IBD in the Elderly 2023

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Disclosures

- **Charles N Bernstein MD:**
- Advisory board – AbbVie Canada, Amgen Canada, Bristol-Myers Squibb Canada, Eli Lilly Canada, JAMP Pharmaceutical, Janssen Canada, Pfizer Canada, Pendopharm Canada, Sandoz Canada, Takeda;
- speaker's bureau – AbbVie Canada, Janssen Canada, Pfizer Canada, Takeda Canada;
- grant/research support – AbbVie Canada, Amgen Canada, Sandoz Canada, Janssen Canada, Pfizer Canada, Takeda
- Educational grants: AbbVie Canada, Eli Lilly Canada, Ferring Canada, Janssen Canada, Organon Canada, Pfizer Canada, Takeda Canada

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The 2023 Impact of Inflammatory Bowel Disease in Canada: Special Populations—IBD in Seniors

Shaffer et al JCAG 2023; 6: S45-S54

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IBD in the Elderly in Canada-FACTS

- 1/88 elderly have IBD (1.14%)
- Prevalence increases by 2.76%/yr
- Incidence is 28.6/100000
- AAPC 0.66 (95% CI, -0.55, 1.52)
- 15% of all persons dx are >65

Shaffer et al JCAG 2023; 6: S45-S54

IBD in the Elderly: What makes it different?

1. Polypharmacy
2. Comorbidities, i.e., DM and use of pred, osteoporosis and risk for fracture, VTE risk
3. Risk for shingles and pneumonia
4. Risk for postoperative complications
5. risk for cognitive impairment
6. Risk for cancer
7. Frailty
8. Access to care

IBD in the Elderly-RX OUTCOMES

- Age >60 assoc with reduced post op prophylaxis (0.2, 95% CI 0.05, 0.76)
- ASUC more treatment failures (28.4%) in >60 than younger adults (12.2%)
- No difference >60 vs <60 for disease related bad outcomes (hospitalizations, surgery, treatment escalation), 0.85 (95% CI 0.58, 1.25)
- Elderly onset UC 3x CMV, 2.4X HSV, 3x all cancer

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Shaffer et al JCAG 2023; 6: S45-S54

ACCESS TO CARE AND INFORMATION

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When a gastroenterologist is involved in care there are better outcomes:
less surgery in UC, higher use of biologicals

Keunzig JCAG 2021

MB, AB, ON population based study

Rural >65 vs urban >65 and likelihood to receive IBD care from gastroenterologist

OR=0.35 (95% CI 0.26, 0.46)

Benchimol Clin Epidemiol 2018

Self-reported mean information technology literacy scores worsened with advancing age

Kaazan JGH Open 2021

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RATES OF INTERNET USE: GENERAL SOCIAL SURVEY (CANADA)

>/=65
2007: 32%
2016: 68%

ALL Canadians <65
2016: 97%

65-69: 81%
70-74: 74%
75-79: 64%
>/=80: 49%

Comorbidities: IBD in the Elderly in Canada

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Comorbidities IBD in the Elderly in Canada

Risk for cardiac disease HR=1.24 (1.07, 1.43)

Risk for cerebrovascular disease HR=1.19, 95% CI 1.01, 1.40)

Risk for Peripheral vascular disease HR=1.36 (95% CI, 1.14, 1.62)

Risk for COPD HR=1.38 (95% 1.12, 1.7)

Risk for cancer HR=1.21 (95% CI 1.04, 1.40)

Risk for DMII HR=1.17 (95% 1.01, 1.35)

Bernstein APT 2021

RESPONSE TO VACCINES

IMID >60 on immunomodulator/ biologic drugs:
Reduced response to mRNA or adenovirus vector vaccine

>60 have lower antibody response and
greater likelihood of nonresponse

Seniors have more rapid decline in antibody levels

Al Janabi Br J Dermatol 2021
Kennedy Gut 2021
Kappelman Am J Gastroenterol 2022

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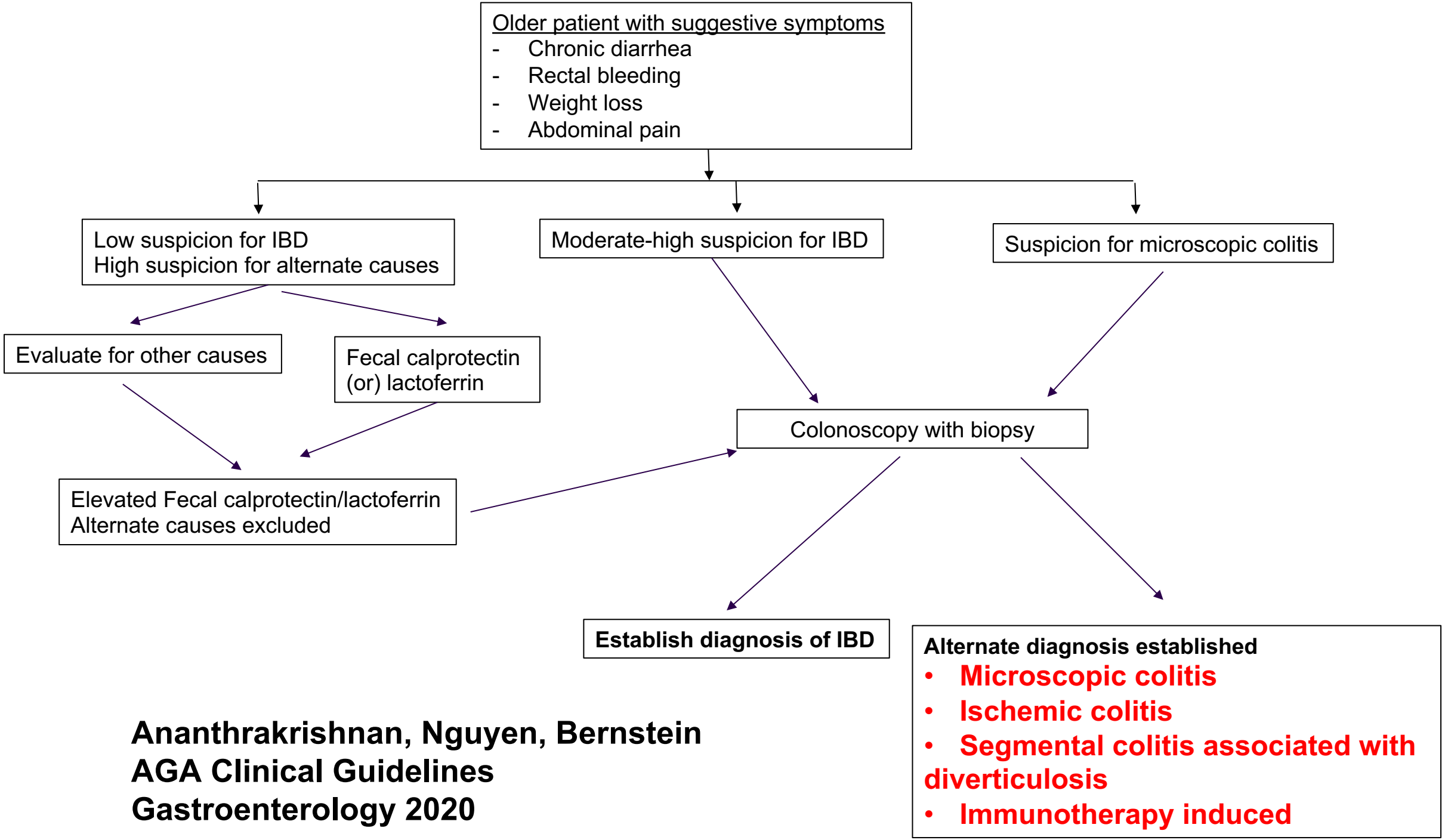


Ananthrakrishnan, Nguyen, Bernstein
AGA Clinical Guidelines
Gastroenterology 2020

Microscopic Colitis

Epidemiology

Age 50-70

F:M 9:1

Incidence 4-5 per 100,000

Chronic watery diarrhea 8-16%

Ethnicity (?)

