Supplementary Tables and Figures

Supplementary Table S1

Clinical characteristics	Ulcerative colitis RWD cohort (Patient-Event) N = 723,263
Age in years (median, full range)	56 (18 – 85)
Sex	
Male	N = 293,112 (40.5%)
Female	N = 430,150 (59.5%)
Engineered Mayo Score (eMS)	
Mild (0-2)	N = 461,854 (63.9%)
Moderate (3-5)	N = 217,478 (30.1%)
Severe (6-9)	N = 43,994 (6.1%)
Clinical Outcomes	
Hospitalization due to UC	N = 106,234 (14.7%)
Death	N = 60,625 (8.4%)
Colectomy	N = 59,333 (8.2%)
Colorectal cancer	N = 17,273 (2.4%)
UC-related Symptoms	
Abdominal pain	N = 481,539 (66.6%)
Diarrhea	N = 434,590 (60.1%)
Rectal bleeding	N = 345,476 (47.8%)
Severe Anemia	N = 41,073 (5.7%)

Table S1: RWD derived UC cohort utilized for model development and simulations.
The overall cohort was used to train the machine learning model to predict the joint effect of patient features and treatments on patient outcomes. However, when predicting the outcomes of the clinical trials in the validation set, a distinct cohort was used for each trial, consisting only of patients who met the eligibility criteria for that specific trial. Importantly, during the prediction process, patient characteristics were utilized, and patients were assigned to the intervention or control arm drugs rather than the actual drugs they received in the RWD.

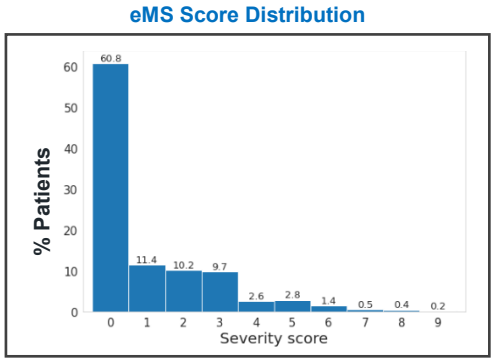
Supplementary Table S2

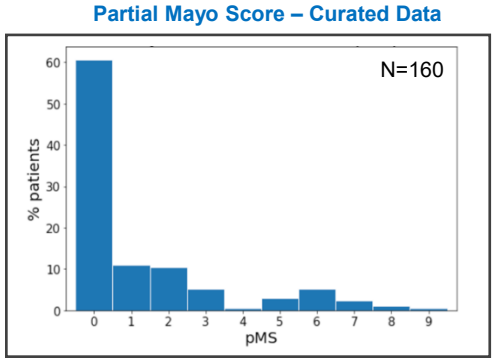
Clinical Characteristics			Elevate-12 Etrasimod group (n=238)	Elevate-12 Placebo group (n=116)	Prediction Cohort (n=29,511)
Age, years			40·3 (13·5)	40·4 (13·3)	44·5 (15·7)
Sex					
	Female		103 (43%)	43 (37%)	17,465 (59.2%)
	Male		135 (57%)	73 (63%)	12,046 (40.8%)
Extent of ulcerative colitis (per investigator)					
	Isolated proctitis		15 (6%)	12 (10%)	5,607 (19%)
	Left-sided colitis or proctosigmoiditis		146 (61%)	63 (54%)	3,835 (13%)
	Pancolitis		77 (32%)	41 (35%)	7,689 (26.1%)
	Missing		0	0	15,178 (51.4%)
Previous ulcerative colitis treatment					
	Corticosteroids		177 (74%)	98 (84%)	20,081 (68%)
	5-aminosalicylic acid		149 (63%)	85 (73%)	20,291 (68.7%)
	Thiopurines		89 (37%)	49 (42%)	4,886 (16.6%)
	Exposed to biologicals or JAK inhibitors		89 (37%)	43 (37%)	6,610 (22.4%)
		TNFα antagonists	57 (24%)	29 (25%)	4,720 (16%)
		Anti-integrin antibodies	33 (14%)	10 (9%)	2,077 (7%)
		Anti-IL-12/23 antibodies	5 (2%)	4 (3%)	260 (0.9%)
		JAK inhibitors	15 (6%)	9 (8%)	152 (0.5%)
Concomitant ulcerative colitis treatment at baseline					
	Corticosteroids		78 (33%)	38 (33%)	3,656 (12.4%)
	5-aminosalicylic acid		201 (84%)	94 (81%)	1,527 (5.2%)

Table S2: Baseline characteristics – Elevate UC 12 vs. Prediction Cohort.

