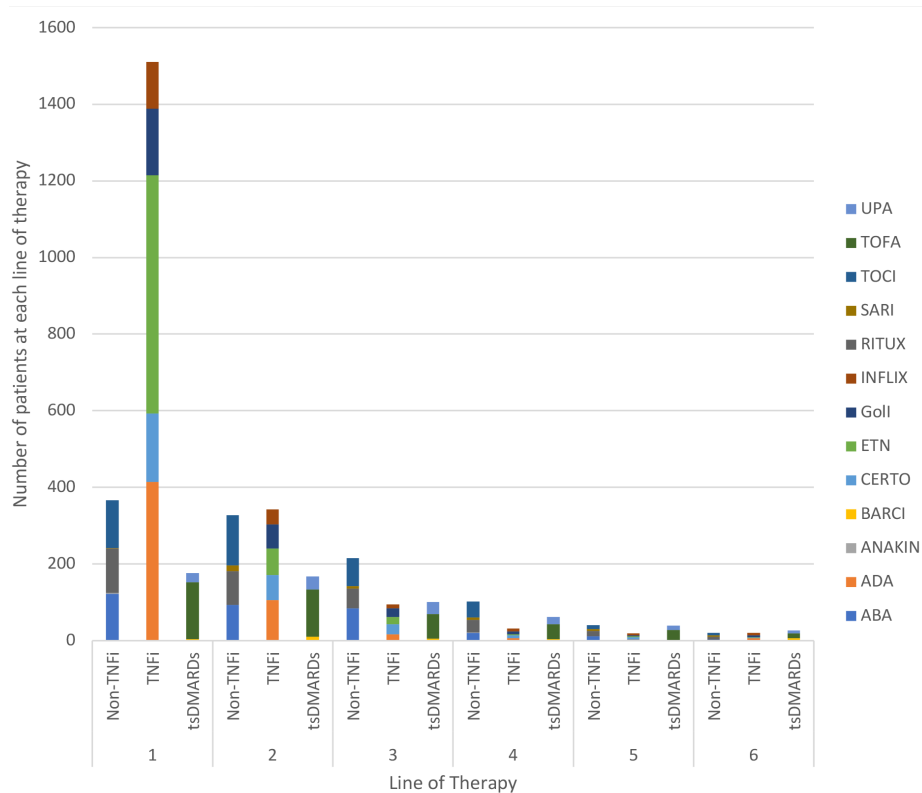
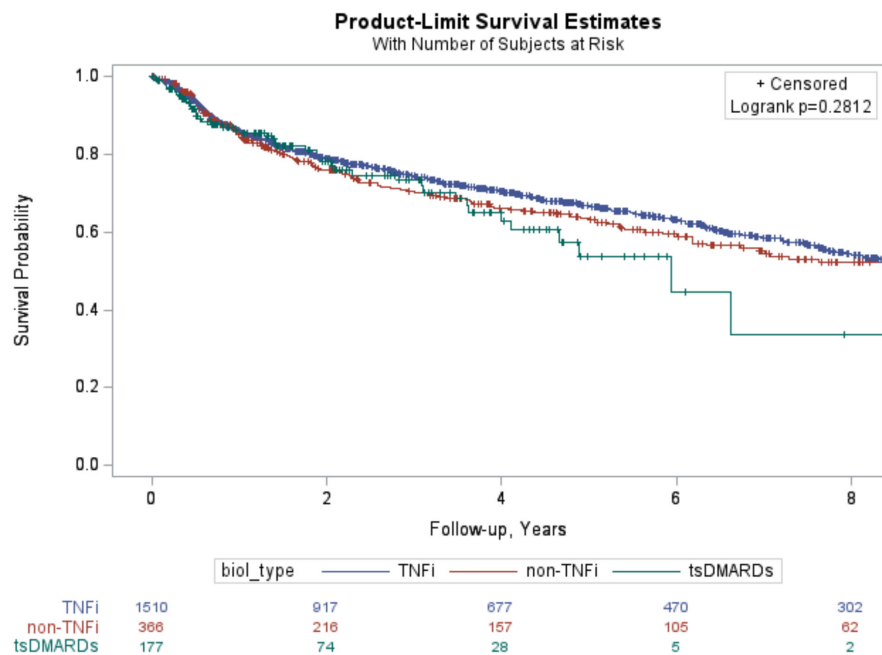


Supplementary Fig. S1. Study flowchart





Supplementary Fig. S3. Time to discontinuation by drug class in line one.

