Tofacitinib dose modifications in refractory ulcerative colitis - a Danish multicentre real-world cohort study

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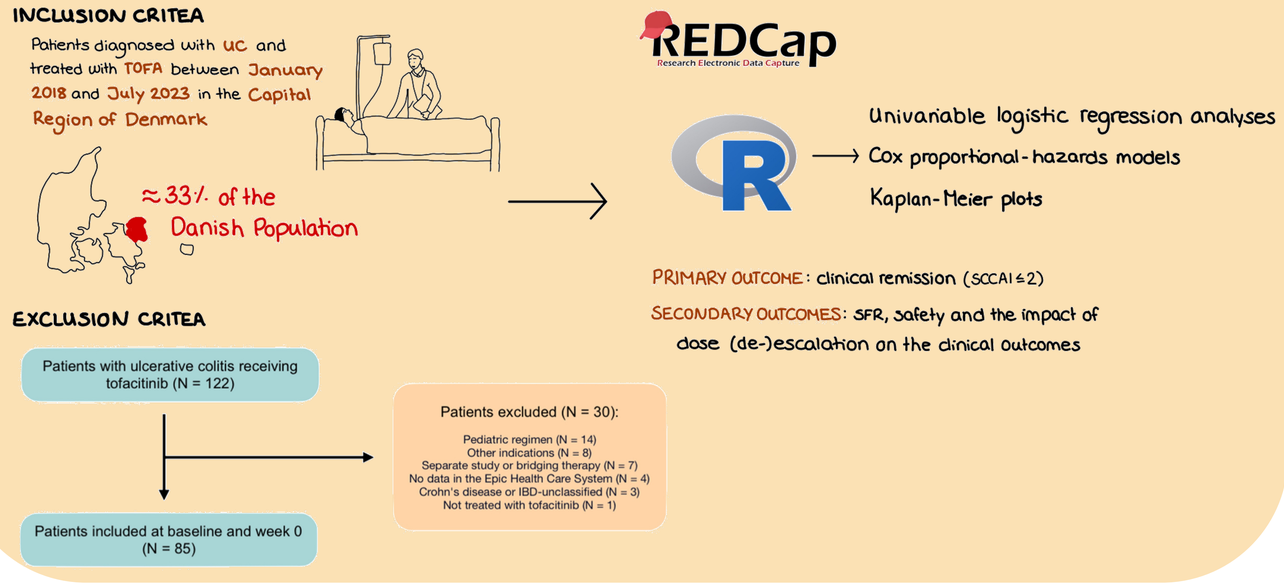
Aims

To evaluate the **effectiveness** and **safety** of dose modifications of TOFA.

