IMPACT OF IBD ON HEALTHCARE SYSTEMS

Gaps Between Evidence and Practice in IBD

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Gaps Between Evidence and Practice in IBD

- Appropriate Disease Course Stratification of IBD patients
- Biologic Dose Escalation in Clinical Practice
- Caring for special populations of IBD patients
  - Prior malignancy
  - Pregnancy
  - Elderly patients
- Appropriate endpoints
  - Clinical Trials versus Important PROs

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Crohn's Disease Is a Chronic, Progressive Destructive Disease… (In Most Cases)

- Typically, inflammatory behavior at presentation → ≈ 50% will develop an intestinal complication within 20 years of diagnosis
- Symptoms do NOT correlate with disease activity
  - Objective assessments necessary to monitor disease course
- Perianal disease → ≈ 25% of patients
- Steroid dependence or resistance → ≈ 50% of patients
- ≈ 80% require hospitalization during disease course
- 10-year risk of major abdominal surgery → 30-55%
- Mortality → 1.4X general population, GI & Lung disease/cancer

Lichtenstein GR et al. ACG Clinical Guidelines: Management of Crohn's disease in adults. *Am J Gastroenterol*. 2018;113:481-517.

Crohn's Disease: Diagnosis and Risk Stratification Are Used to Guide Treatment

- **Location**
- **Extent**
- **Severity**
- **EIMs**

Assess inflammatory status

↓

Assess current and prior disease burden

Assess comorbidities, disease- and therapy-related complications

- **Infections**
- **Strictures**
- **Surgical hx**
- **Adverse rxns**
- **Fistulas**

ACG Crohn's Disease Guidelines

- **IBD type,**
- **location, and**
- **disease activity…**

should be documented in the medical record.

Lichtenstein GR et al. ACG Clinical Guidelines: Management of Crohn's disease in adults. *Am J Gastroenterol*. 2018;113:481-517; Sandborn WJ. *Gastroenterology*. 2014;147(3):702-705.

Treatment Selection for Crohn's Disease: Characterizing Risk

Low-Risk		High-Risk
> 30 years	**Age at diagnosis**	**< 30 years**
Limited	**Anatomic involvement**	**Extensive**
No	**Perianal and/or severe rectal disease**	**Yes**
Superficial	**Ulcers**	**Deep**
No	**Prior surgical resection**	**Yes**
No	**Stricturing and/or penetrating behavior**	**Yes**

Sandborn WJ. *Gastroenterology*. 2014;147(3):702-705; Lichtenstein GR et al. ACG Clinical Guidelines: Management of Crohn's disease in adults. *Am J Gastroenterol*.2018;113:481-517.

Ulcerative Colitis: Assessment of Disease Risk

- Standard assessment of UC disease activity
  - Mild
  - Moderate
  - Severe
- Is insufficient to guide selection of therapy
- Need to assess risk of colectomy

Low Risk for Colectomy

- Limited anatomic extent
- Mild endoscopic disease

High Risk for Colectomy

- Extensive colitis
- Deep ulcers
- Age < 40
- High CRP and ESR
- Steroid-requiring disease
- History of hospitalization
- *C difficile* infection
- CMV infection

Rubin DT et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384–413.

Distinguishing Disease *Activity* vs Disease *Severity*

Activity
Reflects cross-sectional assessment of biologic inflammatory impact on symptoms, signs, endoscopy, histology, and biomarkers

How is your patient TODAY?

Severity
Includes longitudinal (disease course) and historical factors that provide a more complete picture of the prognosis

What has your patient's disease course been like over their history since diagnosis?

Peyrin-Biroulet L et al. *Clin Gastroenterol Hepatol*. 2016;14(3):348-54.e17.

We Need Additional Tools To Manage IBD More Effectively

Currently we are Lacking the Following

- Individual patient prognosticator
  - Surgery
  - Hospitalization
  - Stricture
  - Dysplasia
  - Fistula

Predicting Colectomy Risk

Design: Retrospective study of pt records from January 1, 2017, to December 31, 2017.