Symptoms

Chronic watery diarrhea

Nocturnal stools

Urgency

Incontinence

Abdominal pain

Weight loss

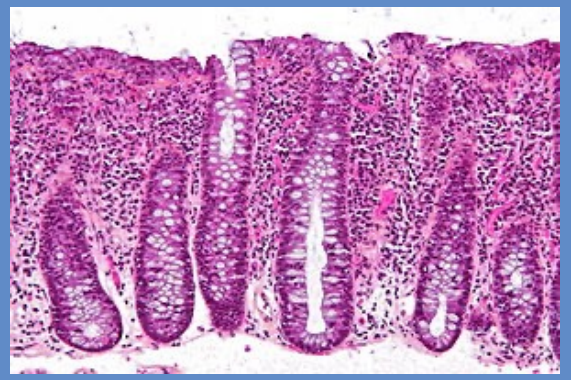
Arthralgias

Fatigue

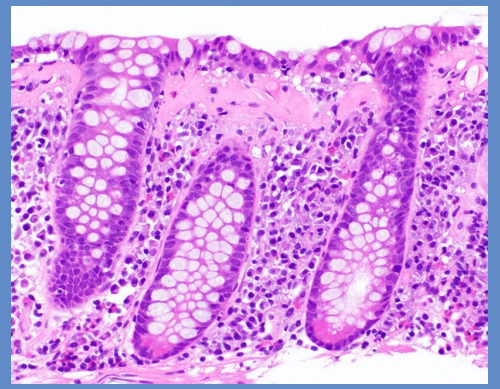
Subtypes

Lymphocytic

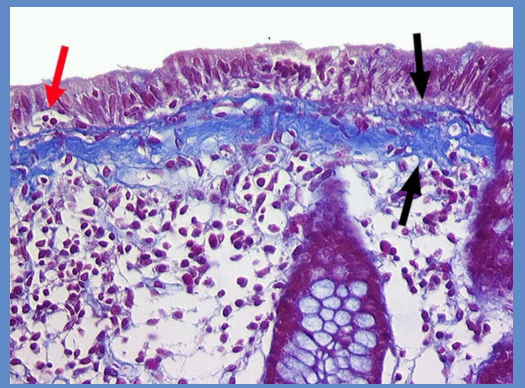
Collagenous



https://librepathology.org/w/index.php?title=Lymphocytic_colitis&mobileaction=toggle_view_desktop



https://www.pathologyoutlines.com/topic/coloncollagenous.html



https://www.webpathology.com/image.asp?n=8&Case=1038

Ananthrakrishnan, Nguyen, Bernstein
AGA Clinical Guidelines
Gastroenterology 2020

New Diagnosis of Inflammatory Bowel Disease

Assess prognostic factors
Assess disease phenotype
Assess psychosocial supports and needs

Mild disease

Severe disease

Assess comorbidity, frailty, and functional status

Fit patient

Frail patient

Health Maintenance

General health maintenance
-Depression screen
-Optimize comorbidity
- colon and non colon cancer screening

Vaccination
- Pneumococcal
- Influenza (annual)
- Inactivated zoster

Induction
-Steroids (preference for budesonide over prednisone)
-Anti-TNF (assess ability to administer and adhere to prescribed regimen)
-Vedolizumab (*maybe slightly favored in those with higher risk of complication)
-Ustekinumab (*maybe slightly favored in those with higher risk of complication)
-Tofacitinib (*higher risk of VTE with 10mg BID in those with cardiac risk factors)

Maintenance
-Anti-TNF (assess ability to administer and adhere to prescribed regimen)
-Vedolizumab (*maybe slightly favored in those with high risk of complication)
-Ustekinumab (* maybe slightly favored in those with high risk of complication)
-rizenkizumab, mirenkizumab, guselkinumab
-Tofacitinib 5mg BID, **upacitinib 30 mg OD**

How robust are the data for treating the elderly with biologicals/JAKs?

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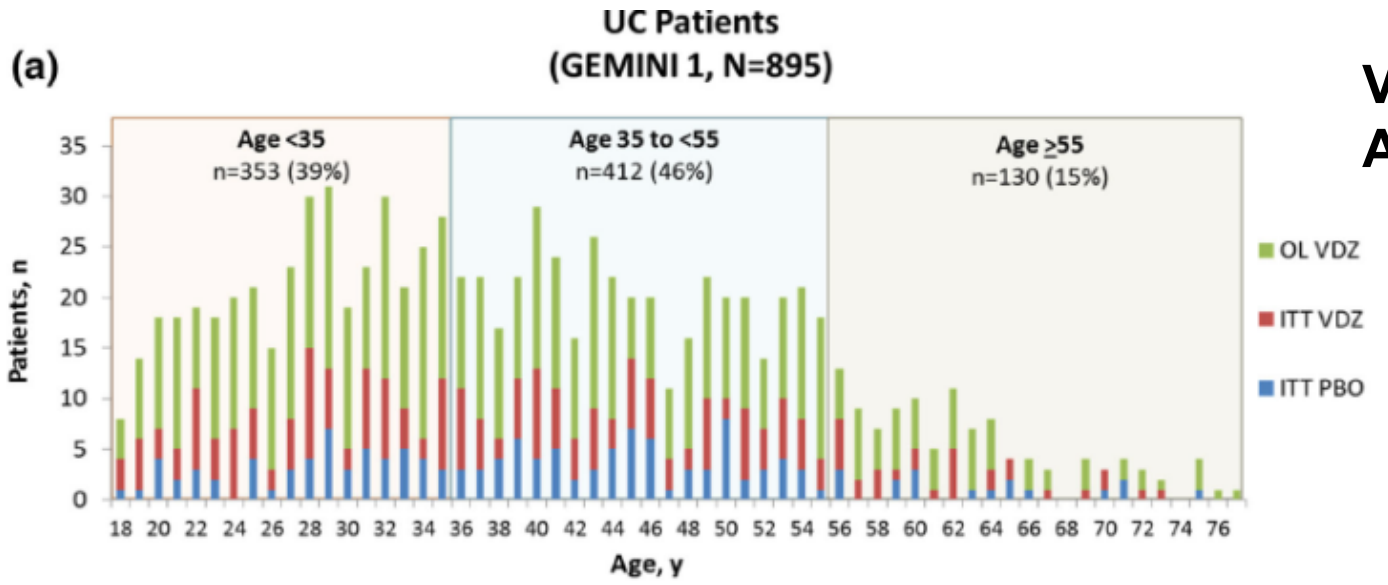
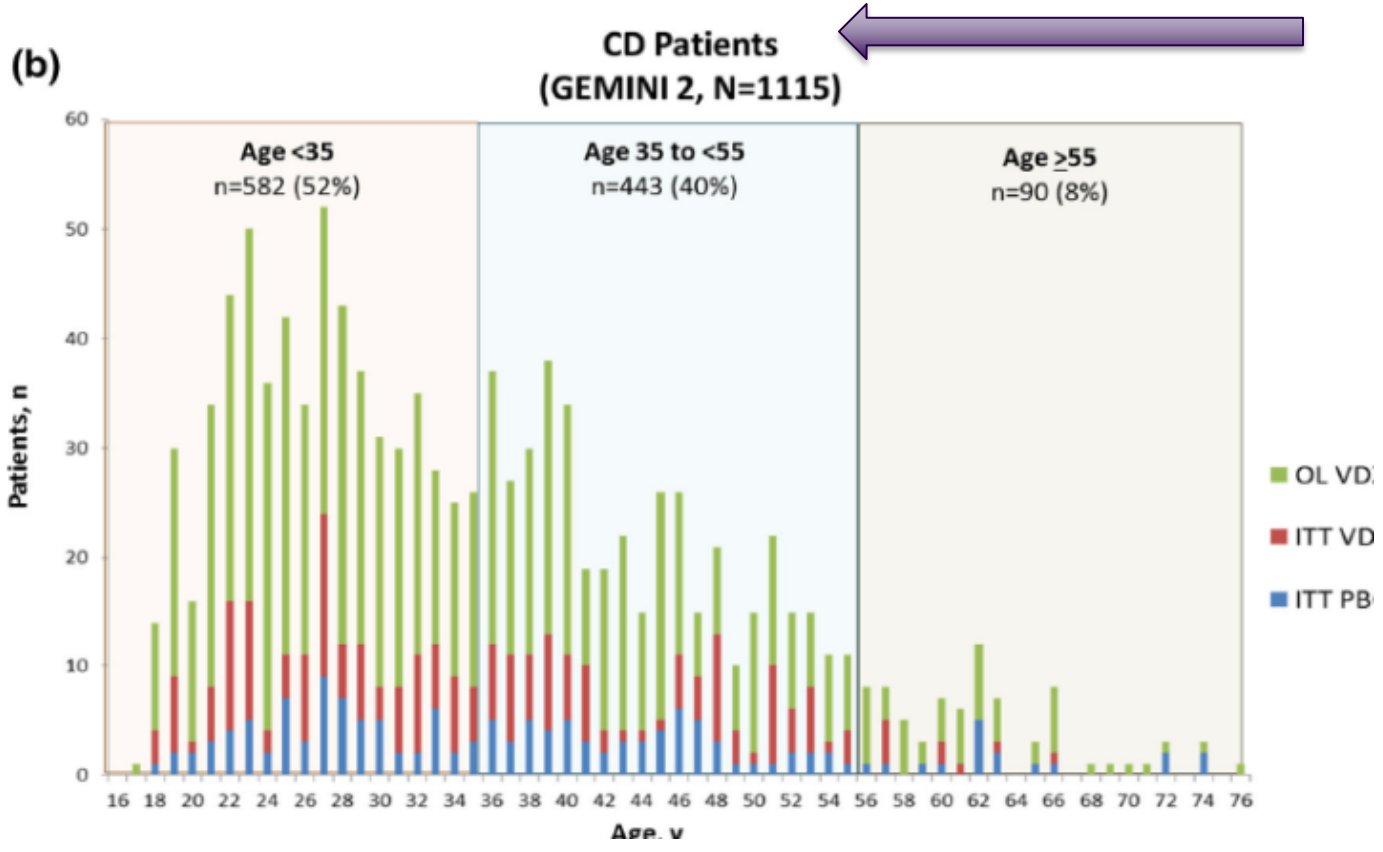
Vedo in UC and CD
Age distribution in UC and CD trials