Supplementary Table S1. Drug survival rate at year 1 to 8 of follow-up by line of therapy.

Line of therapy	Year	Survival rate	95% confidence interval	
Line 1	1	0.85	0.84	0.87
	2	0.78	0.76	0.80
	3	0.74	0.71	0.76
	4	0.69	0.67	0.72
	5	0.65	0.63	0.68
	6	0.62	0.59	0.65
	7	0.57	0.55	0.60
	8	0.53	0.50	0.56
Line 2	1	0.75	0.72	0.77883
	2	0.62	0.58	0.66
	3	0.56	0.52	0.60
	4	0.50	0.45	0.54
	5	0.43	0.38	0.47
	6	0.41	0.36	0.45
	7	0.38	0.33	0.47
	8	0.36	0.31	0.41
Line 3	1	0.74	0.69	0.79
	2	0.58	0.52	0.64
	3	0.50	0.44	0.56
	4	0.43	0.36	0.49
	5	0.36	0.28	0.43
	6	0.33	0.26	0.41
	7	0.28	0.20	0.36
	8	0.19	0.11	0.30
Line 4-6 combined	1	0.73	0.67	0.78
	2	0.59	0.52	0.65
	3	0.49	0.41	0.56
	4	0.40	0.32	0.48
	5	0.32	0.23	0.41
	6	0.24	0.15	0.35
	7	0.24	0.15	0.35
	8	0.24	0.15	0.35

Supplementary Table S2. Response outcomes by line of therapy.

Outcome n=2085	Line 1 n=961 *	Line 2 n=584 *	Line 3 n=282 *	Line 4-6 combined. n=258 *
CDAI change between baseline and 6-month follow-up, mean (SD)	10.2 (13.3)	6.96 (13.7)	6.66 (12.9)	6.33 (13.4)
Minimal clinically important difference for CDAI, n (%)	553 (57.4)	254 (43.5)	114 (40.4)	103 (39.9)
CDAI LDA (<=10), n (%)	479 (49.8)	218 (37.3)	71 (25.2)	62 (24.0)
CDAI remission (<=2.8), n (%)	129 (13.4)	52 (8.9)	22 (7.8)	12 (4.7)

* CDAI was not available for 364 patients at 6 months follow-up for: 156 patients in line 1; 95 patients in line 2; 57 patients in line 3; 56 patients in line 4 /5/6.

Supplementary Table S3. Treatment effectiveness at 6 months by line of therapy stratified by year of AT initiation.

Models weighted for PS (IPTW) and adjusted for selected covariates *				
	CDAI change Difference (95% CI)	CDAI-MCID ORs (95% CI)	CDAI-LDA ORs (95% CI)	CDAI-remission ORs (95% CI)
Patients initiated in 2010 or before				
Line 1	Ref	Ref	Ref	Ref
Line 2	-3.12 (-5.18, -1.06)	0.77 (0.65, 0.91)	0.77 (0.64, 0.93)	0.23 (0.15, 0.36)
Line 3	-6.15 (-11.7, -0.61)	2.06 (1.33, 3.19)	0.27 (0.15, 0.48)	0.97 (0.55, 1.69)
Patients initiated after 2010				
Line of AT therapy				
Line 1	Ref	Ref	Ref	Ref
Line 2	-3.60 (-4.20, -3.00)	0.56 (0.53-0.59)	0.56 (0.54-0.59)	0.64 (0.60-0.69)
Line 3	-3.98 (-4.75 -3.20)	0.50 (0.46-0.54)	0.34 (0.31-0.36)	0.72 (0.64-0.80)
Line 4-6 combined	-5.95 (-6.80, -5.09)	0.42 (0.39-0.46)	0.35 (0.32-0.38)	0.37 (0.32-0.43)

*Adjusted for baseline characteristics (age, sex, disease duration, positive RF, CDAI, drug class, comorbidity number)