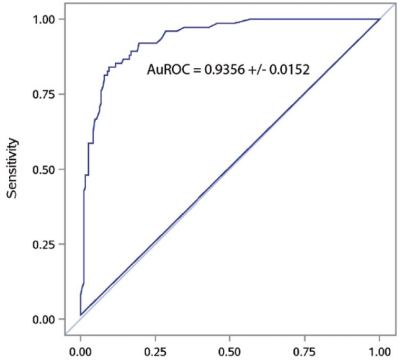
- Cases: had Total Proctocolectomy (TPC) performed for refractory UC after January 1, 2008.
- Controls: had no prior UC surgery.
- Clinical data: assessed 1–12 months preceding TPC or clinic visit for cases and controls, respectively.
- Randomly selected two-thirds of patients to develop a TPC prediction model using multivariable logistic regression.
- One-third was reserved for model validation.
- URL: https://connect.calcapp.net/?app=rxry0p.

TABLE 3. Multivariable Prediction Model for TPC in UC

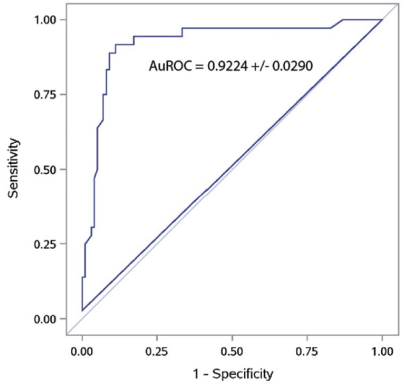
Variable	Coefficient	Odds Ratio	OR 95% LCL	OR 95% UCL	*P*
Intercept	0.02				0.99
Albumin, g/dL	–1.06	0.35	0.15	0.78	0.01
Mayo endoscopic subscore >1	1.17	10.30	4.35	24.37	<0.01
9-point Mayo score >5	0.95	6.63	2.70	16.27	<0.01
Corticosteroid use in last 6 mo	0.64	3.61	1.50	8.70	<0.01

Abbreviations: LCL, lower confidence limit; UCL, upper confidence limit.

Initial Cohort



Validation Cohort



Dalal R et al. *IBD.* 2019;DOI 10.1093/ibd/izz014.

Predicting Response to Medical Therapy

Clinical Gastroenterology and Hepatology 2020;18:2952–2961

Development and Validation of Clinical Scoring Tool to Predict Outcomes of Treatment With Vedolizumab in Patients With Ulcerative Colitis

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BACKGROUND & AIMS: We created and validated a clinical decision support tool (CDST) to predict outcomes of vedolizumab therapy for ulcerative colitis (UC).

METHODS: We performed logistic regression analyses of data from the GEMINI 1 trial, from 620 patients with UC who received vedolizumab induction and maintenance therapy (derivation cohort), to identify factors associated with corticosteroid-free remission (full Mayo score of 2 or less, no subscore above 1). We used these factors to develop a model to predict outcomes of treatment, which we called the vedolizumab CDST. We evaluated the correlation between exposure and efficacy. We validated the CDST in using data from 199 patients treated with vedolizumab in routine practice in the United States from May 2014 through December 2017.

RESULTS: Absence of exposure to a tumor necrosis factor (TNF) antagonist (+3 points), disease duration of 2 y or more (+3 points), baseline endoscopic activity (moderate vs severe) (+2 points), and baseline albumin concentration (+0.65 points per 1 g/L) were independently associated with corticosteroid-free remission during vedolizumab therapy. Patients in the derivation and validation cohorts were assigned to groups of low (CDST score, 26 points or less), intermediate (CDST score, 27–32 points), or high (CDST score, 33 points or more) probability of vedolizumab response. We observed a statistically significant linear relationship between probability group and efficacy (area under the receiver operating characteristic curve, 0.65), as well as drug exposure ($P < .001$) in the derivation cohort. In the validation cohort, a cutoff value of 26 points identified patients who did not respond to vedolizumab with high sensitivity (93%); only the

Abbreviations used in this paper: CDST, clinical decision support tool; CI, confidence interval; CSFREM, corticosteroid-free remission; ITT, intention to treat; OR, odds ratio; TNF, tumor necrosis factor; UC, ulcerative colitis; VDZ, vedolizumab.