Age >55

Yajnik Adv Therap 2017

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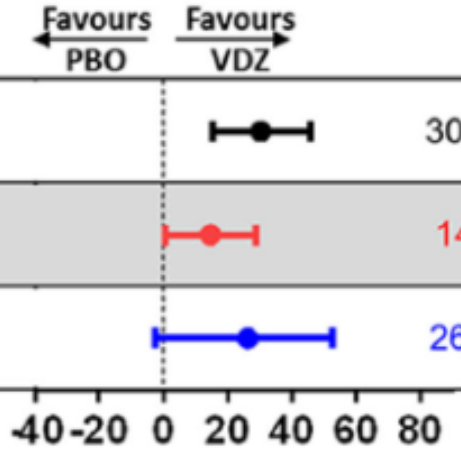
(a)

Age, y	UC patients in clinical response at week 6, n/N (%) PBO	VDZ	Difference from PBO, % (95% CI)
<35	11/53 (20.8)	44/86 (51.2)	30.4 (15.2, 45.6)
35 to <55	25/78 (32.1)	50/107 (46.7)	14.7 (0.7, 28.7)
≥55	2/18 (11.1)	12/32 (37.5)	26.4 (-2.5, 52.6)

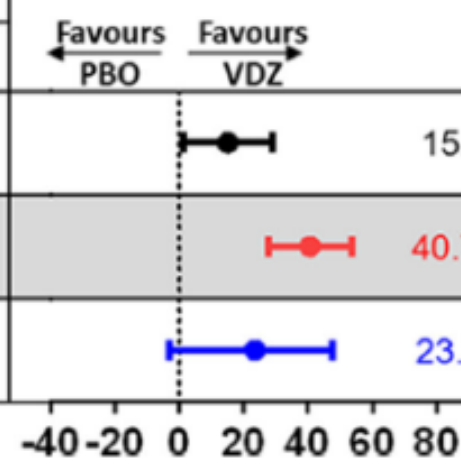


Clinical response at wk 6

UC not quite SS in >55

(b)

Age, y	UC patients in clinical remission at week 52, n/N (%) VDZ/PBO[a]	VDZ/VDZ[b]	Difference from PBO, % (95% CI)
<35	10/54 (18.5)	34/101 (33.7)	15.1 (1.3, 29.0)
35 to <55	6/50 (12)	58/110 (52.7)	40.7 (27.8, 53.7)
≥55	4/22 (18.2)	15/36 (41.7)	23.5 (-3.2, 47.8)

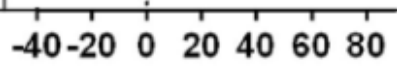


Clin remission at wk 52

33 (4%) >/= 65

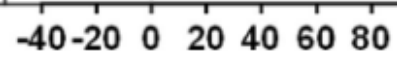
(b)

Age, y	CD patients with enhanced clinical response at week 6, n/N (%) PBO	VDZ	Difference from PBO, % (95% CI)
<35	21/67 (31.3)	31/111 (27.9)	-3.4 (-17.3, 10.5)
35 to <55	14/63 (22.2)	32/96 (33.3)	11.1 (-2.8, 25.1)
≥55	3/18 (16.7)	6/13 (46.2)	29.5 (-6.4, 60.6)



(c)

Age, y	CD patients in clinical remission at week 52, n/N (%) VDZ/PBO[a]	VDZ/VDZ[b]	Difference from PBO, % (95% CI)
<35	15/73 (20.5)	65/173 (37.6)	17.0 (5.3, 28.8)
35 to <55	13/65 (20.0)	42/112 (37.5)	17.5 (4.3, 30.7)
≥55	5/15 (33.3)	9/23 (39.1)	5.8 (-26.5, 37.6)



Clinical response at wk 6

CD not SS in >55

Clin remission at wk 52

23 (2%) >/= 65

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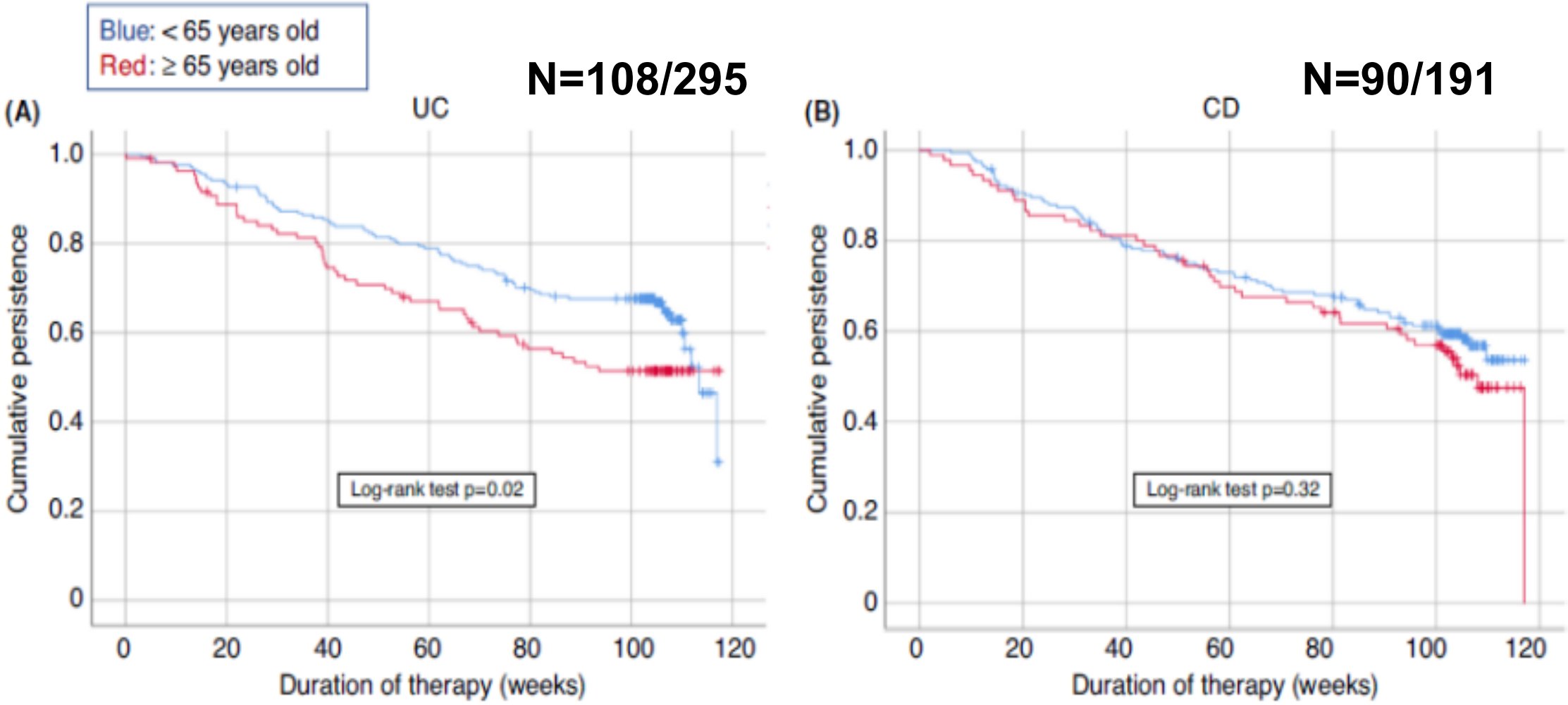
VEDO >/=65 vs <65



UC **Cumulative remission** **CD**

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Pugliese IG-LIVE Study APT 2022

Predictors: VEDO non-persistence in elderly vs <65:

UC:
Only age

CD:
CCI > 2
Previous anti TNF us
Concomitant steroids
Mod-sev vs mild

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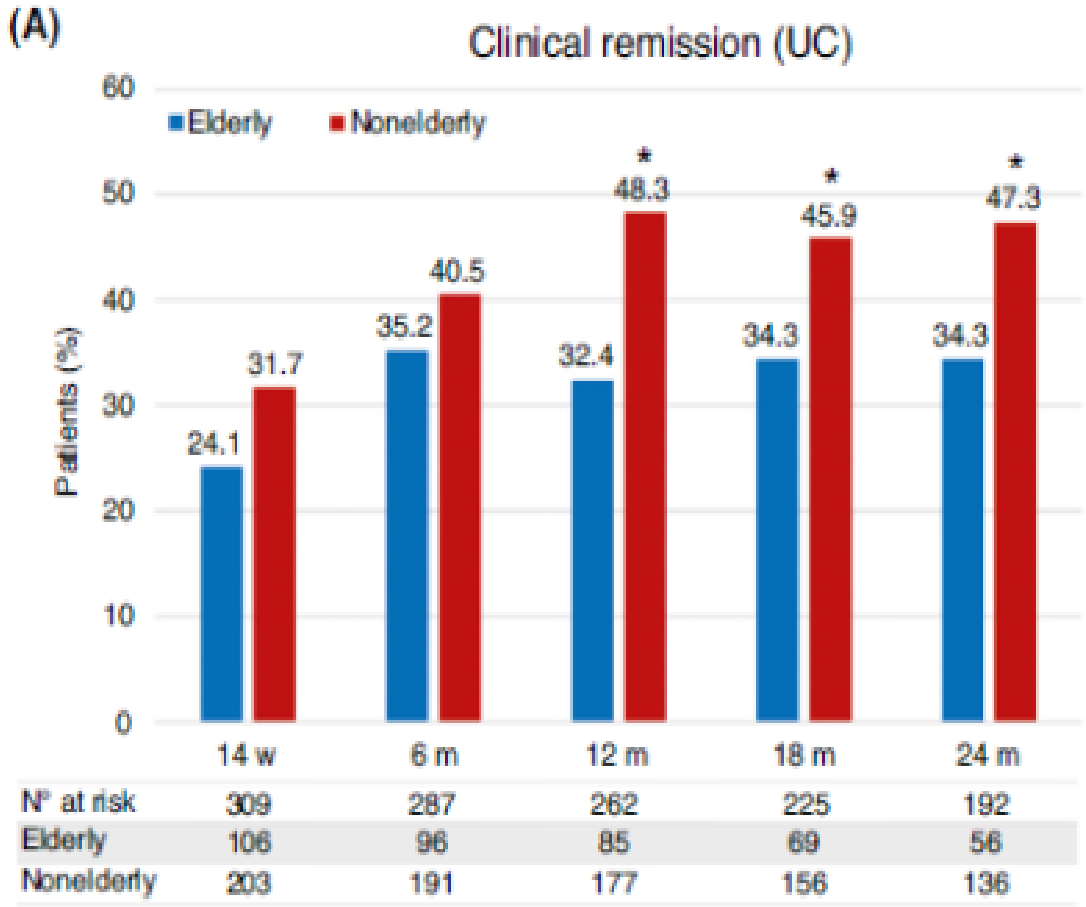
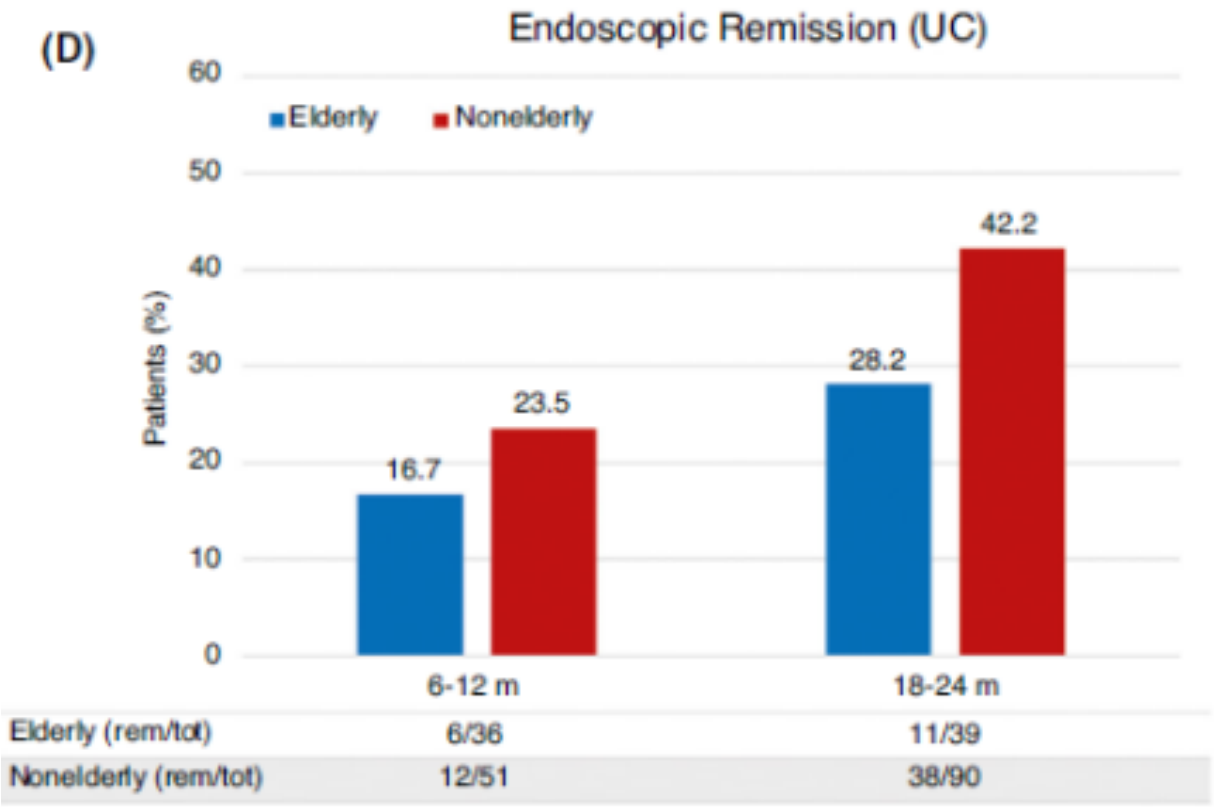
Pugliese IG-LIVE Study APT 2022

