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Development and Validation of a Scoring System to Predict Outcomes of Vedolizumab Treatment in Patients With Crohn's Disease

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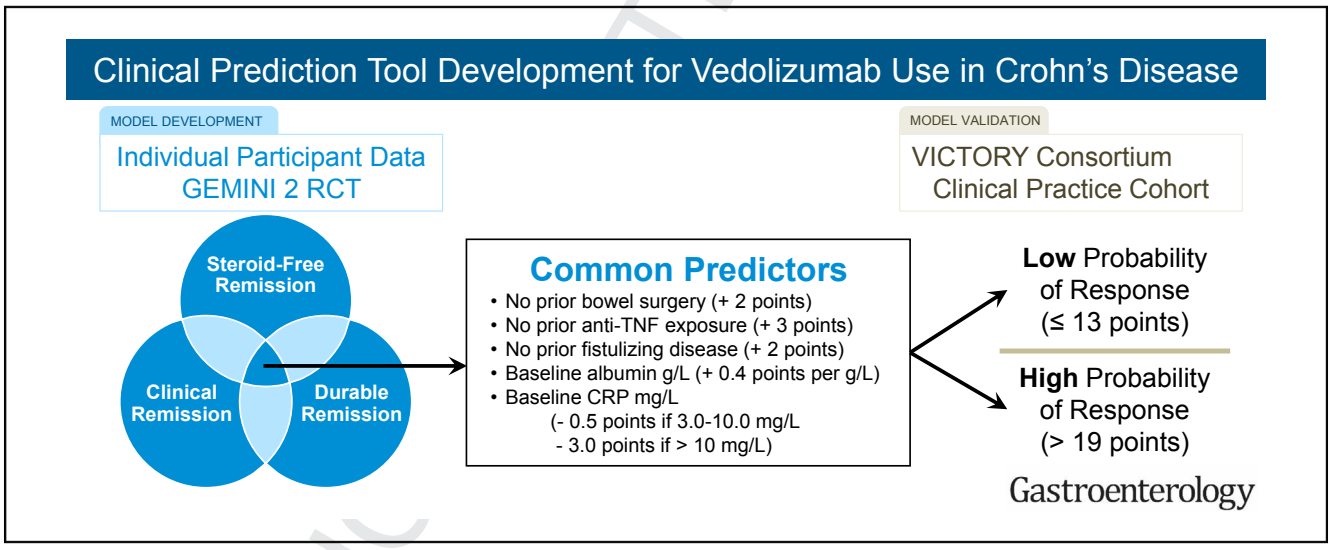

BACKGROUND & AIMS: As more treatment options for inflammatory bowel diseases become available, it is important to identify patients most likely to respond to different therapies. We created and validated a scoring system to identify patients with Crohn's disease (CD) who respond to vedolizumab. **METHODS:** We collected data from the GEMINI 2 phase 3 trial of patients with active CD treated with vedolizumab for 26 weeks (n = 814) and performed logistic regression analysis to identify factors associated with clinical, steroid-free, and durable remission (derivation set). We used these data to develop a clinical decision support tool, which we validated using data from 366 participants in a separate clinical practice observational cohort of patients with active CD treated with vedolizumab for 26 weeks (the VICTORY cohort). We evaluated the ability of this tool to identify patients in clinical remission or corticosteroid-free remission, or those with mucosal healing (MH), clinical remission with MH, or corticosteroid-free remission with MH after vedolizumab therapy using receiver operating characteristic area under the curve (AUC) analyses. The primary outcome was to develop and validate a list of factors associated with achieving remission by vedolizumab in patients with active CD. **RESULTS:** In the derivation analysis, we identified absence of previous treatment with a tumor necrosis factor antagonist (+3 points), absence of prior bowel surgery (+2 points), absence of prior fistulizing disease (+2 points), baseline level of albumin (+0.4 points per g/L), and