Most current article

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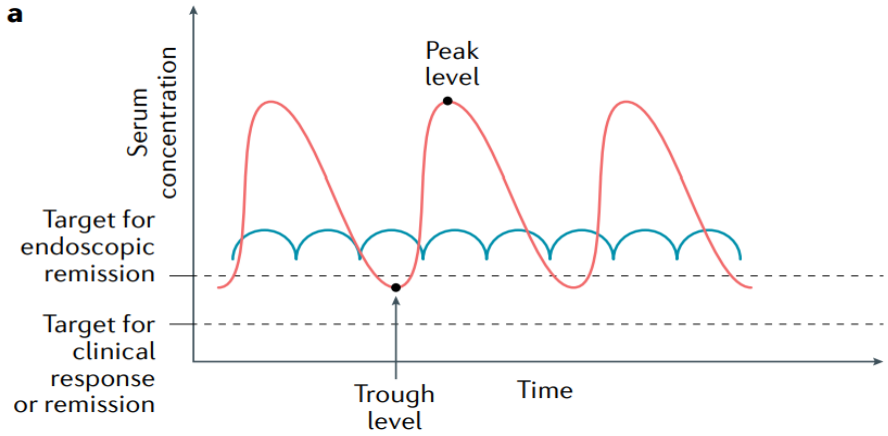
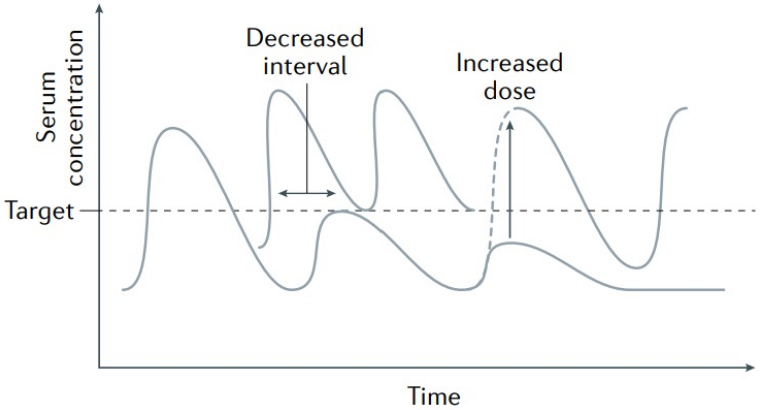
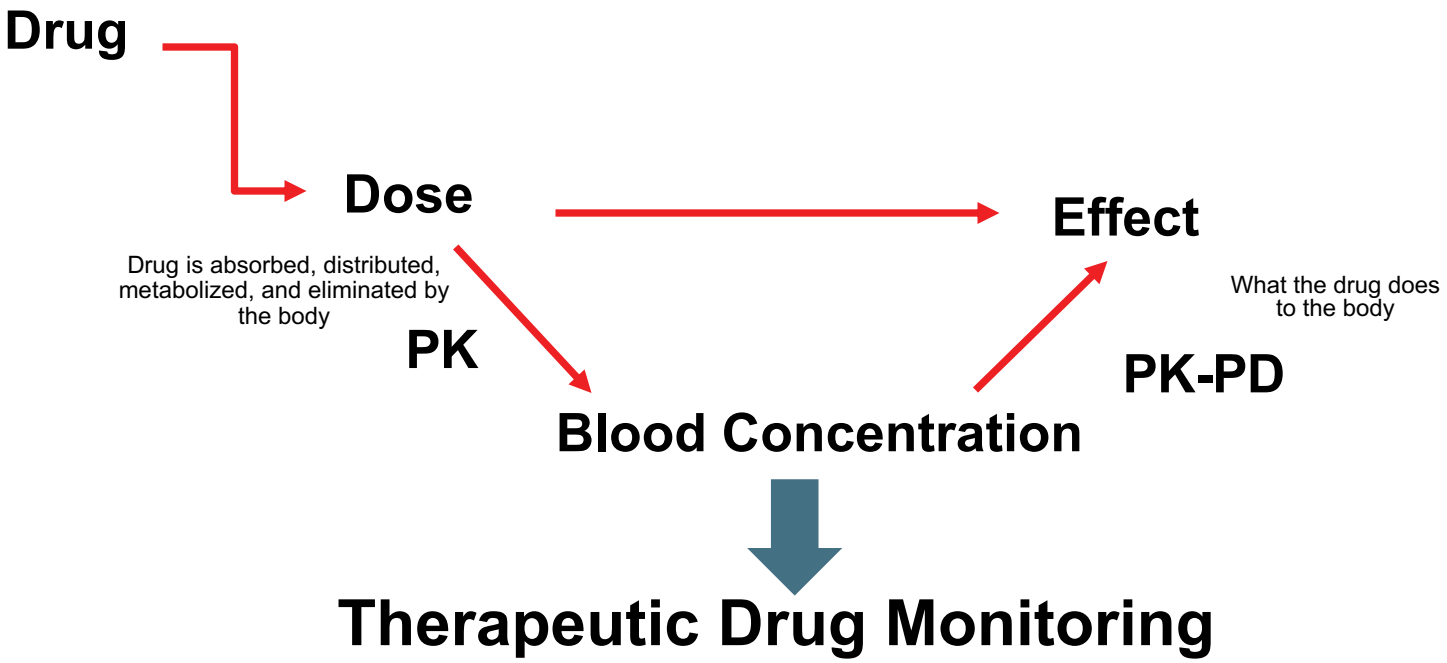
Biologic Dose Escalation in Clinical Practice





What Is Therapeutic Drug Monitoring?



