disclosures

HC-HH is a researcher, consultant, and/or advisor for Pfizer Inc., AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Dermira, Dermavant, DS Biopharma, Galderma, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Eli Lilly, MedImmune, Novartis, Regeneron, Roche, Sanofi Genzyme, and UCB.

JFM is a consultant and/or investigator for Pfizer Inc., AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, LEO Pharma, Novartis, Regeneron, Sanofi, Sun Pharma, and UCB.

DG, EG, CF, AB, DEM, MDB are employees and shareholders of Pfizer Inc. and may own Pfizer stock.

JW is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Aristea Therapeutics, Bausch Health (Ortho Dermatologics), Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dr. Reddy's Laboratories, Eli Lilly, Galderma, Janssen, LEO Pharma, Mindera, Novartis, Regeneron, Sanofi Genzyme, Solius, Sun Pharmaceutical, UCB, and Zerigo Health.

Introduction and Methods

Background

- Dupilumab, a subcutaneously administered monoclonal antibody that blocks IL-4 and IL-13 signaling, is the most common systemic therapy for AD in the United States[1]
- Many patients with AD have a suboptimal response to systemic therapy, including dupilumab[1]
- As the armamentarium of systemic therapies expands, it will become increasingly important to select best treatment options for individual patients

Objective

To identify predictors of nonresponse to dupilumab among patients with AD using ML

Patient Selection

Data source and collection window

- Optum® Market Clarity database (US EHR system and insurance claims)

Eligibility criteria

- Patients ≥12 years of age with AD (*ICD-9/10-CM*: 691.8/L20.x)
- Dupilumab initiation between April 1, 2017, and June 30, 2019 (index date)
- ≥6 months of continuous eligibility before and after the index date
- No participation in a clinical trial within 6 months before and after the index date

Indicators of Nonresponse

Any of the following were considered as indicators of nonresponse to dupilumab

- Dupilumab discontinuation (gap of >60 days' supply)
- Addition of another systemic therapy or phototherapy
- Addition of a high-potency topical corticosteroid not previously used
- AD-related hospital visit
- AD-related ER visit
- Incident skin infection

Statistical Analysis

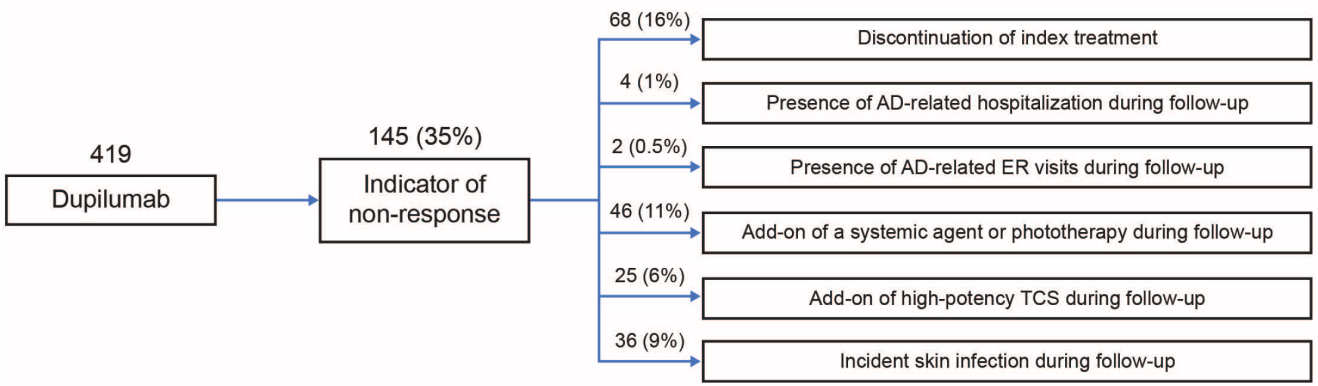
- Predictors of nonresponse were identified using 4 ML classification methods
  - Lasso logistic regression, elastic net logistic regression, random forests, and gradient-boosted trees
- The data set was randomly split into a training data set (80%) and a test data set (20%)
- The most influential predictors were based on absolute values of SHAP[2]

AD, atopic dermatitis; ER, emergency room; IL, interleukin; ML, machine learning; SHAP, Shapley Additive Explanations.

1. Eichenfield LF et al. *Dermatol Ther*. 2020;10:791-806. 2. Shapley LS. *Notes on the n-Person Game—II: The Value of an n-Person Game*. Rand Corporation; 1951.

Nonresponse to Dupilumab Was Observed in 35% of Patients Who Met Selection Criteria

Indicators of Nonresponse During the Postindex Follow-up Period[a]



Baseline Demographics and Medical History

Variable	Patients N=419
Age, mean ± SD, years	44.8 ± 17.3
Women, n (%)	236 (56)
Race, n (%)	
• White	290 (69)
• African American	67 (16)
• Asian	24 (6)
• Unknown	38 (9)
AD family history, n (%)	26 (6)
Disease duration, n (%)	
• 1-2 years	60 (14)
• 2-5 years	116 (28)
• 5+ years	93 (22)
Quan-Charlson Comorbidity Index, mean ± SD	0.9 ± 1.4

