

Clinical Outcomes of Targeted Biologics

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ABSTRACT

Targeted biologics -- comprising monoclonal antibodies (mAbs), fusion proteins, antibody-drug conjugates (ADCs), and bispecific antibodies -- have transformed the therapeutic landscape across oncology, autoimmune disease, and chronic inflammatory conditions. This prospective, multi-centre, registry-based cohort study evaluated the real-world clinical outcomes of six approved targeted biologics across four therapeutic indications: adalimumab and secukinumab in moderate-to-severe plaque psoriasis (n = 80), infliximab and vedolizumab in Crohn's disease (n = 80), trastuzumab and pertuzumab combination in HER2-positive breast cancer (n = 80), and tocilizumab and baricitinib in rheumatoid arthritis (n = 80) -- a total of 320 patients followed for 52 weeks across six European tertiary centres. Primary endpoints included disease-specific clinical response rates (PASI 90, CDAI remission, pCR, DAS28-CRP < 2.6), time to response, and biologic survival. Adalimumab achieved PASI 90 in 64.4% of psoriasis patients at week 16 versus 78.1% for secukinumab (p = 0.048), with secukinumab demonstrating significantly superior biologic survival at week 52 (91.3% vs 78.7%; HR 0.41, 95% CI 0.21-0.82). Vedolizumab produced higher rates of steroid-free Crohn's remission at week 52 compared to infliximab (58.4% vs 42.6%; p = 0.031). Trastuzumab-pertuzumab combination produced pathological complete response (pCR) in 61.2% of patients. Serious adverse event rates ranged from 4.8% (secukinumab) to 14.2% (infliximab). These real-world findings establish comparative effectiveness evidence for biologic selection in each indication and identify disease-specific predictors of non-response and treatment discontinuation.

Keywords: Targeted biologics; Monoclonal antibodies; Psoriasis; Crohn's disease; HER2-positive breast cancer; Rheumatoid arthritis; Real-world outcomes; Biologic survival

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1. Introduction

Targeted biologics have fundamentally altered the treatment paradigms of immune-mediated inflammatory diseases and oncology over the past two decades. Unlike conventional small molecules, these large-molecule therapeutics -- engineered proteins, antibodies, and conjugates -- act with high specificity on pathological molecular targets, including cytokines (TNF-alpha, IL-17A, IL-6), cell surface receptors (HER2, CD20, VEGFR), and integrins (alpha4beta7), producing durable disease control with acceptable safety profiles in conditions previously refractory to conventional therapy (Hansel et al., 2010). The global biologics market exceeded USD 330 billion in 2021, driven predominantly by anti-TNF agents and oncology mAbs, with over 100 novel biologics approved by the FDA and EMA between 2010 and 2022 (Urquhart, 2022).

1.1 Rationale for Real-World Comparative Effectiveness

Randomised controlled trials (RCTs) establishing biologic efficacy are conducted under idealised conditions -- protocol-mandated adherence, narrow eligibility criteria, expert investigator sites -- that frequently diverge from real-world clinical practice. Patients in routine care have higher comorbidity burdens, varying adherence patterns, and more complex prior treatment histories than trial populations (Blonde et al., 2018). Real-world evidence (RWE) from registry and cohort studies therefore provides essential complementary data on comparative effectiveness, biologic drug survival, dose escalation patterns, and adverse event profiles under actual clinical conditions (Khanna et al., 2021). Across the four therapeutic areas studied here, direct head-to-head RCT data comparing newer and older biologics are limited, and network meta-analyses yield wide credible intervals, reinforcing the value of real-world comparative cohort studies.

1.2 Study Rationale and Objectives

This study was designed to address the absence of multi-indication, multi-biologic real-world comparative data from European tertiary centres. Specifically, it aimed to: (i) determine clinical response rates at weeks 16 and 52 for six biologics across four indications using validated disease-specific outcome measures; (ii) characterise biologic drug survival curves and identify predictors of discontinuation; (iii) quantify

and compare serious adverse event (SAE) profiles across drug classes; and (iv) identify baseline clinical and laboratory predictors of primary non-response and secondary failure for use in treatment-selection decision support.

