RESULTS OF A RETROSPECTIVE IGIBD STUDY ON ADALIMUMAB USE IN REAL PRACTICE IN ITALY: THE REAL-LIFE CLINICAL EFFECTIVENESS OF ADALIMUMAB IN ULCERATIVE COLITIS (REALADA-UC) STUDY

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Dott. Alessandro VITELLO

Background

- **Adalimumab (ADA)** has been approved for the treatment of 14 immune-mediated diseases (5 pediatric).

- In Italy since 2014 UC label for adalimumab required **strict observation** of common treatment pathway.

- **Real-life studies** result usually hampered by heterogeneous clinical management.

Aim of the study

To explore clinical effectiveness of Adalimumab in real-world Italian patients

Primary outcome → **Persistence**

Secondary outcomes →

Response and clinical remission

Colectomy rate

Predictors of withdrawal and colectomy

Safety in real-life

IG IBD

Patients and Methods

Coordinating Center: Gastroenterologia AO Mauriziano di Torino

Torino (Mauriziano)

Caltanissetta (M. Raimondi)

Palermo (Villa Sofia-Cervello)

Palermo (Policlinico P. Giaccone)

Messina (G. Martino)

Palermo (Civico)

Catania (Cannizzaro)

Brescia (Spedali Civili)

Reggio Emilia (S. Maria Nuova)

Padova (Azienda Ospedaliera)

Rho (Ospedale di Rho)

Lecce (V. Fazzi)

Roma (S. Camillo Forlanini)

Bari (A. Moro)

Genova (S. Martino)

Roma (Policlinico Gemelli)

Cuneo (S. Croce e Carle)

Torino (S. Giovanni Battista)

346 pts
May 2014-Dec 2018

Rho
Torino
Brescia
Padova
Cuneo
Reggio Emilia
Genova
Roma
Bari
Lecce
Palermo
Messina
Caltanissetta
Catania

IGBD

Results

	346
F/M, n (%)	171 (49)/175 (51)
Age IBD diagnosis, years, n (%)	
< 20	59 (17)
20-45	209 (60)
> 45	78 (23)
Disease duration, years	
Mean ± SD	9.5 ± 8.7
Smoking, n (%)	
Active	24 (7)
Ex-smoker /never	263 (76)
Disease extension (Montreal), n (%)	
E1	16 (5)
E2	120 (35)
E3	210 (61)
Disease activity	
Full Mayo score, *Median (IQR)*	8 (6-9)
Partial Mayo score, *Median (IQR)*	5 (4-7)
Endoscopic Mayo score, *Median (IQR)*	2 (2-3)
CRP (mg/l)	
Mean ± SD	9.4 ± 14.6
Extra-intestinal manifestations, n (%)	80 (23)
Steroid-dependent disease, n (%)	264 (76)
Previous anti-TNFα treatment, n (%)	160 (46)
Previous anti-TNFα discontinuation reason, n (%)	
Primary non-response	16 (10)
Secondary loss of response	74 (46)
Non-infectious adverse event	66 (41)
Infectious adverse event	4 (3)
Combination therapy with IM, n (%)	48 (14)
Combination therapy with corticosteroids, n (%)	138 (40)
Dose of corticosteroids (mg)	
Mean ± SD	25 ± 15
Hemoglobin (g/dl)	
Mean ± SD	12.3 ± 1.84
Body weight (kg)	
Mean ± SD	66.3 ± 12.7

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IGIBD

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Disease extension - Montreal
E3 (61%), E2 (35%), E1 (5%)

Disease activity	
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IG**IBD**

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Disease activity
Median FMS 8 (IQR 6-9)
Endoscopic MS 2 (IQR 2-3)

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Previous anti-TNFα

46%

Secondary loss of response	74 (46)
Non-infectious adverse event	66 (41)
Infectious adverse event	4 (3)
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EIMs
23%