baseline concentration of C-reactive protein (reduction of 0.5 points for values between 3.0 and 10.0 mg/L and 3.0 points for values >10.0 mg/L) as factors associated with remission. In the validation set, our model identified patients in clinical remission with an AUC of 0.67, patients in corticosteroid-free remission with an AUC of 0.66, patients with MH with an AUC of 0.72, patients in clinical remission with MH with an AUC of 0.73, and patients in corticosteroid-free clinical remission with MH with an AUC of 0.75. A cutoff value of 13 points identified patients in clinical remission after vedolizumab therapy with 92% sensitivity, patients in corticosteroid-free remission with 94% sensitivity, patients with MH with 98% sensitivity, patients in deep remission with 100% sensitivity, and patients with corticosteroid-free clinical remission with MH with 100% sensitivity. **CONCLUSIONS:** We developed and validated a scoring system to identify patients with CD most likely to respond to 26 weeks of vedolizumab therapy. Further studies are needed to optimize its accuracy in select populations and determine its cost-effectiveness.

Keywords: IBD; CD; Prediction Model; Biomarker.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

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Vedolizumab (VDZ), a humanized anti-$\alpha_4\beta_7$ integrin monoclonal antibody that selectively targets lymphocyte trafficking to the gut, is currently indicated for the treatment of adult patients with moderately to severely active Crohn's disease (CD) who have failed corticosteroids, immunomodulators, or tumor necrosis factor-alpha (TNFα) antagonist therapy. In the GEMINI 2 phase III trial, approximately one-third of patients were in clinical remission (CREM) or corticosteroid-free clinical remission (CSF-REM) following treatment with VDZ.[1] Although these results are clinically important, the GEMINI 2 trial did not assess for mucosal healing (MH), and the strict inclusion criteria used may limit the generalizability of the results to routine clinical practice.[2]

Real-world data from multiple jurisdictions are now available for VDZ therapy in CD and outcomes are fairly consistent across clinical practice. In the US-based VICTORY (VedolIzumab for Health OuTComes in InflammatORY Bowel Diseases) consortium that evaluated 212 patients with CD, CREM, CSF-REM, and deep remission (CREM + MH) were seen in 35%, 34%, and 26% of patients, respectively, by 12 months.[3] In real-world cohorts and in the GEMINI 2 trial, prior exposure to TNFα-antagonists negatively affected treatment outcomes.[3–5] However, the magnitude of this effect and the influence of other clinical factors on treatment outcomes varied across these studies, making it difficult for clinicians to interpret their relevance to practice.

Clinical prediction models use baseline characteristics to provide an estimate of the value of a therapy on treatment outcomes for an individual patient. Furthermore, the transformation of these models into decision support tools facilitates their application as a component of "precision medicine."[6,7] With the evolving landscape of biologic therapy in CD and increasing treatment choice, a validated prognostic tool for treatment outcomes with VDZ would be of considerable value.[8] We aimed to address this gap by deriving and validating a multivariable clinical prediction model within the GEMINI 2 clinical trial dataset. To improve the ease with which this prediction model can be used at the "bedside," we transformed it into a prognostic clinical decision support tool (CDST) and validated this tool in a cohort of patients with CD treated with VDZ in routine clinical practice.

Methods

We developed and validated a multivariable model to predict CREM with VDZ treatment for patients with active CD.[1,9,10] We further assessed model prediction for MH and deep remission in VDZ-treated patients with CD with endoscopically active disease at baseline.[3] Finally, we transformed this prediction model into a CDST for use in routine practice. This study is reported according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement.[9]

Data Sources and Participants

We used 2 data sources to derive and validate the prediction model and CDST.[1,3] First, the GEMINI 2 trial was used to derive the CREM prediction model, and to derive the CDST. Second, data from the VICTORY consortium were used to externally validate the CREM prediction model, to assess the

Abbreviations used in this paper: **AUC, area under the curve; CD, Crohn's disease; CDST, clinical decision support tool; CREM, clinical remission; CRP, C-reactive protein; CSF-REM, corticosteroid-free remission; MH, mucosal healing; TNFα, tumor necrosis factor-alpha; VDZ, vedolizumab.**

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