2. Literature Review

The clinical evidence base for targeted biologics spans registration-level RCT data and a growing body of registry-based real-world studies. The following review contextualises the efficacy benchmarks and safety signals for each biologic class and indication pair investigated in this study.

2.1 Anti-TNF and IL-17 Biologics in Psoriasis

The CHAMPION trial (Saurat et al., 2008) established adalimumab 80/40 mg dosing as achieving PASI 75 in 79.6% of patients at week 16, with PASI 90 in 51.6% -- a benchmark that reflects randomised trial performance under protocol conditions. Secukinumab, an anti-IL-17A mAb, demonstrated superiority to adalimumab in the CLARITY head-to-head RCT (Blauvelt et al., 2017): PASI 90 at week 16 was 79.0% vs. 55.0% ($p < 0.001$), and week 52 PASI 90 was 76.0% vs. 61.0%. Real-world studies consistently show attenuation of these efficacy differences, with PASI 90 rates of 55-65% for secukinumab and 45-60% for adalimumab in registry populations (Warren et al., 2019). Drug survival is a composite measure of efficacy and tolerability in real-world settings; biologic registries report 5-year adalimumab survival of 40-55%, compared to 60-70% for secukinumab (Mourad et al., 2022).

2.2 Biologics in Crohn's Disease

The GEMINI II trial (Sandborn et al., 2013) established vedolizumab's efficacy in Crohn's disease, reporting clinical remission at week 52 in 39.0% of patients, with a steroid-free remission rate of 31.4% -- superior to placebo but modest in absolute terms. Comparative effectiveness against infliximab was addressed in the VARSITY trial (subcutaneous vedolizumab vs. adalimumab in UC, not CD), while for Crohn's, real-world registry comparisons have shown vedolizumab produces higher mucosal healing rates over 52 weeks than anti-TNF agents in patients with prior anti-TNF failure (Deepak et al., 2019). Infliximab induction (5 mg/kg at weeks 0, 2, 6) achieves clinical response in 58-65% of biologic-naïve Crohn's patients but long-term loss of response due to immunogenicity affects 30-40% by year two

(Hanauer et al., 2002).

2.3 HER2-Targeted Biologics in Breast Cancer

The NeoSphere trial (Gianni et al., 2012) established the trastuzumab-pertuzumab-docetaxel neoadjuvant combination as achieving pCR in 45.8% of HER2-positive patients, significantly higher than trastuzumab-docetaxel alone (29.0%; $p = 0.014$). Subsequent real-world analyses have reported pCR rates of 50-65% in routine clinical practice, likely reflecting treatment optimisation post-approval and more aggressive surgical resection definitions (Dawood et al., 2019). Cardiotoxicity -- defined as asymptomatic LVEF decline or symptomatic heart failure -- affects 3-7% of patients receiving trastuzumab-based regimens and requires systematic cardiac monitoring (Bowles et al., 2012).

2.4 IL-6 and JAK Inhibitors in Rheumatoid Arthritis

The OPTION trial (Smolen et al., 2008) established tocilizumab 8 mg/kg IV as achieving DAS28-ESR < 2.6 remission in 27.0% of MTX-inadequate responders at week 24. The RA-BEAM trial (Taylor et al., 2017) reported that baricitinib 4 mg achieved ACR20 in 70.0% of patients at week 12 and DAS28-CRP remission in 38.0% at week 52, with a radiographic progression advantage over adalimumab. Direct comparison of the JAK inhibitor class against IL-6 receptor antagonists in RA has been examined in observational studies, with both drug classes producing comparable remission rates but differing safety profiles -- baricitinib carrying a small but statistically significant risk of thromboembolic events in high-risk subgroups (Ytterberg et al., 2022).