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Combination therapy
IM (14%), Corticosteroids (40%)
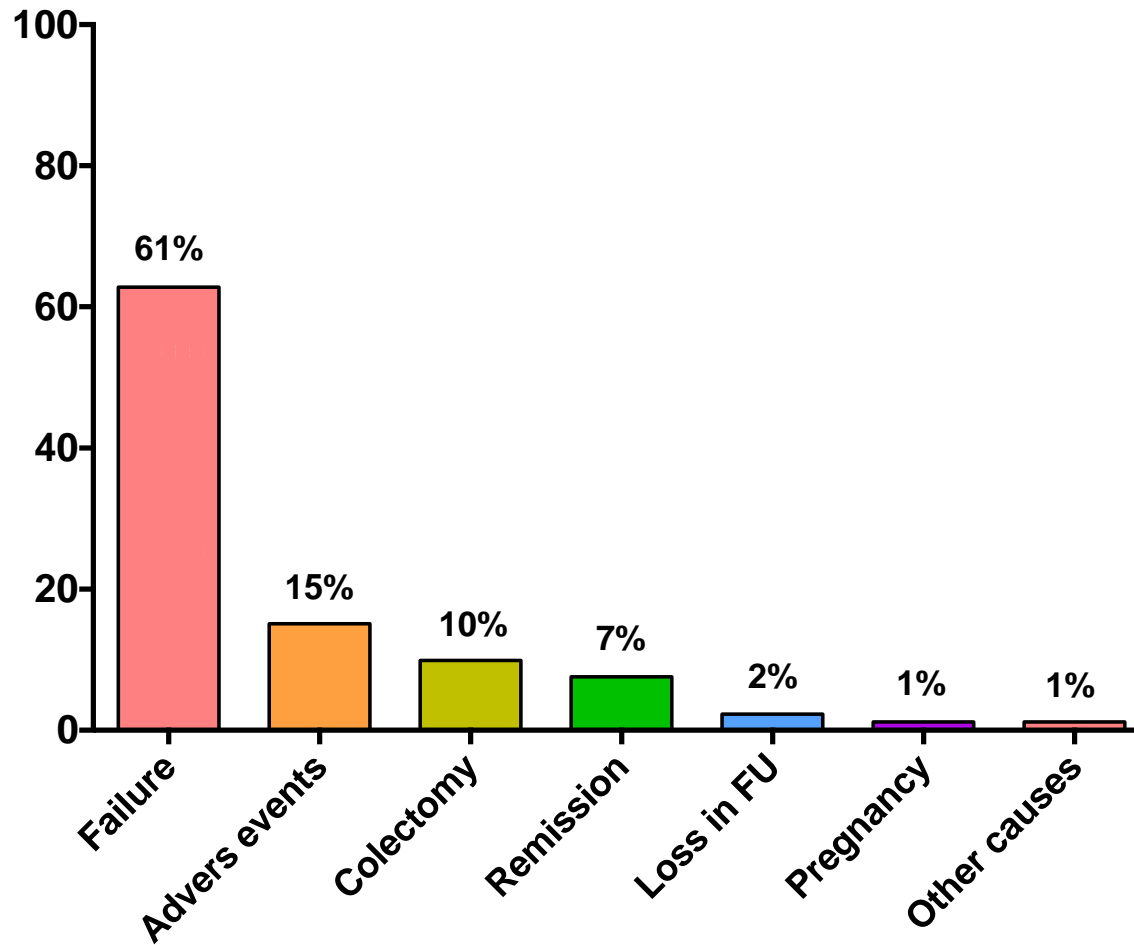
Results

Persistence (cumulative probability)
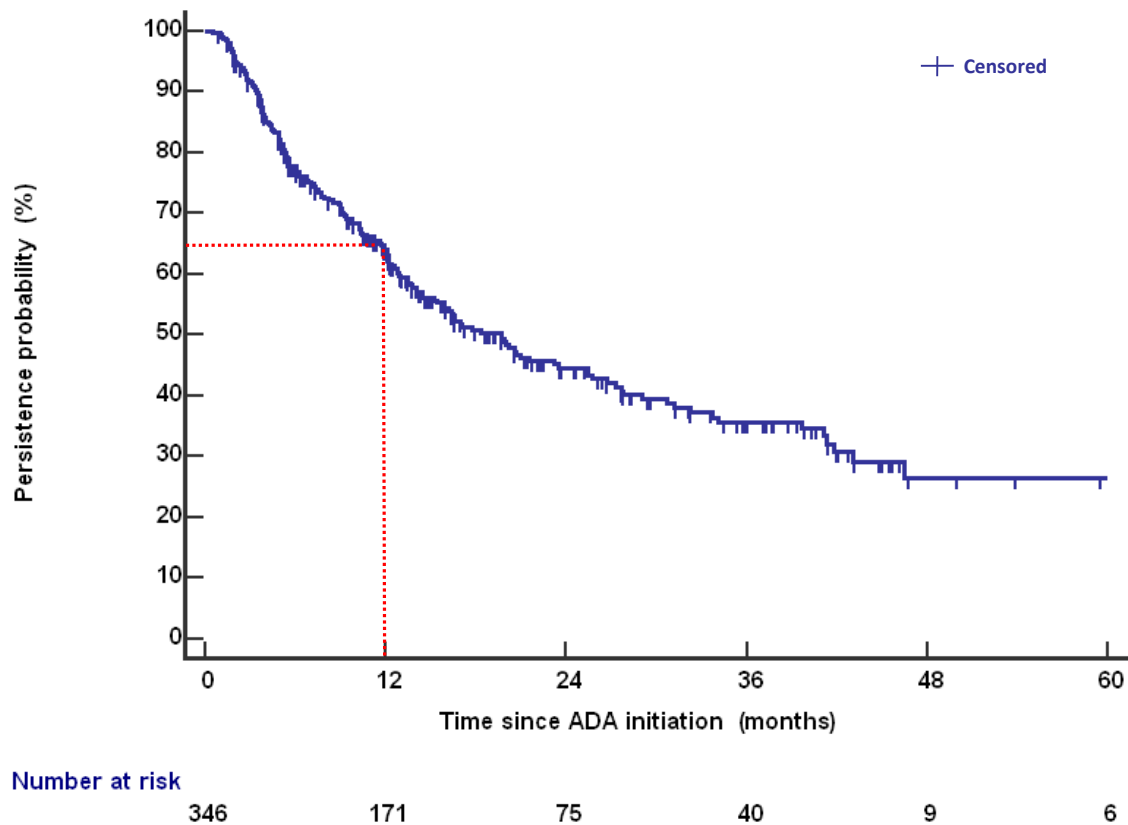
The cumulative probability of continuing ADA therapy over one year was 64%