PK = pharmacokinetic; PK-PD = pharmacokinetic/pharmacodynamic.

Gale Encyclopedia of Nursing and Allied Health. Encyclopedia.com. Accessed March 7, 2021.
http://www.encyclopedia.com/medicine/encyclopedias-almanacs-transcripts-and-maps/therapeutic-drug-monitoring

Definitions

- Pharmacokinetics – Is currently defined as the study of the time course of drug absorption, distribution, metabolism, and excretion. Clinical pharmacokinetics is the application of pharmacokinetic principles to the safe and effective therapeutic management of drugs in an individual patient.
- Pharmacodynamics – Refers to the relationship between drug concentration at the site of action and the resulting effect, including the time course and intensity of therapeutic and adverse effects. The effect of a drug present at the site of action is determined by that drug's binding with a receptor.

Biologic Therapy: Why Should We Monitor?

- Optimize first biologic
  - The first biologic = the best opportunity
  - The earlier in the course of disease we treat the more beneficial and the less disease progression
- Assess outcomes of drug (trough) and antibody level:
  - Inadequate drug
  - Antibody positive
  - Wrong drug class

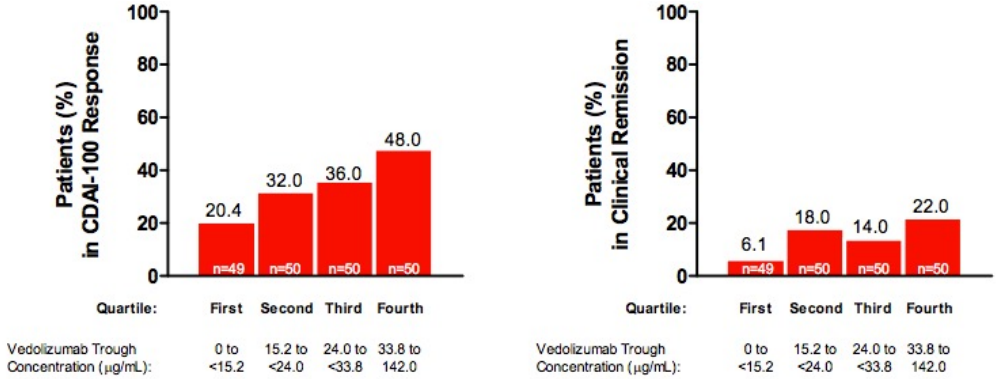
Lichtenstein GR. *Therap Adv Gastroenterol*. 2013;6(4):269-93.

General Concepts

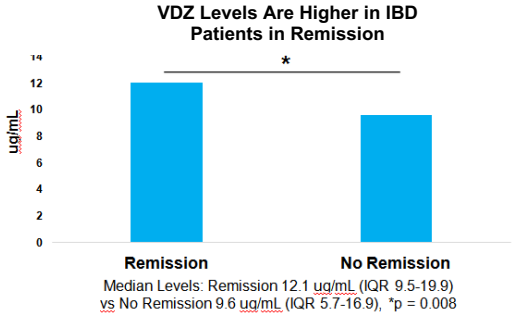
- Higher drug levels – without antibodies are associated with better remission rates and better rates of mucosal healing
  - Anti-TNF agents – Infliximab, Adalimumab, Golimumab, Certolizumab Pegol
  - Anti-integrins – Vedolizumab
  - Anti-interleukin-12/23 – Ustekinumab
- Evolving prospective data to suggest routine TDM should be done for treatment with biologics
- PROactive TDM makes good sense

Therapeutic Drug Monitoring – Vedolizumab

Clinical response and remission at week 6 by VDZ trough in GEMINI 2 (CD)



Higher VDZ trough in IBD patients in clinical and CRP remission during maintenance



Low trough levels of vedolizumab at Week 6 (<19.0 µg/mL) associated with need for additional doses (given at Week 10 and then every 4 weeks) in small prospective study (n=47)