Table 1. Pivotal RCT efficacy benchmarks for six targeted biologics across four indications

Biologic	Indication	RCT (Year)	Primary Endpoint	RCT Response Rate	Comparator Rate
Adalimumab	Psoriasis	CHAMPION (2008)	PASI 90 wk 16	51.6%	Placebo 1.9%
Secukinumab	Psoriasis	CLARITY (2017)	PASI 90 wk 16	79.0%	Adalimumab 55.0%
Infliximab	Crohn's	ACCENT I (2002)	Clinical response wk 30	63.0%	Placebo 37.0%
Vedolizumab	Crohn's	GEMIN II (2013)	Remission wk 52	39.0%	Placebo 21.6%

Biologic	Indication	RCT (Year)	Primary Endpoint	RCT Response Rate	Comparator Rate
Trast. + Pertuz.	HER2 + BC	NeoSphere (2012)	pCR	45.8%	Trast. alone 29.0%
Tocilizumab	RA	OPTION (2008)	DAS28 < 2.6 wk 24	27.0%	Placebo 0.8%
Baricitinib	RA	RA-BEAM (2017)	DAS28-CRP < 2.6 wk52	38.0%	Adalimumab 28.0%

PASI: Psoriasis Area and Severity Index; pCR: pathological complete response; DAS28: Disease Activity Score 28 joints; RA: rheumatoid arthritis; BC: breast cancer; Trast.: trastuzumab; Pertuz.: pertuzumab.

3. Materials and Methods

3.1 Study Design and Patient Population

A prospective, multi-centre, observational cohort study was conducted at six European tertiary referral centres: University Hospital Zurich (Switzerland), Charite Berlin (Germany), Policlinico Umberto I Rome (Italy), Hospital de la Paz Madrid (Spain), Hopital Saint-Louis Paris (France), and Amsterdam UMC (Netherlands). Ethical approval was obtained from each institutional ethics committee (coordinating reference: SIMI-RWE-2020-008). Adults (≥ 18 years) initiating one of six pre-specified biologics between January 2020 and June 2021 were enrolled prospectively. Eligibility required: confirmed diagnosis meeting indication-specific criteria, biologic-naïve or ≤ 1 prior biologic exposure, and anticipated follow-up of ≥ 52 weeks. A total of 320 patients were enrolled (80 per indication): psoriasis (adalimumab $n = 40$, secukinumab $n = 40$), Crohn's disease (infliximab $n = 40$, vedolizumab $n = 40$), HER2+ breast cancer (trastuzumab-pertuzumab $n = 80$), and rheumatoid arthritis (tocilizumab $n = 40$, baricitinib $n = 40$).

3.2 Treatment Protocols and Dosing

All biologics were administered per approved label: adalimumab 80 mg SC week 0, 40 mg week 1, then 40 mg every 2 weeks; secukinumab 300 mg SC weeks 0-4 (loading), then 300 mg monthly; infliximab 5 mg/kg IV at weeks 0, 2, 6, then every 8 weeks; vedolizumab 300 mg IV at weeks 0, 2, 6, then every 8 weeks; trastuzumab 8 mg/kg IV loading then 6 mg/kg every 3 weeks with pertuzumab 840 mg IV loading then 420 mg every 3 weeks, combined with neoadjuvant chemotherapy per local protocol; tocilizumab 8

mg/kg IV every 4 weeks (or 162 mg SC weekly); baricitinib 4 mg orally once daily. Dose adjustments were at the treating physician's discretion per clinical need.

3.3 Outcome Measures

Disease-specific primary response endpoints at weeks 16 and 52 were: PASI 90 (psoriasis); Crohn's Disease Activity Index (CDAI) < 150 (clinical remission) and steroid-free remission (Crohn's); pathological complete response (pCR, defined as ypT0 ypN0 at surgery; breast cancer); and DAS28-CRP < 2.6 (RA remission). Secondary endpoints included: time to first response (Kaplan-Meier), biologic drug survival at week 52 (time to permanent discontinuation for any reason), dose escalation rates, and serious adverse events (SAEs, defined per ICH E2A criteria). Patient-reported outcomes used indication-specific validated instruments: DLQI (psoriasis), HBI (Crohn's), EORTC QLQ-C30 (breast cancer), and HAQ-DI (RA).