Clinical remission

UC

Endoscopic remission





24 months

18-24 months

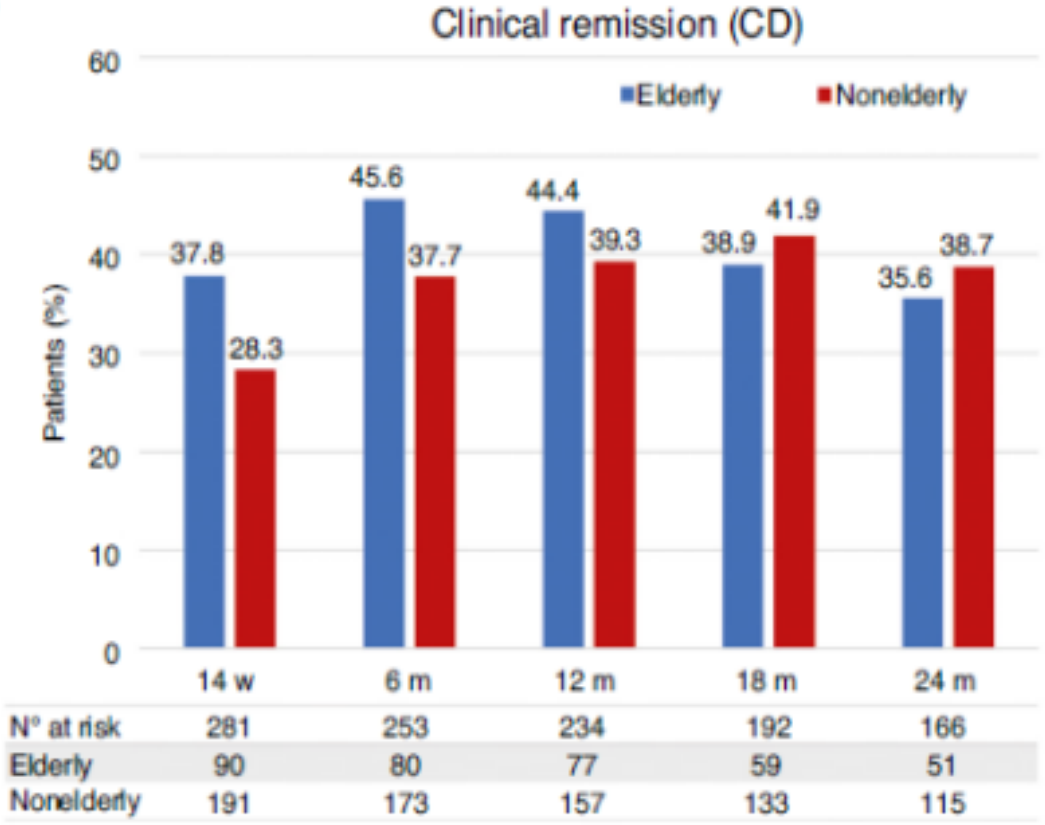
Pugliese IG-LIVE Study APT 2022

Clinical remission

CD

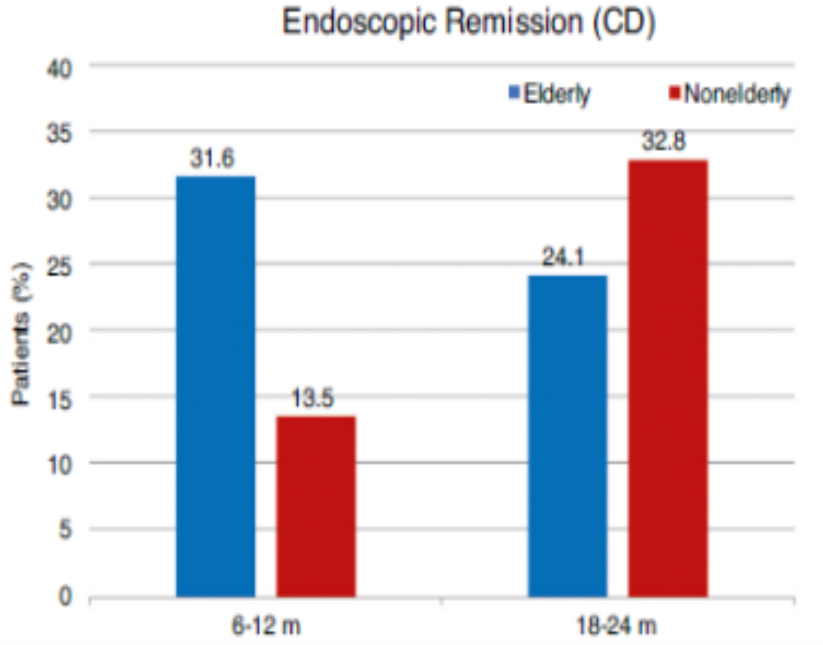
Endoscopic remission

(A)



	14 w	6 m	12 m	18 m	24 m
N° at risk	281	253	234	192	166
Elderly	90	80	77	59	51
Nonelderly	191	173	157	133	115

(D)



	6-12 m	18-24 m
Elderly (rem/tot)	6/19	7/20
Nonelderly (rem/tot)	5/37	29/61

24 months

18-24 months

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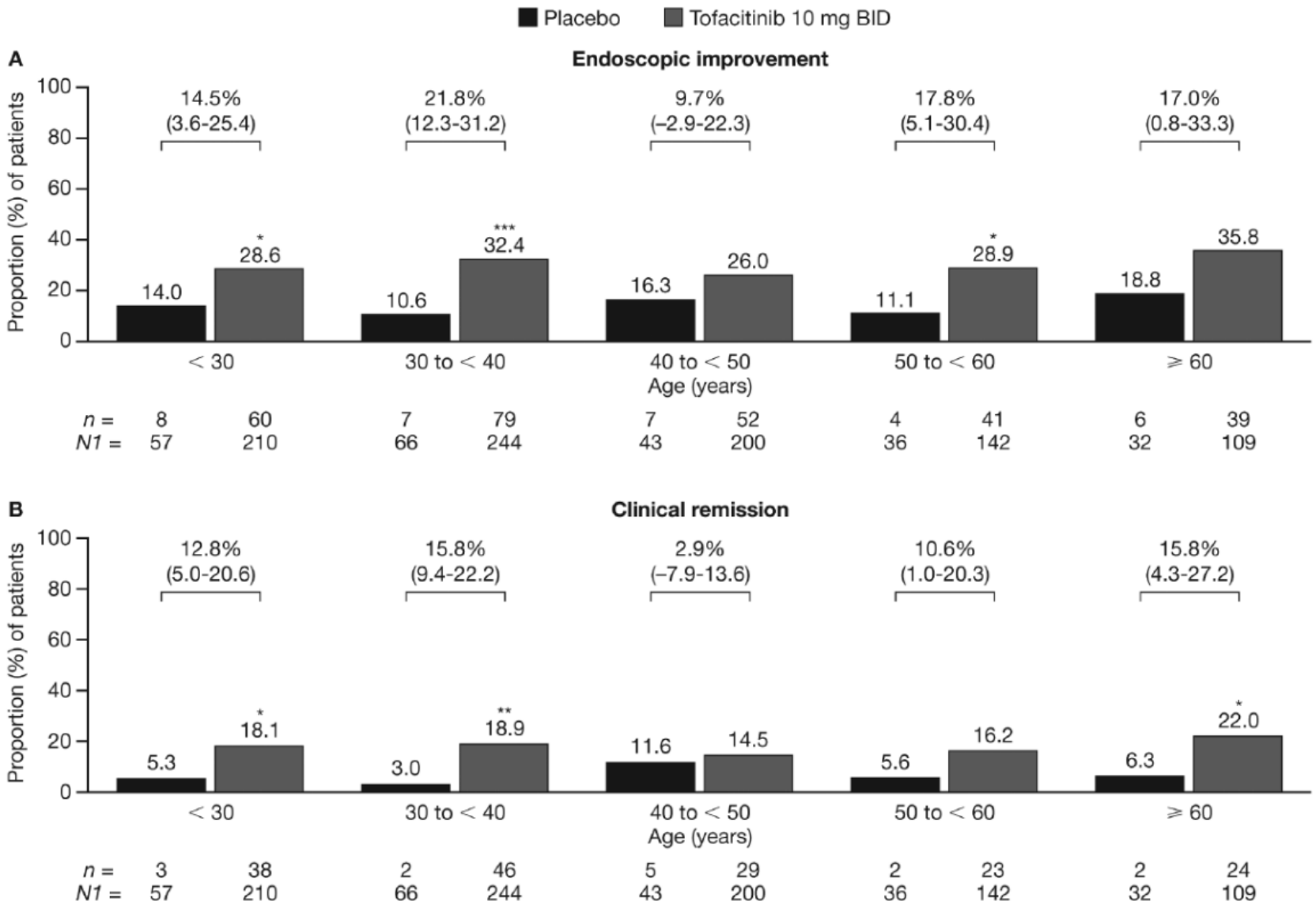
Pugliese IG-LIVE Study APT 2022

Ustekinumab in elderly in ENEIDA Registry

Remission	>60 (n=212)	<60 (n=436)
Wk 16	51.4%	54.6%
Wk 32	54.5%	53%
Wk 54	57.8%	51.1% p=0.21
Adverse events	11.2%	14.2%
Severe infection	7.3%	7.1%

Casas-Deza JCC 2023-

Tofactinib Induction program in UC- 8 weeks



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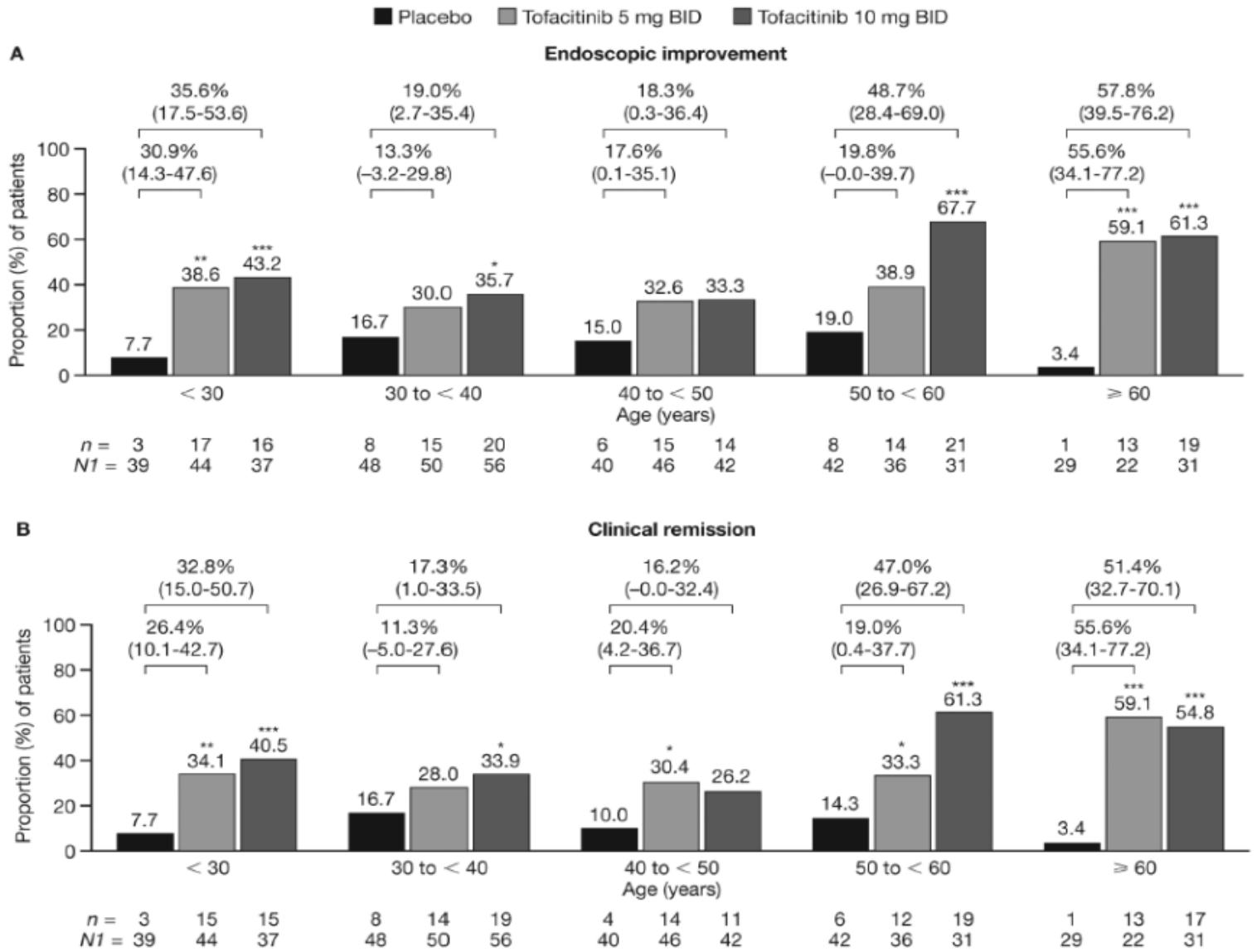
Lichtenstein IBDJ 2023

Tofactinib Maintenance program in UC- 52 weeks



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Tofactinib Induction and Maintenance program in UC

Table 4. Treatment-emergent AEs reported in the Overall Cohort from the tofacitinib UC clinical program.

