DOP Session 12: Clinical Trials and Diagnostics

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DOP101
Maintaining remission after an episode of steroid-responsive Acute Severe Ulcerative Colitis: what is the best strategy?

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Background: The best maintenance therapy after a steroid-responsive acute severe ulcerative colitis (ASUC) episode remains poorly studied and is not addressed in current guidelines. We aimed to compare the impact of different treatment strategies following hospitalization for steroid-responsive ASUC.

Methods: Multicentric, multinational, retrospective cohort study including patients hospitalized with ASUC, between 2010-2021, who responded to intravenous steroids (Oxford Criteria). Patients were categorized according to treatment instituted after discharge - 5ASA, immunomodulators (IMM) and advanced therapy (AT). AT was considered as the reference for comparison. Our primary outcome was a composite of time until disease progression (need for steroids, need for therapy change, new hospitalization or colectomy); secondary outcomes were each event analyzed separately. Survival analysis and multivariate cox regression were performed.

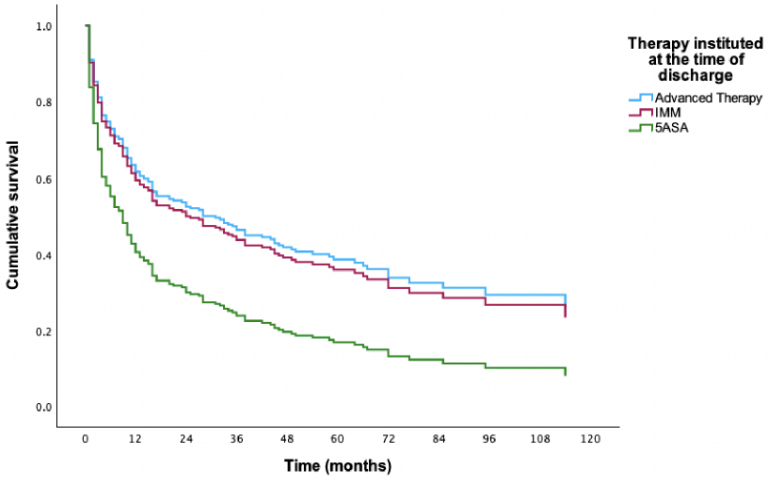
Results: 271 steroid-responsive patients from 19 countries were included; median-age at diagnosis was 33 (IQR 25-48) years, 49% were male, 49% had extensive colitis at diagnosis; median disease duration was 26 (IQR 3.0-92.3) months. Following hospitalization for steroid responsive ASUC, 34% of patients received 5-ASA as a maintenance therapy, 23% IMM and 43% AT. During a median follow up of 59 months (IQR 38-92), 68% had disease progression: new course of steroids was needed in 40%, therapy change in 54%, new hospitalization in 33% and colectomy in 10%. In univariate analysis, patients treated with 5-ASA had a trend towards earlier disease progression, compared to AT (HR 1.37, CI 95% 0.99-1.91, p=0.06), earlier need for steroids (HR 1.70, CI 95% 1.11-2.59, p=0.014) and therapy change (HR 1.68, CI 95% 1.15-2.43, p=0.007). In

Figure(s)/Table(s): see next page

multivariate analysis, adjusting for age and disease extension at diagnosis, disease duration, use of AT prior to ASUC hospitalization, and period of hospitalization (2010-2015 vs 2016-2021), patients treated with 5-ASA had a higher risk of disease progression compared to both IMM (HR 1.50, CI 95% 1.02-2.21, p=0.041) and AT (HR 1.86, CI 95% 1.26-2.74, p=0.002) – Figure 1. No differences were seen between IMM and AT in uni- and multivariate analysis. Shorter disease duration (HR 0.99, CI 95% 0.99-0.99, p=0.007), and prior use of AT (HR 1.67, CI 95% 1.13-2.47, p=0.010) were also associated with higher risk of disease progression – Table 1.

Conclusion: After an episode of steroid-responsive ASUC, shorter disease duration and prior use of advanced therapy were risk factors for disease progression. Approximately 1/3 of patients was treated with 5ASA alone. This strategy was also associated with a higher risk of poor outcomes and should be avoided.

Figure 1. Differences in disease progression (defined by need of steroids, therapy change, new hospitalization or colectomy) in patients with steroid-responsive ASUC, comparing different treatment regimens at discharge – 5ASA, IMM and advanced therapy – and adjusted for age at diagnosis, disease extension, disease duration, advanced therapy prior to ASUC hospitalization and date of hospitalization.



5-ASA vs advanced therapy (reference) - HR 1.86, CI 95% 1.26-2.74, p=0.002; 5-ASA vs IMM (reference) - HR 1.50, CI 95% 1.02-2.21, p=0.041; IMM vs advanced therapy (reference) - HR 1.18, CI 95% 0.73-1.66, p=0.636.

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Table 1. Factors associated to disease progression (defined by need of steroids, therapy change, new hospitalization or colectomy) in patients with steroid-responsive ASUC – univariate and multivariate cox regression.

	Univariate analysis			Multivariate analysis		
	HR	**CI 95%**	**p-value**	**HR**	**CI 95%**	**p-value**
Age at diagnosis, years	1.003	0.994-1.013	0.467	1.000	0.990-1.010	0.978
Smoking habits at diagnosis						
Smoker	ref.	ref.	ref.	ref.	ref.	ref.
Non-smoker	0.083	0.941-2.682	0.083	1.669	0.983-2.836	0.058
Ex-smoker	0.068	0.963-2.931	0.068	1.647	0.935-2.901	0.084
Disease at diagnosis						
E2/E1	ref.	ref.		ref.	ref.	
E3	1.107	0.830-1.478	0.489	1.088	0.807-1.467	0.579
Disease duration, months	0.998	0.996-1.000	**0.013**	0.998	0.996-0.999	**0.007**
Corticotherapy prior to hospitalization						
No	ref.	ref.				
Yes	1.027	0.768-1.373	0.859			
Advanced therapy prior to hospitalization						
No	ref.	ref.		ref.	ref.	
Yes	1.378	0.983-1.931	0.063	1.673	1.132-2.473	**0.010**
Clostridioides Difficile infection						
No	ref.	ref.				
Yes	0.542	0.173-1.696	0.292			
CMV infection						
No	ref.	ref.				
Yes	0.766	0.377-1.555	0.460			
sMayo during hospitalization						
2	ref.	ref.				
3	1.248	0.891-1.748	0.198			
Hospitalization date						
2010-2015	ref.	ref.		ref.	ref.	
2016-2021	1.245	0.892-1.738	0.197	1.299	0.909-1.857	0.151
Therapy instituted at discharge						
Advanced therapy	ref.	ref.		ref.	ref.	
5ASA	1.374	0.990-1.907	0.057	1.856	1.258-2.738	**0.002**
IMM	0.917	0.625-1.344	0.656	1.104	0.733-1.662	0.636

CI – Confidence Interval; CMV – *Citomegalovirus*; HR – Hazard Ratio; sMayo – Mayo Endoscopic Subscore.