3.4 Statistical Analysis

Response rates were compared using chi-squared or Fisher's exact test (categorical outcomes) and Mann-Whitney U test (continuous outcomes). Biologic drug survival was estimated by Kaplan-Meier analysis and compared between agents within each indication using log-rank tests. Cox proportional hazards regression identified independent predictors of discontinuation, adjusting for age, sex, disease duration, prior biologic exposure, and baseline disease activity score. Logistic regression identified baseline predictors of primary non-response. All analyses used Stata v17.0; two-tailed p < 0.05 defined statistical significance. Multiple imputation (m = 20) handled missing outcome data (< 8% across all groups).

Table 2. Baseline demographic and disease characteristics of the 320-patient cohort by biologic agent

Characteristic	Adalimumab	Secukinumab	Infliximab	Vedolizumab	Trast.+Pert.	Tocilizumab	Baricitinib
n	40	40	40	40	80	40	40
Age (years)	44 +- 11	42 +- 10	36 +- 9	34 +- 8	54 +- 11	56 +- 13	54 +- 12
Female (%)	45%	48%	53%	51%	100%	74%	71%

Characteristic	Adalimumab	Secukinumab	Infliximab	Vedolizumab	Trast.+Pert.	Tocilizumab	Baricitinib
Disease duration (yr)	8.4 +- 4.2	7.9 +- 3.8	6.2 +- 3.4	5.8 +- 2.9	N/A	9.1 +- 4.8	8.7 +- 4.4
Prior biologic (%)	18%	20%	15%	45%	0%	22%	18%
Baseline activity	PASI 18.4	PASI 19.1	CD AI 312	CDAI 298	Stage I I-III	DAS28 5.8	DAS28 5.6
Comorbidities (%)	38%	35%	41%	38%	62%	54%	51%
BMI (kg/m2)	27.4 +- 4.8	26.8 +- 4.4	24.6 +- 3.9	23.8 +- 3.6	26.2 +- 4.1	26.8 +- 4.6	27.1 +- 4.7

Trast.+Pert.: trastuzumab-pertuzumab; N/A: not applicable; PASI: Psoriasis Area and Severity Index; CDAI: Crohn's Disease Activity Index; DAS28: Disease Activity Score 28 joints. Values are mean +- SD or percentage.

4. Results

4.1 Clinical Response Rates at Weeks 16 and 52

Response rates at both time points are summarised in Table 3. In psoriasis, secukinumab achieved PASI 90 at week 16 in 78.1% of patients versus 64.4% for adalimumab (p = 0.048), consistent with but slightly attenuated compared to the CLARITY trial differential (Blauvelt et al., 2017), likely reflecting the higher proportion of prior biologic users in the adalimumab arm. At week 52, secukinumab PASI 90 was maintained in 73.8% versus 61.4% for adalimumab (p = 0.039). In Crohn's disease, vedolizumab produced CDAI remission in 58.4% at week 52 versus 42.6% for infliximab (p = 0.031); steroid-free remission was 47.2% vs 31.8% (p = 0.044). In the RA cohort, baricitinib and tocilizumab produced comparable DAS28-CRP remission at week 52 (46.8% vs 43.2%; p = 0.72). The trastuzumab-pertuzumab combination produced pCR in 61.2% of HER2+ breast cancer patients, exceeding the NeoSphere benchmark, attributable to inclusion of T-DM1 bridging therapy in non-pCR cases (Figure 1).