	18 to <30 years	30 to <40 years	40 to <50 years	50 to <60 years	≥60 years	<65 years	≥65 years
	Tofacitinib All[a] (N= 270)	Tofacitinib All[a] (N= 311)	Tofacitinib All[a] (N= 251)	Tofacitinib All[a] (N= 181)	Tofacitinib All[a] (N= 144)	Tofacitinib All[a] (N= 1080)	Tofacitinib All[a] (N= 77)
AEs, *n* (%)	220 (81.5)	253 (81.4)	219 (87.3)	159 (87.8)	129 (89.6)	912 (84.4)	68 (88.3)
SAEs, *n* (%)	42 (15.6)	55 (17.7)	49 (19.5)	37 (20.4)	40 (27.8)	202 (18.7)	21 (27.3)
Severe AEs, *n* (%)	38 (14.1)	48 (15.4)	43 (17.1)	26 (14.4)	23 (16.0)	164 (15.2)	14 (18.2)
Discontinuation due to AEs, *n* (%)	14 (5.2)	23 (7.4)	26 (10.4)	26 (16.4)	30 (23.3)	99 (10.9)	20 (29.4)
Dose reduction or temporary discontinuation due to AEs, *n* (%)	16 (5.9)	24 (7.7)	29 (11.6)	14 (7.7)	23 (16.0)	91 (8.4)	15 (19.5)

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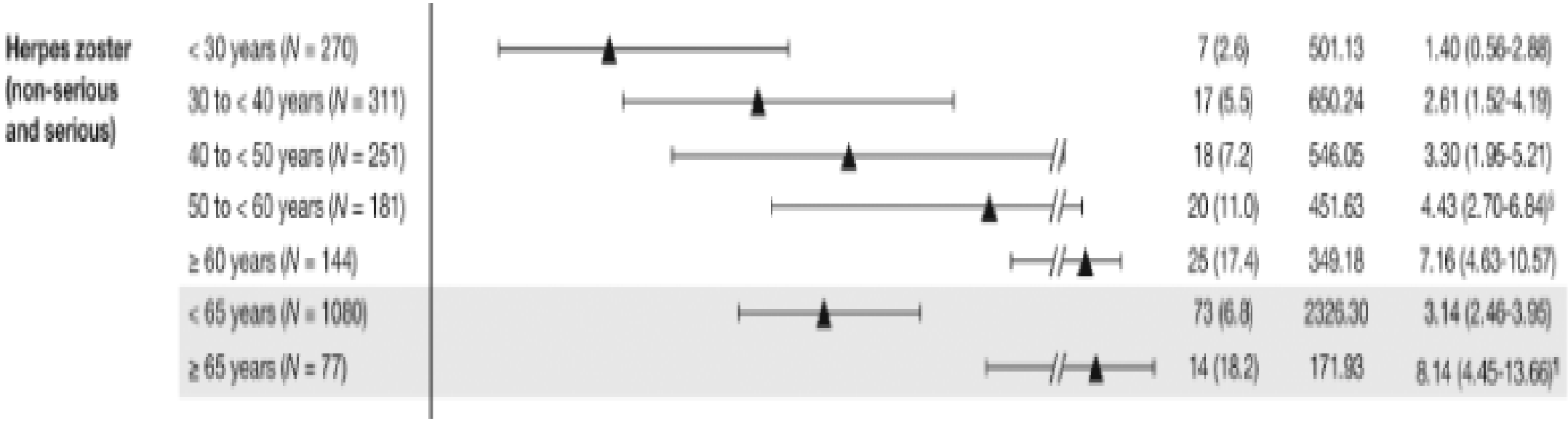
Lichtenstein IBDJ 2023

Tofactinib Induction and Maintenance program in UC

HZV infections



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ACT-1; ACT-2; PURSUIT-SC; PURSUIT-MAINT (Older v Younger)

N=231

N=2257

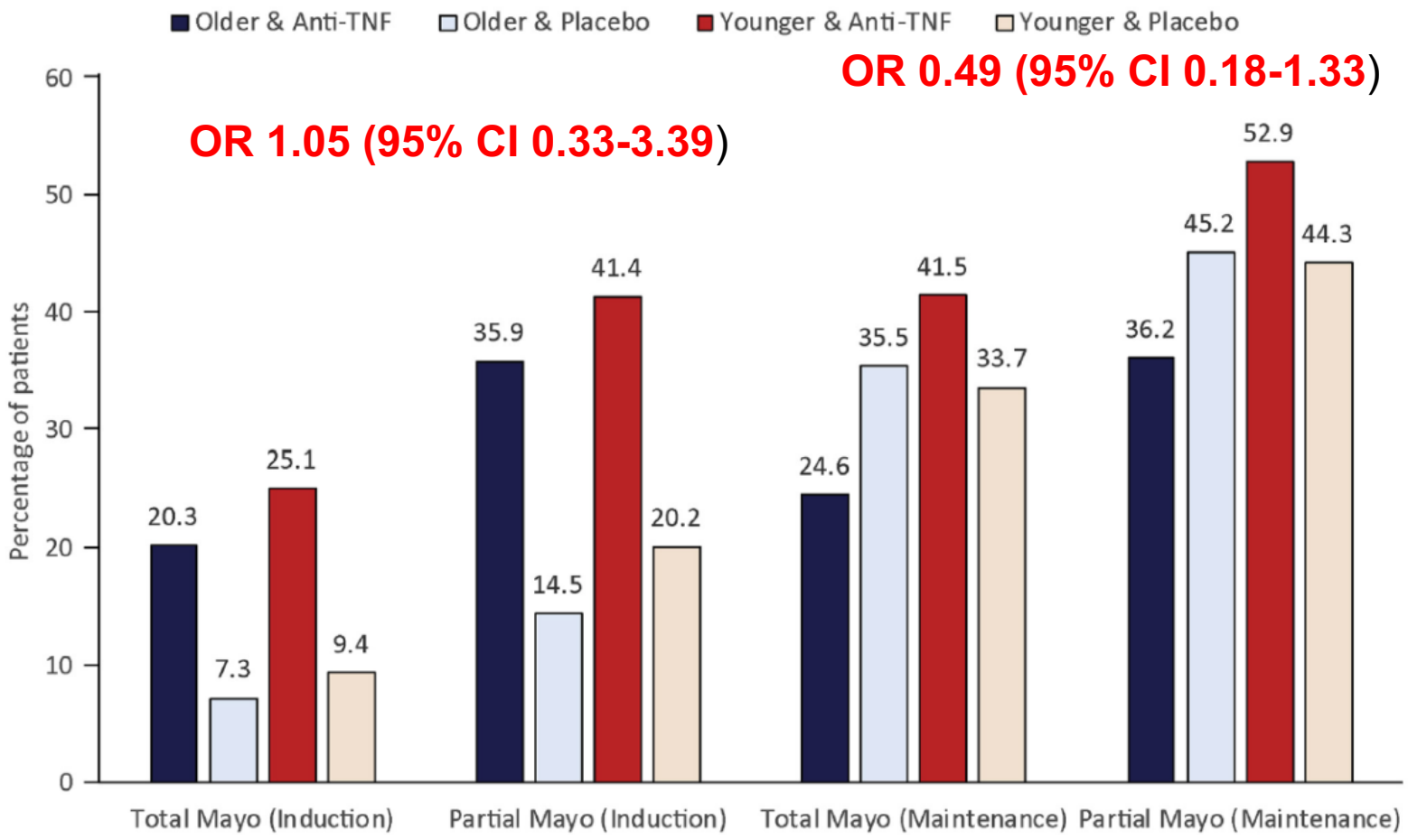

Figure 2. Percentage in clinical remission among all patients who underwent trial randomization, stratified by age and randomization status. TNF, tumor necrosis factor.