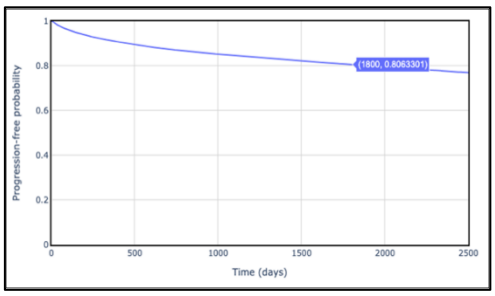
Supplementary Figure S1

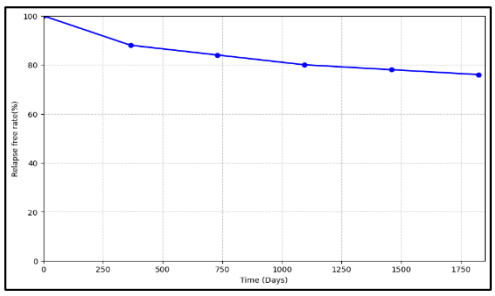
a





b





c

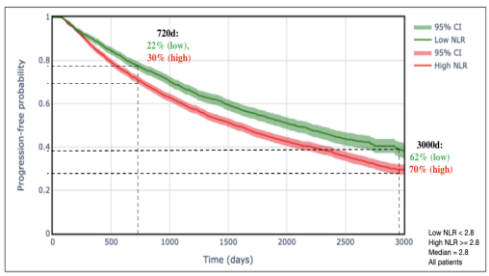
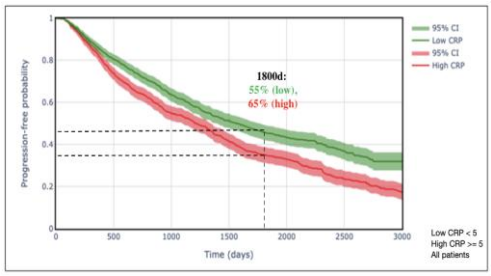
	Relapse-free survival – low / high NLR groups	**Relapse-free survival – low / high CRP groups**
eMS-retrospective Analysis		
External Validation	**(Kurimoto, et. al., 2023)** After 1 year: NLR:Low – 84% NLR:High – 68% After 4 years: NLR:Low – 53% NLR:High – 36%	**(Lee, et. Al., 2020)** After 60 months (1-Poor outcome) Adalimumab CRP:Low – 62% CRP:High - 65% Infliximab CRP:Low – 5% CRP:High - 65%

Figure S1: The eMS score successfully captures UC disease course over time and is internally coherent and concordant with previous published estimates. The eMS ability to monitor disease progression was validated through analysis of absolute progression rates relative to literature, relapse rates across time after diagnosis; and clinical relapse vs literature relapse data by neutrophil/lymphocyte ratio and CRP strata.
a) Distribution of eMS at the index date in the study UC real-world dataset compared to Partial Mayo Scores derived from curated physician-notes datasets.
b) Progression-free survival for patients analyzed using the engineered eMS compared to relapse-free survival outcomes reported by Dahlgren et al., 2022.
c) Relapse-free survival, analyzed using the engineered eMS, stratified by biomarkers, Neutrophil-to-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP) levels. The results were compared to relapse-free survival probabilities reported in the indicated retrospective studies.

Supplementary Figure S2

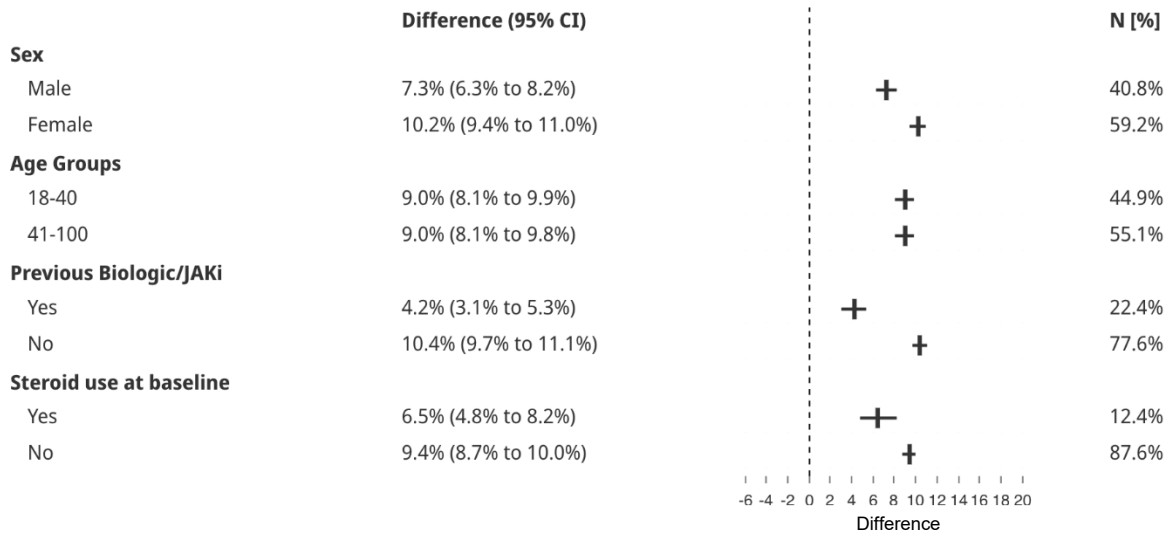


Figure S2: Predicted effect sizes (difference in treatment arm remission rate minus placebo remission rate) for patient subgroups within the Elevate UC 12 trial cohort. The original trial reported an observed effect size of 6.6% for patients with prior Biologics/JAK inhibitor treatment, compared to the predicted effect size of 4.2%. For patients without prior treatment, the observed effect size was 11.9%, while the predicted value was 10.4%. No additional subgroup outcomes were reported in the original trial.