

Supplementary Web Appendix

Drug Survival on TNF Inhibitors in Patients with RA: Comparison of Adalimumab, Etanercept & Infliximab

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eTable 1 Studies investigating / showing TNF inhibitor drug survival trends over time in RA^a

Register Country	Author Year	Period	n	Findings
DANBIO Denmark	Hetland et al 2008[10]	2000-2005	1813	Seemingly no change in 1y drug surv [not tested]: 2000/01: 73%; 2005: 69%
SCQM Switzerland	Du Pan et al 2009[1]	1997-2006	2364	Later year associated with greater discontinuation [Not only first TNFi start]
BIOBADASER Spain	Gomez-Reino 2012[5]	2000-2009	2907	Decreasing 1y drug survival, driven by more stops/switches due to inefficacy Adjustment for TNFi, clinical activity, and concomitant treatment
ARTIS Sweden	Simard et al 2011[4]	1999-2008 (1999-2007 for drug survival)	9612 on 1 st TNFi	Decreasing 1y drug survival - Greater share stops/switches due to inefficacy - Smaller share stops/switches due to adverse events 25-30% discontinued within 1y Time on any bio-therapy: 82% of person-time over first 6y
BSRBR United Kingdom	Hyrich et al 2011[3]	2001-2008	11216	<i>“Drug survival remained relatively stable over the study years”</i> <i>“There was a minimal trend towards improved drug survival at both 1 and 2 years”</i>
SCQM Switzerland	Du Pan et al, 2012[31]	? ^b -2009	1485	<i>“A time trend for increasing rates of drug discontinuation exists in recent years”</i> [Analysis of drug survival after TNFi failure]
PharMetrics United States	Yazici et al, 2009[12]	2000-2005	9074	Time to switching decreased over time

^a All studies included time with low etanercept supply (2000-2003) & the pre-adalimumab period (2000-2002); TNFi = TNF inhibitor

^b Question marks indicate that the follow-up year is unclear

eTable 2 European studies of head-to-head comparisons of TNF inhibitor drug survival in RA^a

Register Country	Author Year	Period	n	Findings	General
SSATG Sweden	Geborek et al, 2002[17]	1999-2000	166 ETA 135 INF	No difference in 20 month drug survival ETA/INF:79%/75%	
Netherlands	Flendrie et al, 2003[8]	1997-2003	120 INF 16 ETA 94 ADA	No between-drug difference 1y drug survival: INF 66% / ETA 74% / ADA 73%	INF: AEs more common cause for discontinuation
RABBIT Germany	Zink et al, 2005[18]	2001-2003	511 ETA 343 INF	No difference between ETA and INF in 12m drug survival (69% vs 65%)	Lower drug survival than in RCTs
France	Duclos et al, 2006[19]	1997-2004	770 (440 RA)	No difference between INF, ETA, ADA (P=.48) 1/2y INF,ETA,ADA: 63%, 64%, 68% / 48%, 51%, 60%	
SSATG Sweden	Kristensen et al, 2006[13]	1999-2004	1161	INF vs ETA 3x greater risk of discontinuation 1y overall: 69% vs 89% 1y combo/mono: 58% vs 85% / 47% vs 74%	ETA & INF [ADA excluded] Main focus on impact of concomitant DMARDs
BIOBADASER Spain	Gomez-Reino et al, 2006[32]	2000-2004	4706 RA AS PsA other	1y / 2y drug survival overall: 83% / 75% 1y / 2y drug survival in switchers: 68% / 60% INF lower survival than ETA & ADA (1 st & 2 nd line)	Focus: Switching (compare)
Tertiary center France	Brocq et al, 2007[16]	1999-2005	442 (304 RA)	1y/2y drug survival ETA: 87% / 68% ADA: 83% / 66% INF: 68% / 46% (sig lower)	In AS patients: INF > ETA
DANBIO Denmark	Ostergaard et al, 2007[33]	? ^b -2002	378 INF 39 ETA	1y drug survival INF/ETA: 71%/73% (P=.04)	
DREAM Netherlands	Kievit et al, 2008[2]	2003-2007	916 (1y: 707)	INF worse than ADA & ETA (1y) Discontinuation: 31% vs 22% & 21%	ADA & ETA: Better and cheaper than INF
NOR-DMARD Norway	Heiberg et al, 2008[14]	2000-2006? ^b	847 RA 172 PsA 249 AS	1y drug survival in RA INF/ETA/ADA: 63%/70%/62% Adjusted: ETA better survival than INF & ADA Adjusted in 1 st TNFi only: No difference	Drug survival in RA, AS, PsA
RABBIT Germany	Strangfeld et al, 2009[34]	2001-2006	1769	36m drug discontinuation INF/ETA/ADA: Co-med MTX: 62% / 46% / 51% Co-med LEF: 67% / 53% / 63%	Focus on co-medication with MTX or LEF (compare[13, 35])

^a INF=Infliximab; ETA=Etanercept; ADA=Adalimumab

^b Question marks indicate that the follow-up year is unclear

eTable 2 (contd) European studies making head-to-head comparisons of TNF inhibitor drug survival in RA^a

Register Country	Author Year	Period	n	Findings	General
SCQM Switzerland	Du Pan et al, 2009[1]	1997-2006	2364	INF worse than ETA & ADA (1y/2y: 78%, 82%, 84% / 58%, 65%, 66%) INF vs ETA+ADA HR 1.24, driven by AEs (no difference in discontinuation due to inefficacy)	DAS28: higher=shorter drug survival
LOHREN Italy	Marchesoni et al, 2009[15]	1999-? ^b	1064	ETA > INF and ADA at 36m (P=0.03) 62.5% > 49.1% & 53.6% Adj HR (ETA ref): ADA 1.45, P=.02; INF 1.50, P=.01	
DANBIO Denmark	Hetland et al, 2010[7]	2000-2007	2326 On 1 st TNFi	2y drug survival ETA/ADA/INF = 56%/52%/41% Adj. Hazard Ratios INF vs ETA: 1.98 (1.63-2.40) INF vs ADA: 1.35 (1.15-1.58) ADA vs ETA: 1.47 (1.20-1.80)	INF: Lowest response, remission & drug survival ADA: Best response ETA: Best drug survival

eTable 3 US studies making head-to-head comparisons of TNF inhibitor drug survival in RA

Register Country	Author Year	Period	N	Findings	General
PharMetrics United States	Tang et al, 2008[36]	2001-2004	1242	1y drug survival INF, ETA, ADA: 78%, 73%, 71% INF longer drug survival than ETA & ADA	
PharMetrics United States	Yazici et al, 2009[12]	2000-2005	9074	INF longer drug survival than ETA & ADA <i>Time to switching decreased over time</i>	50% on INF at 2y follow-up
CORRONA United States	Greenberg et al, 2011[20]	2002-2008	2242 728 INF 640 ETA 874 ADA	1/2y drug survival INF, ETA, ADA in bio-naïve: 76%, 72%, 68% / 63%, 53%, 53% Odds Ratios ADA vs INF: 1.4 (95%CI 1.1-1.8) ETA vs INF: 1.3 (95%CI 1.0-1.6)	Dosing differences vs European studies for INF and ADA[2, 7] Disease activity low or moderate in most patients, contrasting with European data

^a INF=Infliximab; ETA=Etanercept; ADA=Adalimumab

^b Question marks indicate that the follow-up year is unclear