Results

Reasons for ADA discontinuation
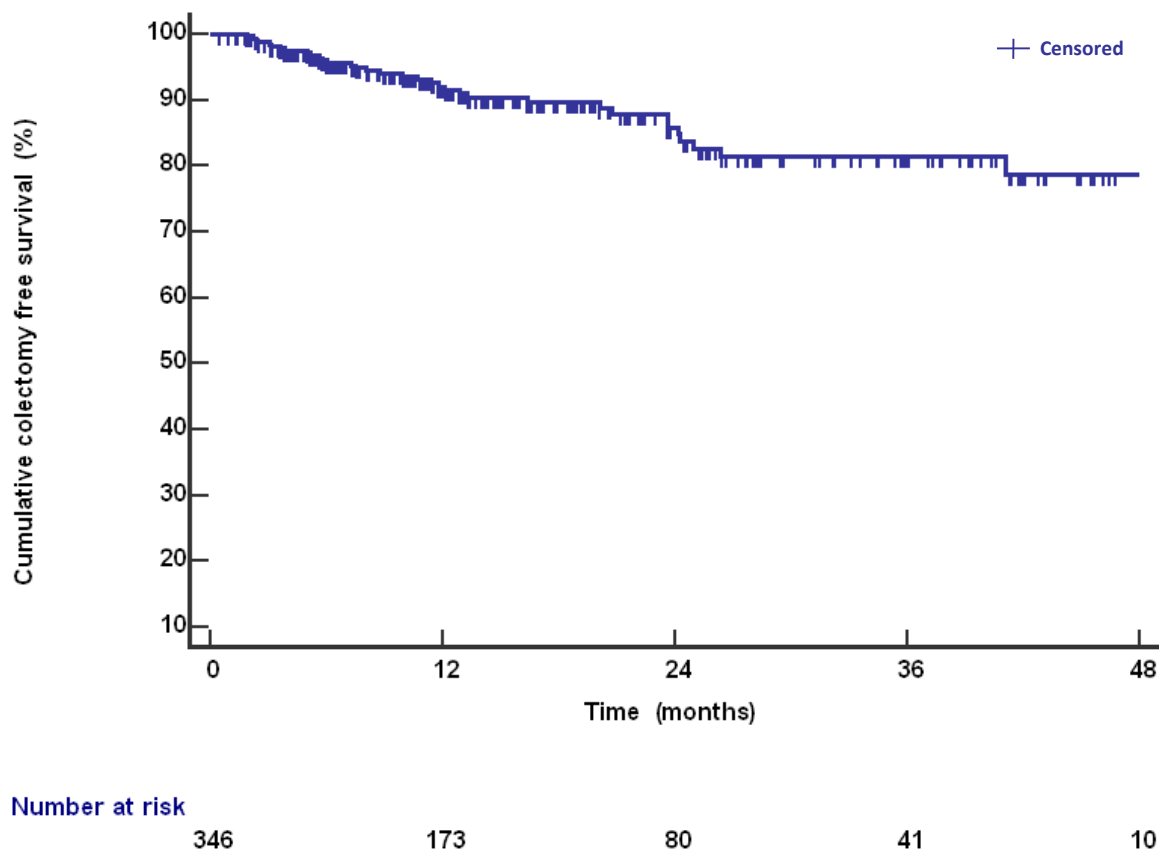
Results

Clinical response and remission

	CLINICAL EFFECTIVENESS (Investigator's opinion)	CLINICAL RESPONSE (Delta PMS ≥2)	CLINICAL REMISSION (PMS ≤2)
Week 8	283/346 (**82%**)	243/346 (**70%**)	176/346 (**51%**)
Week 24	206/346 (**60%**)	191/346 (**55%**)	173/346 (**50%**)
Week 52	154/346 (**45%**)	144/346 (**42%**)	142/346 (**41%**)

ITT analisis

➔ **ADA optimization (EW): 42%**, 6.6 month (IQR 3.2-14.2). 45% of patients with ADA optimization avoid withdrawal, **NNH 5.4** (95% CI 3.5-12.7)

➔ Endoscopic evaluation only in 70/346 patients (20%), 17.7 months (IQR 10.8-27.3) with **Mucosal healing** (Endoscopic Mayo Score 0-1) achieved in 34/70 **(48.5%)** of cases

Results

Colectomy

Cumulative colectomy-free survival was 92%, 85%, and 80% at 12, 24, and 36 months, respectively

Results

Adverse events

ADVERSE EVENTS	TOTAL	TIME to AE (months)
	68/346 (19.7%)	**11 (IQR 5-20)**
Allergic reactions	n= 4	1 (IQR 0.3-5)
Infections	n= 8	5 (IQR 3-11)
Skin disorders	n= 7	8 (IQR 4-20)
Rheumatological disorders	n= 7	5 (IQR 1-15)
Malignancy	n= 2	21 (IQR 3-40)

Results

	Time to Adalimumab stop			Time to Colectomy		
Predictors (Cox regression)	Univariate P	Multivariate P	HR	Univariate P	Multivariate P	HR
Male gender	.181			.113		
Age ≥ 60, naïve	.994					
Age at diagnosis ≥ 40 y				<.001	**.003**	3.26
Disease duration > 5 y	.004	**<.001**	0.64	.658		
Current smoker	.579			.761		
Extensive colitis (E3)	.403			.037	**.041**	2.28
Severe activity at baseline	.001	**.018**	1.59	<.001	**.001**	2.45
CRP > 10 mg/L	.228			.468		
EIMs	.020	NS		.281		
Steroid-dependent disease	.582			.786		
Concomitant thiopurines	.066	NS		.644		