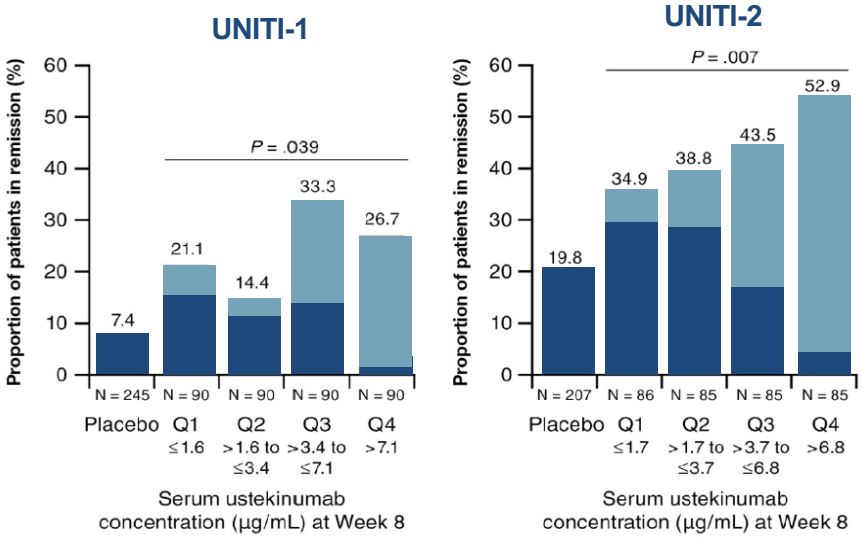
OR 2.65 (95% CI 1.24-5.66) for clinical/CRP remission if VDZ level > 10.9

Sandborn WJ et al. *NEJM.* 2013; Ungaro R et al. *AIBD*. 2016; Williet N et al. *CGH*. 2017.

Therapeutic Monitoring for Ustekinumab

- Apparent exposure-response relationship in UNITI trials
- Thresholds associated with better outcomes
  - Maintenance >0.8 – 1.35 µg/mL (Clinical remission)
  - Maintenance >4.5 µg/mL (Endoscopic response)
- Maintenance <0.5 µg/mL associated with worse outcomes

Clinical Remission in UNITI Trials By Serum Ustekinumab Concentration



1. Adedokun OJ et al. *Gastroenterology*. 2018;154(6):1660-1671; 2. Battat R et al. *Clin Gastroenterol Hepatol*. 2017; 15(9):1427-1434.

Caveats

- Lack of adequately powered randomized prospective placebo controlled primary data assessing these outcomes (dose escalation of the biologic) in a large randomized placebo-controlled trials
- Prohibitive Costs to assess this in prospective, randomized, placebo clinical trials
- Real World Experience data exists
- PROactive TDM makes good sense – but studies not well designed

Caring for Special Populations of IBD Patients

- Prior malignancy
- Pregnancy
- Elderly patients

Pregnancy

- 1.6 million people have IBD in USA
- ~ 1/2 are women
- Most carry the diagnosis during their reproductive years

Shah SC et al. *Gastroenterology*. 2018;155:1079-1089.e3 Picture from: prenate.com

The Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes (PIANO) Study

- Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes
- Prospective observational study
- Pregnant women with IBD at 30 US centers between Jan 2007 to present, over 1600 patients
- Questionnaires at study intake, each trimester, delivery and 4, 9 and 12 months after birth
- Offspring enrolled after 2010 assessed for developmental milestones at 12, 24, 36 and 48 months after estimated due date

The PIANO Registry: 2021 Results

- 2007-2019
- 1490 completed pregnancies
- 1431 live births
- 1 yr infant outcomes in 1010

Group	Pregnancy Outcome
None **N=379**	
Group A: IM **N=42**	
Group B: Biologic **N-642**	C-Section
Group AB: **IM plus a biologic** **N=227**	C-Section

- Drug exposure did not increase rate of congenital malformations, spontaneous abortions, preterm birth, low birth weight and infections during first year of life
- Spontaneous abortion before 20 weeks independently associated with:
  - Active disease HR 3.41;95% CI 1.51-7.69
  - Prior spontaneous abortion HR 2.17;95% CI, 1.05-4.49
- Preterm birth associated with increased infant infection OR 1.73, 95% CI 1.19-2.51

Mahadevan U et al. Pregnancy and Neonatal Outcomes after Fetal Exposure to Biologics and Thiopurines Among Women with Inflammatory Bowel Disease. *Gastroenterology*. 2021. 160:1131-1139.