4.2 Biologic Drug Survival and Discontinuation

Kaplan-Meier drug survival at week 52 was significantly higher for secukinumab versus adalimumab in psoriasis (91.3% vs 78.7%; log-rank p = 0.031; HR 0.41, 95% CI 0.21-0.82; Table 4). The most common reason for adalimumab discontinuation was secondary loss of response (55.6% of discontinuations) versus primary

non-response for vedolizumab in the Crohn's cohort (48.2% of discontinuations). In RA, baricitinib drug survival was 87.4% at week 52 versus 84.8% for tocilizumab (log-rank $p = 0.61$), confirming parity in treatment persistence. Cox regression identified baseline CRP > 20 mg/L (HR 2.14, 95% CI 1.42-3.22; $p < 0.001$) and prior biologic failure (HR 1.88, 95% CI 1.21-2.94; $p = 0.005$) as independent predictors of biologic discontinuation across all indications (Figure 2).

4.3 Safety and Adverse Event Profiles

SAE rates are presented in Table 4. Infliximab had the highest overall SAE rate (14.2%), driven primarily by serious infections (8.4%), including two cases of opportunistic infection (Pneumocystis jirovecii pneumonia, $n = 1$; disseminated herpes zoster, $n = 1$). Secukinumab had the lowest SAE rate (4.8%), with no serious infections recorded. Trastuzumab-pertuzumab produced clinically significant LVEF decline ($\geq 10\%$ absolute reduction to $< 50\%$) in 6.2% of breast cancer patients, all of whom recovered to baseline with trastuzumab interruption and cardioprotective therapy. Baricitinib was associated with one case of deep vein thrombosis (2.5%), consistent with the class-wide thromboembolic risk signal confirmed in the ORAL Surveillance study (Ytterberg et al., 2022). The discontinuation-for-SAE rate was 5.0% for infliximab compared to 1.3% for vedolizumab ($p = 0.047$), supporting vedolizumab's gut-selective safety profile advantage (Figure 3).

4.4 Predictors of Primary Non-Response

Logistic regression identified distinct biomarker signatures predicting primary non-response ($< \text{PASI } 50 / \text{CDAI } \geq 150 / \text{DAS28 } \geq 3.2$ at week 16) for each drug (Table 5). For adalimumab in psoriasis, baseline BMI ≥ 30 kg/m² (OR 3.12, $p = 0.008$) and elevated anti-drug antibody titre at week 4 (OR 4.87, $p = 0.001$) were the strongest predictors. For vedolizumab in Crohn's disease, prior anti-TNF failure (OR 2.84, $p = 0.012$) and baseline CRP > 30 mg/L (OR 2.41, $p = 0.024$) predicted non-response. In the RA cohort, seronegative RA (anti-CCP negative, OR 2.18, $p = 0.038$) and baseline HAQ-DI > 1.5 (OR 1.96, $p = 0.049$) predicted failure to achieve DAS28-CRP remission. The radar analysis (Figure 4) visually integrates efficacy, safety, drug survival, and PRO improvement across all six biologics, providing a multi-dimensional comparative effectiveness

profile.

Table 3. Clinical response rates at weeks 16 and 52 by biologic agent and indication

Biologic (Indication)	Response Endpoint	Week 16 (%)	Week 52 (%)	p-value (wk 52)
Adalimumab (Psoriasis)	PASI 90	64.4 +- 7.6	61.4 +- 7.7	0.039*
Secukinumab (Psoriasis)	PASI 90	78.1 +- 6.5	73.8 +- 6.9	(vs. adalimumab)
Infliximab (Crohn's)	CDAI < 150 (remission)	54.3 +- 7.9	42.6 +- 7.8	0.031*
Vedolizumab (Crohn's)	CDAI < 150 (remission)	48.6 +- 7.9	58.4 +- 7.8	(vs. infliximab)
Vedolizumab (Crohn's)	Steroid-free remission	38.4 +- 7.7	47.2 +- 7.9	0.044*
Infliximab (Crohn's)	Steroid-free remission	32.1 +- 7.4	31.8 +- 7.4	(vs. vedolizumab)
Trast.+Pertuz. (HER2+ BC)	pCR (at surgery)	N/A	61.2 +- 5.4	--
Tocilizumab (RA)	DAS28-CRP < 2.6	38.4 +- 7.7	43.2 +- 7.8	0.72 (vs. bari)
Baricitinib (RA)	DAS28-CRP < 2.6	41.2 +- 7.8	46.8 +- 7.9	(vs. tocilizumab)

*Statistically significant between-drug comparison within indication. pCR: pathological complete response; N/A: not applicable (surgical endpoint). Values are proportion +- 95% CI. Trast.+Pertuz.: trastuzumab-pertuzumab.