Methods

Retrospective cohort study



Results

Baseline characteristics

Characteristics	Total number of patients (N = 85)	De-escalation of TOFA (N = 59)	No de-escalation of TOFA (N = 26)	*P* value
Sex				.188
Male	53 [62.4]	40 [67.8]	13 [50.0]	
Female	32 [37.6]	19 [32.3]	13 [50.0]	
Age at diagnosis, y	26.8 [22.5-37.7]	27 [22.5-38.5]	26 [22.3-35.5]	.879
Disease duration when initiating TOFA, y	6.3 [2.4-9.8]	6.3 [2.7-9.6]	6.2 [1.7-9.7]	.935
Age when initiating TOFA, y	34.2 [26.3-46.6]	34.2 [26.5-46.1]	34 [25.3-48.5]	.932
BMI	24.4 [21.5-28.3]	24.4 [21.2-28.0]	24 [22-29.5]	.658
BMI ≥ 30	13 [20.6]	8 [13.8]	5 [26.3]	.508
Indication for TOFA				.627
Acute severe disease	17 [20.0]	13 [22.0]	4 [15.4]	
Chronic active disease	68 [80.0]	46 [78.0]	22 [84.6]	
Disease extent[a]				.675
E1	7 [8.2]	5 [8.5]	2 [7.7]	
E2	27 [31.8]	17 [28.8]	10 [38.5]	
E3	51 [60.0]	37 [62.7]	14 [53.8]	
Comorbidities				
Chronic illnesses	31 [36.5]	22 [37.3]	9 [34.6]	.814
Previous cancer	2 [2.4]	2 [3.4]	0 [0]	1.00
Prior VTE	2 [2.4]	0 [0]	2 [7.7]	.091
Previous HZ	3 [3.5]	2 [3.4]	1 [3.8]	1.00
Smoking status				.909
Never	53 [63.9]	35 [62.5]	18 [69.2]	
Previous	27 [32.5]	19 [33.9]	8 [30.8]	
Less than once a week	1 [1.2]	1 [1.8]	0 [0]	
Daily	1 [1.2]	1 [1.8]	0 [0]	
Prior treatments				
Topical 5-ASA	74 [87.1]	50 [84.7]	24 [92.3]	.491
Systemic 5-ASA	80 [94.1]	56 [94.9]	24 [92.3]	.639
Thiopurines	65 [76.5]	43 [72.9]	22 [84.6]	.234
Topical steroids	47 [55.3]	32 [54.2]	15 [57.7]	.768
Systemic steroids	85 [100]	59 [100]	26 [100]	
Methotrexate	8 [9.4]	4 [6.8]	4 [15.4]	.241
Cyclosporine	1 [1.2]	0 [0]	1 [3.8]	.306
Prior biologic treatments				
IFX	79 [92.9]	55 [93.2]	24 [92.3]	1.00
ADA	17 [20.0]	11 [18.6]	6 [23.1]	.638
GOL	15 [17.6]	8 [13.6]	7 [26.9]	.215
VDZ	48 [56.5]	31 [52.5]	17 [65.4]	.772
UST	18 [21.2]	11 [18.6]	7 [26.9]	.389
Miri	1 [1.2]	0 [0]	1 [3.8]	.306
Number of prior biologic treatments				.069
Zero	4 [4.7]	3 [5.1]	1 [3.8]	
One	26 [30.6]	18 [30.5]	8 [30.8]	
Two	22 [25.9]	20 [33.9]	2 [7.7]	
Three	23 [27.1]	13 [22.0]	10 [38.5]	
Four	8 [9.4]	4 [6.8]	4 [15.4]	
Five	2 [2.4]	1 [1.7]	1 [3.8]	
Concomitant medication at baseline				
Topical 5-ASA	35 [41.2]	24 [40.7]	11 [42.3]	.888
Systemic 5-ASA	39 [45.9]	27 [45.8]	12 [46.2]	.973
Immunomodulators	3 [3.5]	2 [3.4]	1 [3.8]	1.00
Topical steroids	4 [4.7]	3 [5.1]	1 [3.8]	1.00
Systemic steroids	27 [31.8]	19 [32.2]	8 [30.8]	.896
Biologics	4 [4.7]	4 [6.8]	0 [0]	.308
None	22 [25.9]	15 [25.4]	7 [26.9]	.884
History of UC-related surgery	0 [0]	0 [0]	0 [0]	

Table 1. Baseline characteristics based on TOFA de-escalation.

- 62.4% male; 95.3% bio-exposed, 64.8% ≥2 prior biologic failures; 60.0% extensive colitis.

Safety profile

- No cases of SAEs.
- AEs occurred in 40 patients (47.1%); most commonly hypercholesterolemia, anaemia, and nausea.
- No significant association with dosing escalation
- 16 patients (43.8%) required dose escalation due to SLR. Of these, 43.8% recaptured clinical remission.

Clinical remission, SFR, and clinical response

Time point	W8	W52
Clinical remission	43.4%	35.3%
SFR	34.9%	29.4%
Clinical response	54.2%	35.3%

SFR during 52 weeks

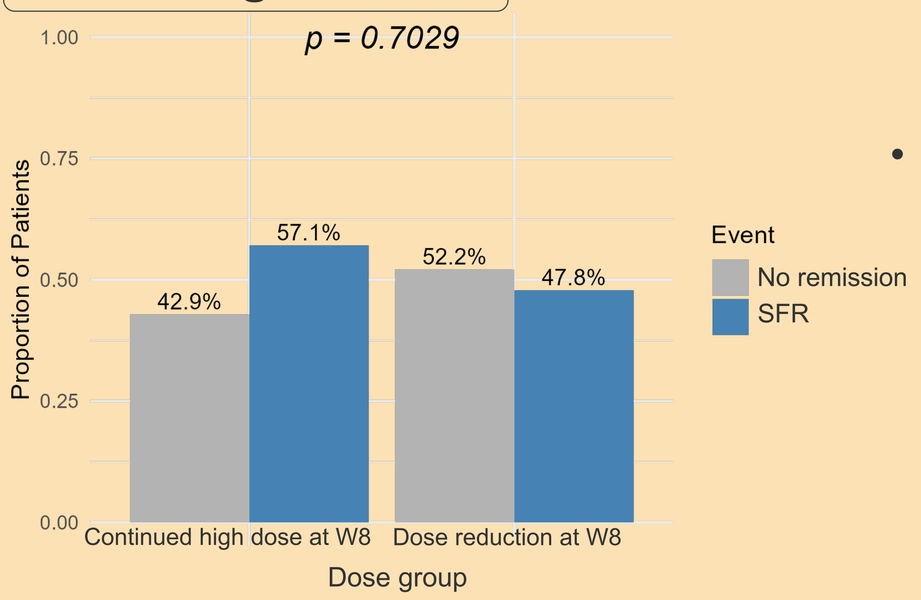


Figure 1. SFR during 52 weeks according to TOFA dosing groups at W8.