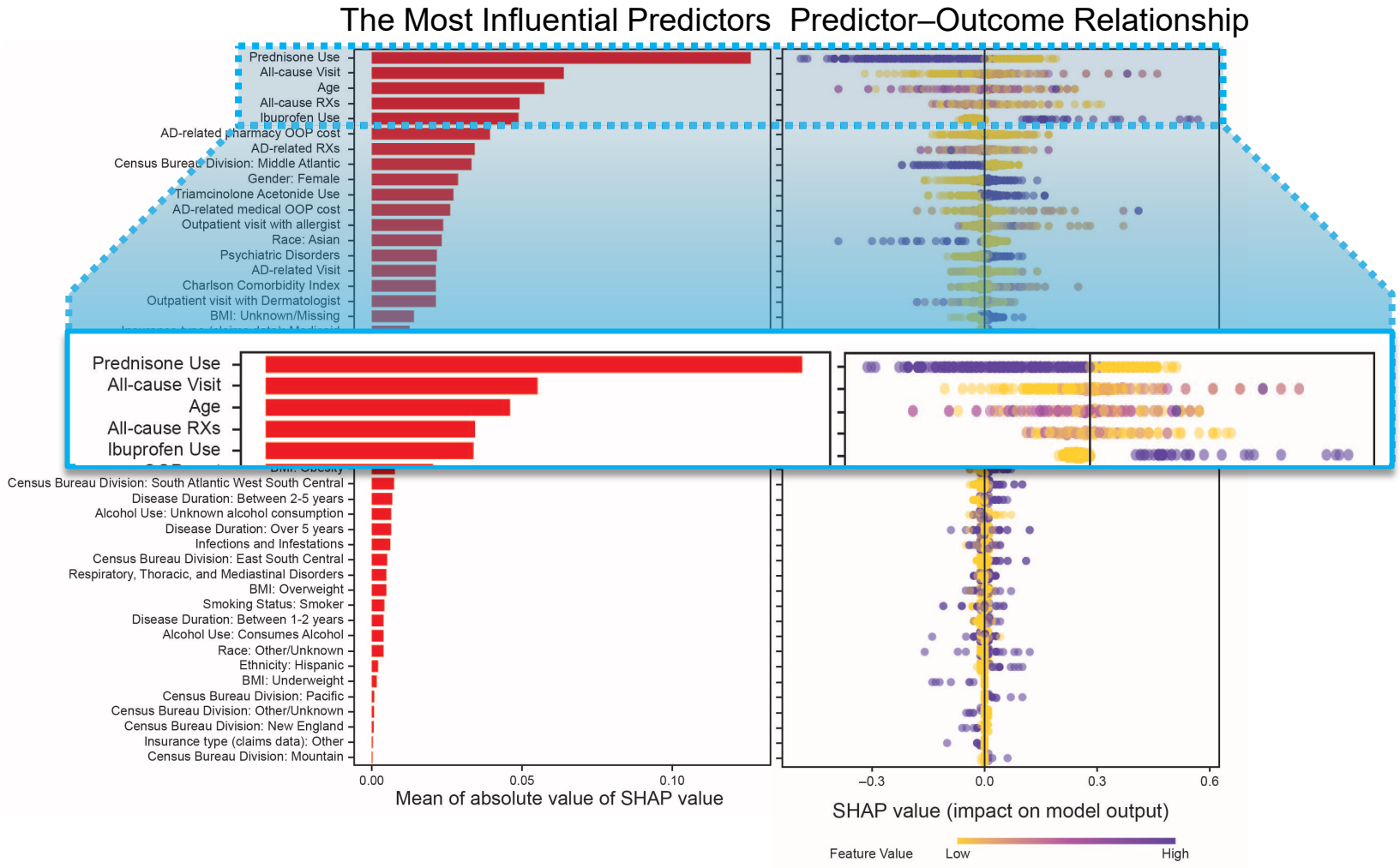
- 419 patients fulfilled selection criteria
- 145 (35%) experienced ≥1 indicator of nonresponse and 18 (4%) experienced ≥2 indicators in the 6-month postindex period
- The most common individual indicator of nonresponse was discontinuation of dupilumab (16%)

AD, atopic dermatitis; ER, emergency room; TCS, topical corticosteroid.

[a]Patients could experience ≥1 indicator of nonresponse.

The Most Common Predictors of Nonresponse Were a Claim for Ibuprofen and Quan-Charlson Comorbidity Index Value of 3 or 4

- A random forest model exhibited the highest accuracy (69%) among the 4 ML classification models
- Levels of nonresponse were **highest** among patients who had a claim for ibuprofen (69%), had a Quan-Charlson Comorbidity Index value of 3 or 4 (59%), resided in the Mountain census region (58%), and had no concomitant medication claims (55%)
- Levels of nonresponse were **lowest** among patients with few (but ≥1) AD-related physician visits (29%), those who were ≤25 years of age (28%), and those who resided in the Middle Atlantic census region (28%), among others



SHAP values are estimators of the influence of predictors in the context of all other predictors

BMI, body mass index; ML, machine learning; OOP, out of pocket; RX, prescription; SHAP, Shapley Additive Explanation.

Conclusions and Limitations

- This analysis of health records and claims data confirms earlier findings that patients with AD who initiate systemic therapy, including dupilumab, might face a significant risk for nonresponse
- These data can be used to support clinical decision making and optimization of disease management
- Key limitations
  - Retrospective, nonrandomized design
  - Proxy variables used instead of gold-standard clinical measures
  - Treatment adherence to previously administered topical therapies, which is difficult to assess, not featured in current analysis
  - Prescription claims data not capturing intended use
  - Demographic and health history data charts not complete for all patients