Corticosteroids at baseline	.087	NS		.092	NS	
ADA optimization	.040	NS		.394		
Previous Anti-TNFα	.744			.543		
W8 clinical effectiveness	<.001	**<.001**	0.27	<.001	**.002**	0.32
W8 variation in PMS	.023	NS		.849		
Anemia (Hb < 12 g/dl)	.425			.216		
Body weight ≥ 80 kg	.423			.624		

Results

	Predictors (Cox regression)					
	Time to Adalimumab stop			Time to Colectomy		
	Univariate P	Multivariate P	HR	Univariate P	Multivariate P	HR
Male						
Age ≥						
Age at diag						6
Disease d						
Curren						
Extensive						3
Severe activ						6
CRP >						
E						
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Concomitant thiopurines	.066	NS		.644		
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Body weight ≥ 80 kg	.423			.624		

Time to Adalimumab stop
Disease duration >5 y, **HR** 0.64
Severe activity at baseline, **HR** 1.59
W8 effectiveness, **HR** 0.27

Results

	Predictors (Cox regression)					
	Time to Adalimumab stop			**Time to Colectomy**		
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Body weight ≥ 80 kg	.423			.624		

Time to Colectomy

Age at diagnosis ≥ 40 y, **HR** 3.26

Extensive colitis (E3), **HR** 2.28

Severe activity at baseline, **HR** 2.45

W8 effectiveness, **HR** 0.32

Discussion

- Large (346 patients) retrospective study with homogeneous data capturing

- Persistence was satisfactory: 64% in 1 year (8% intentionally stopping in well being)

- Short-term effectiveness very high (82%), majorly impacting on long-term persistence in treatment

- No safety signal emerged

- Colectomy in 35/346 cases (10%): significant protective effect of ADA on the short-medium term risk of colectomy.

IG·IBD

Thank you for your attention