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ACT-1; ACT-2; PURSUIT-SC; PURSUIT-MAINT

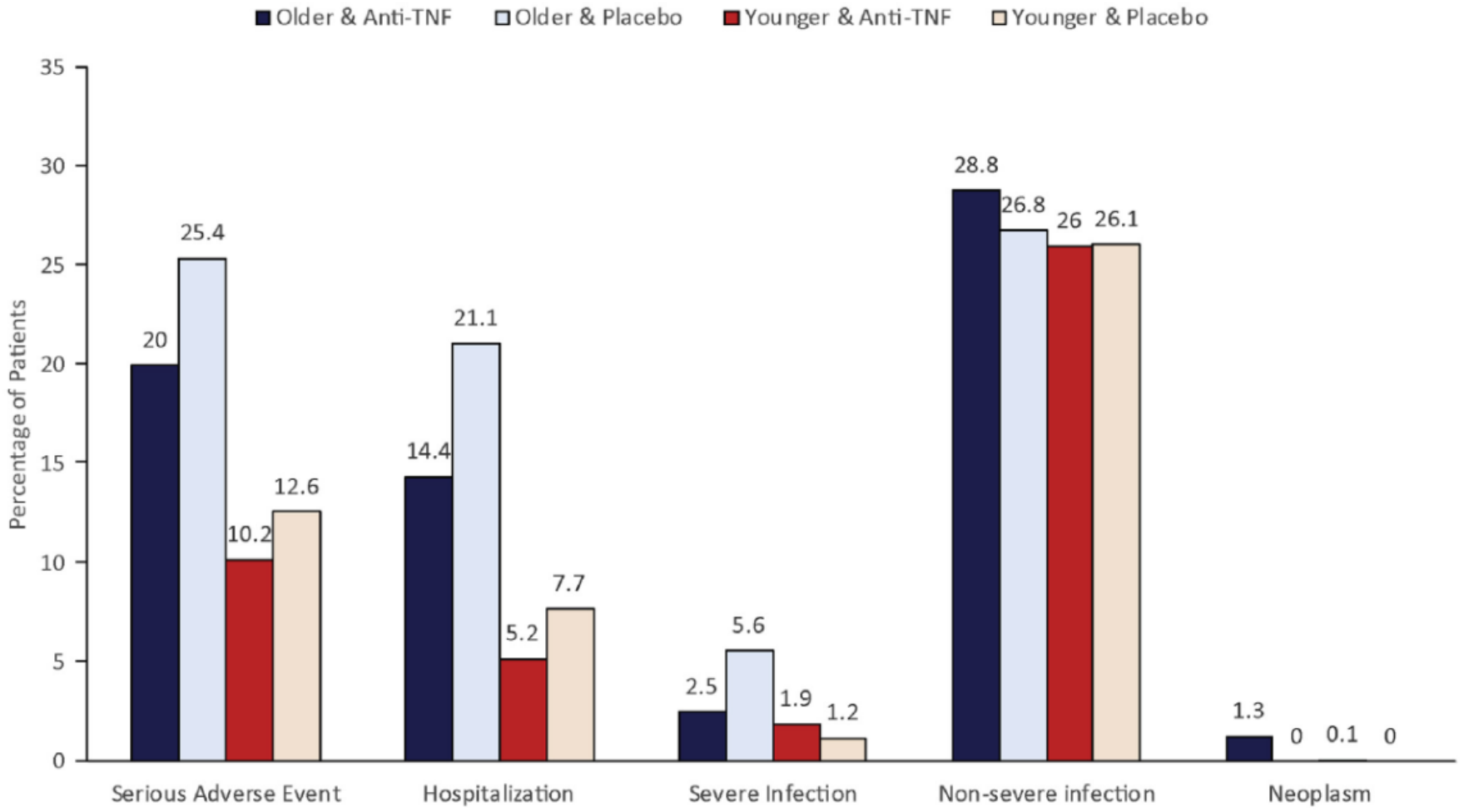

Figure 1. Percentage of safety events among all patients who underwent trial randomization, stratified by age and randomization status. TNF, tumor necrosis factor.

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ACT-1; ACT-2; PURSUIT-SC; PURSUIT-MAINT

Table 2. Logistic Regression Evaluating Age as a Predictor of Safety Events and Efficacy Rates With Random Effects for Trial in Ulcerative Colitis Patients on Anti-Tumor Necrosis Factor Therapy (Randomized Only)

	Odds ratio	Confidence interval	*P* value
Adverse events			
Serious adverse event	2.20	1.51–3.22	<.001[a]
Hospitalization	3.12	2.05–4.76	<.001[a]
Severe infection	1.83	0.82–4.07	.14
Non-severe infection	1.09	0.78–1.51	.63
Neoplasm	10.6	2.83–39.6	<.001[a]
Total Mayo score (induction)	0.78	0.51–1.19	.25
Total Mayo score (maintenance)	0.65	0.41–1.06	.08
Partial Mayo score (induction)	0.79	0.56–1.11	.17
Partial Mayo score (maintenance)	0.63	0.40–1.00	.051

NOTE. Adjusted for immune modulators, corticosteroids, gender, and weight. Odds ratios refer to comparisons in safety or efficacy rates between older patients in remission on any biologic therapy and younger patients on any biologic therapy.

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ACT-1; ACT-2; PURSUIT-SC; PURSUIT-MAINT

Table 3. Logistic Regression Evaluating Interaction of Age and Treatment in Predicting Safety Events and Efficacy Rates With Random Effects for Trial in Ulcerative Colitis Patients (Randomized Only)

	Ratio of odds ratio	Confidence interval	*P* value
Adverse events			
Serious adverse event	0.83	0.38–1.81	.63
Hospitalization	0.93	0.39–2.19	.87
Severe infection	0.22	0.04–1.10	.07
Non-severe infection	1.12	0.55–2.28	.75
Total Mayo score (induction)	1.05	0.33–3.39	.93
Total Mayo score (maintenance)	0.49	0.18–1.33	.16
Partial Mayo score (induction)	1.23	0.51–2.95	.65
Partial Mayo score (maintenance)	0.51	0.19–1.35	.18

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HUMIRA

Table 10. Rates of Registry TEAEs According to Age Group

AE	<40 Years n=2,981 PY=9,681.1 E (E/100 PY)	40 to 59 Years n=1,717 PY=6,009.3 E (E/100 PY)	≥60 Years n=327 PY=990 E (E/100 PY)	*P*-value[a]
Any AE	3,594 (37.1)	2,115 (35.2)	415 (41.9)	0.004
SAE	2,392 (24.7)	1,422 (23.7)	315 (31.8)	<0.001
SAE at least possibly related to Humira[b]	341 (3.5)	230 (3.8)	56 (5.7)	0.008
AE leading to discontinuation	449 (4.6)	250 (4.2)	67 (6.8)	0.003
Any infection	816 (8.4)	420 (7.0)	97 (9.8)	<0.001
Serious infection[c]	485 (5.0)	243 (4.0)	64 (6.5)	0.001
Opportunistic infection other than oral candidiasis and TB	10 (0.1)	7 (0.1)	4 (0.4)	0.117
Active TB	7 (<0.1)	3 (<0.1)	0	NE
Latent TB	4 (<0.1)	3 (<0.1)	0	NE
Injection site reaction	12 (0.1)	10 (0.2)	0	NE
Demyelinating disorder	5 (<0.1)	3 (<0.1)	0	NE
AE leading to death	14 (0.1)	21 (0.3)	17 (1.7)	<0.001
Deaths including non-treatment emergent deaths	15 (0.2)	28 (0.5)	20 (2.0)	<0.001