Active Disease Associated With Increased Risk of Adverse Pregnancy Outcomes

Meta-analysis: 28 studies

	Low Birth Weight (OR)	Preterm Birth OR	Small for Gestational Age OR	Spontanious Abortion OR	Stillbirths OR
Women with	3.81 (95% confidence	2.42 [95% CI 1.74-	1.48 [95% CI 1.19-	1.87 [95% CI	2.27 [95% CI 1.03-
active IBD	interval [CI] 1.81-8.02)	3.35]	1.85]	1.17-3.0]	5.04]
c/w inactive IBD					

Subgroup Analysis	Active Ulcerative Colitis	Active Crohn's Disease
Increased Risk	Low birth weight preterm birth, spontaneous abortion	Preterm birth, small for gestational age, spontaneous abortion

Kim A et al. *Journal of Crohn's and Colitis*. 2021, 719-732.

Safety of Biologic Therapy in the Elderly

Clinical Gastroenterology and Hepatology 2019;17:1736–1743

SYSTEMATIC REVIEWS AND META-ANALYSES

Safety of Biologic Therapy in Older Patients With Immune-Mediated Diseases: A Systematic Review and Meta-analysis

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e108. Learning Objective–Upon completion of this activity, successful learners will be able to define the diagnosis, natural history, and treatment of IBD in older individuals.

BACKGROUND & AIMS: **Management of immune-mediated inflammatory diseases often requires lifelong immunosuppression. Increasing numbers of older patients have inflammatory diseases and are particularly vulnerable to risks of immune suppressive therapies—particularly infections and malignancies.**

METHODS: **We systematically searched PubMed/Medline and Embase to identify eligible studies that examined the safety of biologic therapies in older patients with immune-mediated inflammatory diseases (inflammatory bowel disease, rheumatoid arthritis, psoriasis). Included studies provided information on patients who began receiving therapy with a biologic agent when they were older than 60 years and a control population (either younger users of biologics or older patients who did not use biologics). Information of on overall pooled rates of infections, malignancy, and mortality were extracted. A DerSimonian and Laird random effects model was used to calculate pooled odds ratios (ORs) and 95% CIs.**

RESULTS: **Our meta-analysis included 14 unique studies that comprised 4719 older users of biologics, 13,305 younger users of biologics, and 3961 older patients who did not use biologics. The pooled prevalence of infections in older and younger users of biologics was 13% and 6% respectively, yielding a pooled random effects odds ratio of 2.28 (95% CI, 1.57–3.31). Older age was associated with a significant increase in risk of malignancy (OR, 3.07; 95% CI, 1.98–4.62) compared to younger age. Older users of biologics had a 3-fold increase in risk of infection compared to patients who did not use biologics (OR, 3.60; 95% CI, 1.62–8.01), but there were no significant differences in odds of malignancy (0.54, 95% CI, 0.28–1.05) or death (OR, 1.52; 95% CI, 0.44–5.28) compared to older patients who did not use biologics.**

CONCLUSION: **In a systematic review and meta-analysis of studies on the safety of biologic therapies in older patients with inflammatory diseases, we found that older users of biologic agents have an increased risk of infections compared with younger users or older patients who do not use biologics. Large, prospective cohort studies are needed to examine safety of biologic therapy in older patients with immune-mediated diseases**

Keywords: Anti-TNF Therapy; Elderly; Autoimmune Disease; Inflammatory Bowel Disease; Rheumatoid Arthritis; Psoriasis; Safety; Tumor Necrosis Factor; IBD; Drug.

With the rising life expectancy worldwide and improvements in treatment of various immune-mediated diseases (IMDs), the number of older individuals with an IMD will continue to expand. Treatment of older patients with a chronic IMD can pose certain unique challenges. Advanced age is a risk factor for several comorbidities such as cardiovascular disease,[1] diabetes,[2] and cancer which complicate the use of immunosuppressive therapy.[3] In addition, there may be age-related changes in the pharmacokinetic properties of therapy, including absorption, distribution, and excretion, when compared with the younger age population.[4]

The cornerstone of treatment for IMDs remains lifelong immunosuppression. In particular, monoclonal antibodies targeting various inflammatory cytokines have emerged as a key component of the therapeutic algorithm for inflammatory bowel diseases (IBD) (eg, Crohn's disease, ulcerative colitis), rheumatoid arthritis (RA), and psoriasis. In each of these diseases, biologic therapies are effective for both inducing and maintaining

Abbreviations used in this paper: CI, confidence interval; IBD, inflammatory bowel disease; IMD, immune-mediated disease; OR, odds ratio; RA, rheumatoid arthritis.