- Clinical remission and response at W8 was associated with SFR at W52 or treatment discontinuation due to remission (unadjusted OR 46.25, 95% CI 8.78-856.81, p<0.001).

SLR and dosing strategy at W8

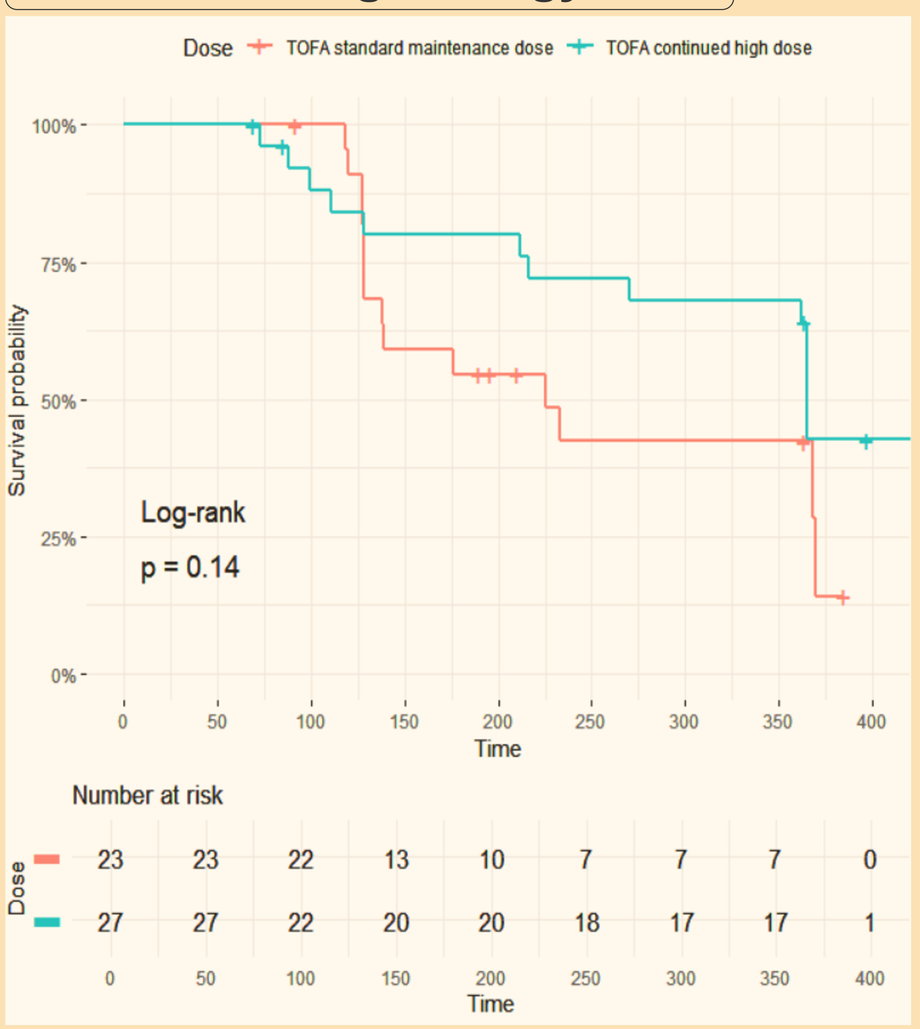


Figure 2. KM-plot illustrating the difference in SLR risk between patients deescalating to TOFA standard maintenance dose or continuing high dose therapy after W8.

- Among patients continuing high-dose therapy after induction, about 60.0% without prior clinical remission eventually achieved so within four months.
- No significant difference in SLR risk between patients continuing high-dose TOFA vs de-escalation at W8. Cox HR 1.86 [95% CI 0.82–4.25]).

Conclusions

TOFA is **effective** and **generally safe** for inducing and maintaining clinical remission in bio-exposed patients with refractory UC. Furthermore, **individualized dosing** of TOFA dependent on induction response was in this study safe and may **improve long-term outcome**.