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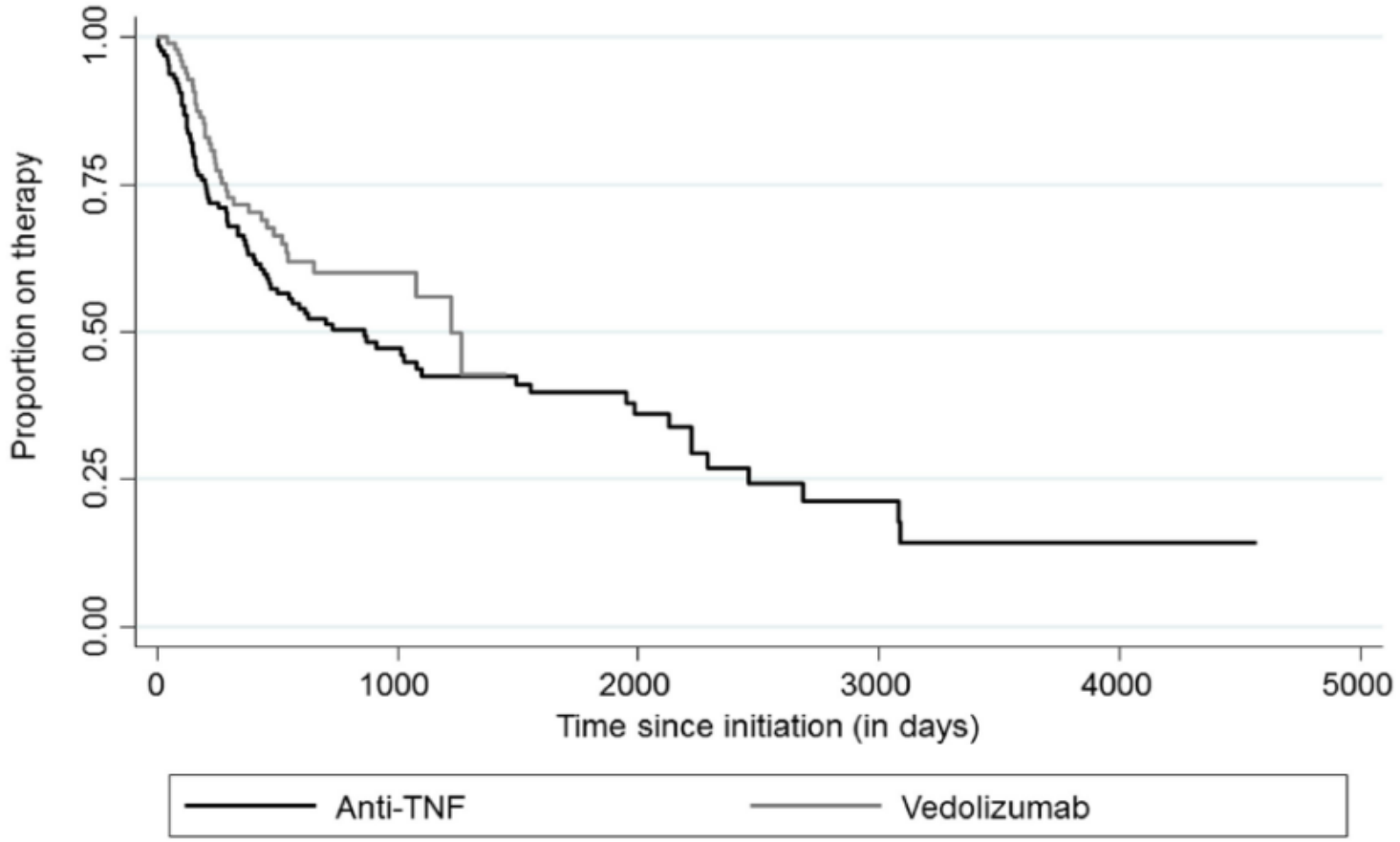
PYRAMID Colombel 2017

Anti TNF and Vedo in persons >65



Adar APT 2019

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Anti TNF (n=131) and Vedo (n=103) in persons >60

Multivariable analysis of odds of study outcomes for anti-TNF compared to vedolizumab)

(a) Crohn's disease

Outcome	Multivariable odds ratio+	95% confidence interval	P-value
Remission at 3 months	2.82	1.18 – 6.76	0.03
Remission at 6 months	1.34	0.62 – 2.88	0.58
Remission at 12 months	0.79	0.35 – 1.79	0.57
Infection at 1 year	1.00	0.37 – 2.73	0.89

(b) Ulcerative colitis

Outcome	Multivariable odds ratio+	95% confidence interval	P-value
Remission at 3 months	1.74	0.74 – 4.13	0.29
Remission at 6 months	1.69	0.73 – 3.91	0.38
Remission at 12 months	1.68	0.67 – 4.18	0.27
Infection at 1 year	1.89	0.61 – 5.78	0.31

+Adjusted for type of IBD, combination immunomodulator use, race/ethnicity, and site of recruitment

Adar APT 2019

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Anti TNF (n=131) and Vedo (n=103) in persons >60

40% of vedo were naïve to anti TNF
60% (anti TNF) and 69% (Vedo) on steroids at initiation
1/3 of each group on immunomodulators

Significant infections 20% (anti TNF) 17% (Vedo) p=0.54

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	Age (years)	52-week Maintenance Treatment Period (FORTIFY) n (%)		
		Withdrawal (PBO SC) N = 184	RZB 180 mg SC N = 179	RZB 360 mg SC N = 179
Adverse events	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	1 (100) 78 (72.9) 49 (72.1) 7 (87.5)	1 (50.0) 64 (64.0) 49 (79.0) 14 (93.3)	1 (50.0) 74 (71.2) 48 (75.0) 6 (66.7)
Serious AE	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 11 (10.3) 11 (16.2) 1 (12.5)	0 9 (9.0) 9 (14.5) 4 (26.7)	0 13 (12.5) 10 (15.6) 1 (11.1)
AE leading to discontinuation	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 3 (2.8) 2 (2.9) 1 (12.5)	0 2 (2.0) 0 1 (6.7)	0 3 (2.9) 3 (4.7) 0
Serious infections	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 4 (3.7) 3 (4.4) 0	0 2 (2.0) 2 (3.2) 1 (6.7)	0 8 (7.7) 0 0
Opportunistic infections excluding tuberculosis and herpes zoster	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 0 0 0	0 1 (1.0) 0 0	0 0 1 (1.6) 0
Herpes zoster	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 0 1 (1.5) 0	0 1 (1.0) 0 1 (6.7)	0 0 0 0
Hypersensitivity	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 10 (9.3) 7 (10.3) 0	0 8 (8.0) 8 (12.9) 2 (13.3)	0 6 (5.8) 6 (9.4) 0
Hepatic events	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 2 (1.9) 2 (2.9) 0	0 3 (3.0) 1 (1.6) 1 (6.7)	0 3 (2.9) 3 (4.7) 1 (11.1)
Injection site reactions	<18[b] ≥18–<40[c] ≥40–<65[d] ≥65–80[e]	0 7 (6.5) 2 (2.9) 0	0 2 (2.0) 7 (11.3) 0	0 8 (7.7) 3 (4.7) 0

N=32 ≥ 65 (5.9%)

Rizenkizumab in CD RCTs

Colombel DDW 2023

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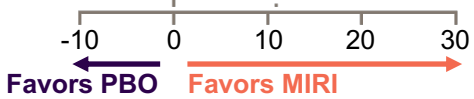
N=14 ≥ 65 (5.9%)

	Risk Difference % (95% CI)	PBO n (%)	MIRI n (%)	Diff %
All Patients		39 (13.3)	210 (24.2)	10.9
Pooled Age Group 1				
<65		36 (13.1)	199 (25.0)	11.9
≥65		3 (15.8)	11 (15.3)	
Pooled Age Group 2				
<40		23 (15.5)	109 (27.7)	12.2
≥40		16 (11.0)	101 (21.3)	10.3
Sex				
Male		20 (12.1)	105 (19.8)	7.7
Female		19 (14.7)	105 (31.1)	16.3
Ethnicity				
Hispanic/Latino		1 (8.3)	7 (21.9)	
Non-Hispanic/Non-Latino		33 (14.8)	155 (24.8)	10.0
Race				
American Indian/Alaska Native		2 (100.0)	2 (20.0)	
Asian		8 (11.8)	63 (28.3)	16.5
Black/African American		0 (0.0)	2 (20.0)	
White		28 (12.8)	142 (23.1)	10.3
Multiple		1 (50.0)	0 (0.0)	
Geographic Region 1				
North America		3 (6.4)	26 (18.8)	12.5
Europe		13 (12.0)	69 (22.0)	9.9
Other		23 (16.5)	115 (27.6)	11.1



	Risk Difference % (95% CI)	PBO n (%)	MIRI n (%)	Diff %
Geographic Region 2				
Asia		9 (14.3)	60 (28.4)	14.2
North America		3 (6.4)	26 (18.8)	12.5
Central America/South America		2 (40.0)	4 (22.2)	
East Europe		7 (13.5)	38 (26.6)	13.1
West Europe		6 (10.7)	31 (18.1)	7.4
ROW (rest of the world)		12 (16.9)	51 (27.3)	10.4
Baseline Weight Group 2				
<100 kg		36 (13.0)	196 (24.3)	11.3
≥100 kg		3 (17.6)	14 (22.6)	
Baseline BMI Group 1				
Underweight (<18.5 kg/m^2)		5 (17.9)	13 (23.6)	
Normal (≥18.5 and <25 kg/m^2)		19 (12.8)	125 (27.7)	15.0
Overweight (≥25 and <30 kg/m^2)		9 (11.8)	46 (19.5)	7.6
Obese (≥30 and <40 kg/m^2)		6 (15.4)	22 (19.3)	3.9
Extreme obese (≥40 kg/m^2)		0 (0.0)	4 (33.3)	
Tobacco Use				
Never		30 (15.2)	145 (25.0)	9.9
Current		2 (11.8)	11 (25.6)	
Former		7 (8.9)	54 (22.0)	13.1

BMI=Body Mass Index; CI=Confidence Interval; Diff=Unadjusted Risk Difference; MIRI=Mirikizumab; PBO=Placebo.
D'Haens G, et al. *N Engl J Med*. 2022;388(26):2444-2455.

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IBD and the ELDERLY

The prevalence of IBD amongst the elderly is going to continue to grow

We must have clinical trial data geared to this demographic