Most current article

1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2018.12.032

Risk Factors in Elderly IBD Patients

Hong SH et al. *Ther Adv Gastroenterol.* 2021, Vol. 14: 1–15 DOI: 10.1177/ 1756284821102339.

Use of Biologics in Patients With Prior Malignancy

Clinical Gastroenterology and Hepatology 2022;20:88–95

Vedolizumab or Tumor Necrosis Factor Antagonist Use and Risk of New or Recurrent Cancer in Patients With Inflammatory Bowel Disease With Prior Malignancy: A Retrospective Cohort Study

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BACKGROUND & AIMS: Treatment of patients with inflammatory bowel diseases (IBD; Crohn's disease (CD), ulcerative colitis (UC) who have a prior history of cancer pose a unique challenge. The impact of Vedolizumab (VDZ) on the risk of new or recurrent cancers in patients with a previous malignancy is unknown.

METHODS: This was a retrospective study of patients with IBD with a history of current or prior cancer who were subsequently initiated on VDZ, tumor necrosis factor α antagonists (anti-TNF), or had no immunosuppressive therapy after the index cancer diagnosis. The occurrence of a new primary cancer or recurrent cancer was ascertained on follow-up. Multivariable Cox-proportional hazard models were used to determine the independent effect of post-cancer treatment on new/recurrent cancer.

RESULTS: The study included 96 patients exposed to VDZ after a prior diagnosis of cancer who were compared to 184 and 183 patients exposed to anti-TNF or no immunosuppressive therapy, respectively. The most common primary cancer were solid tumors (50%). Over a median of 6.2 person-years of follow-up, 18 patients on VDZ developed new (7) or recurrent (11) cancer corresponding to a rate of 22 per 1000 person-years after cancer diagnosis. In a multivariable Cox-model, after adjusting for confounders, there was no increase in the risk of new or recurrent cancer with VDZ (HR 1.38 95% CI 0.38 – 1.36) or anti-TNF therapy (HR 1.03, 95% CI 0.65 – 1.64), when compared to no IS.

CONCLUSIONS: Neither Vedolizumab nor TNF-antagonists were associated with increased risk of new or recurrent cancers in patients with prior malignancy.

Keywords: Cancer Recurrence; Biologics; IBD.

Immunosuppression through use of conventional immunomodulators (azathioprine, mercaptopurine), biologic agents, or small molecules forms the foundation for the treatment of the inflammatory bowel diseases (IBD) Crohn's disease (CD) and ulcerative colitis (UC).[1] The emergence of such agents over the past 3 decades has revolutionized the ability to treat IBD, reducing disease-related surgery and hospitalization. However, such immunosuppression is associated with serious safety concerns, including the potential for treatment-related complications.[2] Of particular interest to patients is the impact of such medications on cancer risk, including incident cancer and recurrences in those with prior malignancy.[3] The latter is an increasingly pressing problem with the rising burden of IBD in older patients and therapeutic algorithms more frequently encouraging early use of immunosuppressive therapy to achieve optimal disease outcomes.[4,5]

Several cohort studies have shown that thiopurines are associated with an increase in the risk of lymphoma and nonmelanoma skin cancer (NMSC).[6] Also, tumor necrosis factor-α antagonists (anti-TNF) may be associated with an increased risk of melanoma and

Abbreviations used in this paper: anti-TNF, tumor necrosis factor-α antagonists; CD, Crohn's disease; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease; NMSC, nonmelanoma skin cancer; no IS, no immunosuppression; UC, ulcerative colitis; VDZ, vedolizumab.

Most current article

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https://doi.org/10.1016/j.cgh.2020.10.007

Critique:

- Small studies
- Uncontrolled
- Retrospective
- Varied malignancies
- Different malignancy stages at time of inclusion
- No specific prespecified treatment protocols
- Potential of bias for those treated vs those not treated

Challenges in IBD

- Disease Classification

Potential Solution:

- Define Novel IBD subtypes / sub-phenotypes that align to molecular biomarkers
- Artificial Intelligence / Machine Learning can be used to standardize and enhance traditional endoscopy, histology, and radiology methods
- Incorporate longitudinal assessment (of biomarkers and phenotype) and broad ethnic representation in the above

Ricciuto A et al. *Gastroenterology*. 2022, 162(7): 1815-1821.DOI:https://doi.org/10.1053/j.gastro.2022.02.049.

Appropriate Endpoints

- Endpoints

Issues:

- There is a lack of criterion standard, precision medicine–appropriate endpoints.
- Such endpoints must be objective, clearly defined, reproducible, attainable within a sensible timeframe, and deeply rooted in disease biology and, thus, causally associated with clinically meaningful long-term outcomes.
- Clinical activity indices, despite being highly relevant for patients and regulatory agencies, are not suitable, given their subjective nature and imperfect correlation with inflammatory activity.
- Even seemingly “hard” outcomes, such as surgery, hospitalization, and treatment escalation, are suboptimal because they lack standardized definitions and may reflect physician practices and/or patient preferences.

Ricciuto A et al. *Gastroenterology*. 2022, 162(7): 1815-1821.DOI:https://doi.org/10.1053/j.gastro.2022.02.049.

Appropriate Endpoints

- Endpoints

Issues:

- Regulatory agencies are increasingly embracing objective outcomes, such as endoscopy and histology in trial design, but have simultaneously mandated patient-reported outcomes (PROs) as coprimary endpoints.
- Although the importance of the patient experience cannot be undermined, PROs capture a construct driven not only by inflammation but by a myriad of other influences.
  - Anatomy
  - Diet
  - Microbiome
  - Functional processes

Ricciuto A et al. *Gastroenterology*. 2022, 162(7): 1815-1821.DOI:https://doi.org/10.1053/j.gastro.2022.02.049.

Appropriate Endpoints

- Endpoints

Issues:

- PROs and endpoints like mucosal healing dilutes the objectivity of the latter.
- The differential biological determinants of clinical activity and endoscopic healing are illustrated by the PROgECT trial, in which a colonic gene expression signature predicted mucosal healing in patients with UC treated with golimumab while showing no association with clinical response or remission.
- An additional unknown is the optimal timepoint at which to assess outcomes for each therapy, reflecting our incomplete understanding of pharmacodynamics.

Ricciuto A et al. *Gastroenterology*. 2022, 162(7): 1815-1821.DOI:https://doi.org/10.1053/j.gastro.2022.02.049.

Appropriate Endpoints

- Endpoints

Issues:

- There is also a need to account for variability in drug systematically applied across studies.
- Although overlap is to be expected with endpoints identified through initiatives such as Selecting Therapeutic Targets in IBD, discrepancies are anticipated (regarding PROs, for example), which must be reconciled moving forward.
- Although endoscopic, histologic, and radiographic endpoints are likely the most objective and appropriate of currently available outcome measures, they are far from perfect.
- None encapsulates the totality of the concepts of inflammatory burden, disease severity, and prognosis, and all have operational challenges, such as optimal indices/cutoffs and training standards.

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Challenges in IBD

- Disease Classification

Potential Solution:

- Define Novel IBD subtypes / sub-phenotypes that align to molecular biomarkers.
- Artificial Intelligence p/ Machine Learning can be used to standardize and enhance traditional endoscopy, histology, and radiology methods.
- Incorporate longitudinal assessment (of biomarkers and phenotype) and broad ethnic representation in the above.

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Challenges in IBD

- Endpoints

Potential Solution:

- Achieve consensus on a set of clearly defined, reproducible and objective endpoints (clinical activity indices, rather than patient-reported outcomes)
- Leverage Artificial Intelligence/Machine Learning to automate/optimize the assessments
- Develop molecular biomarkers associated with disease biology and progression (preferably a peripheral marker to facilitate frequent monitoring and treatment modification).
- Dedicate efforts to further elucidating drug mechanism of action to inform optimal time for outcome assessment

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Challenges in IBD

- Therapies

Potential Solution:

- There is a need for additional targeted IBD therapies.
- Use of combination therapy may allow overcoming the “ceiling effect” observed in most clinical trials.
- There is a need to strive to deepen the understanding of Pharmacodynamics and pharmacokinetic mechanisms to facilitate optimized and patient tailored medication performance.
- The use of TDM- and dashboard –based dosing are a start, but insufficient.
- Leverage Artificial Intelligence / Machine learning methods to optimize choice of drug(s) and drug doses (e.g., phenotypic personalized medicine).

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Impact of IBD on Healthcare Systems

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