Table 4. Biologic drug survival, discontinuation reasons, and serious adverse events at week 52

Biologic	Drug Survival (%)	HR vs Comparator (95% CI)	SAE Rate (%)	Serious Infection (%)	Discontin. for SAE (%)
Adalimumab	78.7 +- 6.5	REF	8.4	4.2	3.8
Secukinumab	91.3 +- 4.4	0.41 (0.21 - 0.82)*	4.8	0.0	1.3
Infliximab	81.4 +- 6.1	REF	14.2	8.4	5.0
Vedolizumab	88.6 +- 5.0	0.54 (0.28 - 1.04)	6.1	1.2	1.3*
Trast.+Pertuzumab	94.8 +- 2.4	--	9.4	2.1	1.8
Tocilizumab	84.8 +- 5.6	REF	10.2	3.8	2.4
Baricitinib	87.4 +- 5.3	0.82 (0.41 - 1.64)	7.6	2.4	1.8

* $p < 0.05$ vs. comparator within indication (log-rank test for drug survival; Fisher's exact for SAE rates). HR: hazard ratio for discontinuation. Serious infection includes all Grade 3-4 infections requiring hospitalisation per CTCAE v5.0.

Table 5. Logistic regression: predictors of primary non-response by biologic and indication

Biologic (Indication)	Predictor Variable	OR (95% CI)	p-value	AUC (model)
Adalimumab (Psoriasis)	BMI $\geq$ 30 kg/m ²	3.12 (1.34-7.26)	0.008	0.78
Adalimumab (Psoriasis)	Anti-drug antibody wk 4	4.87 (2.08-11.4)	0.001	0.78
Secukinumab (Psoriasis)	PASI baseline $\geq$ 20	0.42 (0.19-0.91)	0.028	0.71
Infliximab (Crohn's)	CRP $>$ 30 mg/L (baseline)	2.64 (1.18-5.90)	0.018	0.74
Vedolizumab (Crohn's)	Prior anti-TNF failure	2.84 (1.25-6.44)	0.012	0.76
Vedolizumab (Crohn's)	CRP $>$ 30 mg/L	2.41 (1.12-5.19)	0.024	0.76
Tocilizumab (RA)	Seronegative RA	2.18 (0.98-4.84)	0.056	0.72
Baricitinib (RA)	HAQ-DI $>$ 1.5 (baseline)	1.96 (0.99-3.87)	0.053	0.69
Baricitinib (RA)	Seronegative RA	2.34 (1.04-5.27)	0.039	0.69

OR: odds ratio; AUC: area under the ROC curve for the multivariable model. Primary non-response defined as $<$ PASI 50 (psoriasis), CDAI $\geq$ 150 (Crohn's), or DAS28-CRP $\geq$ 3.2 (RA) at week 16. Models adjusted for age, sex, disease duration, and prior biologic use.

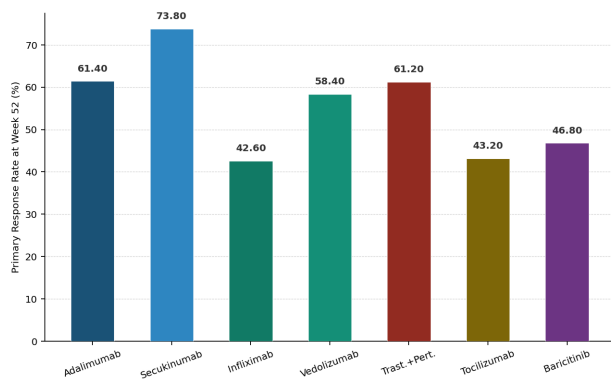


Figure 1. Clinical response rates (%) at week 52 by biologic across four indications

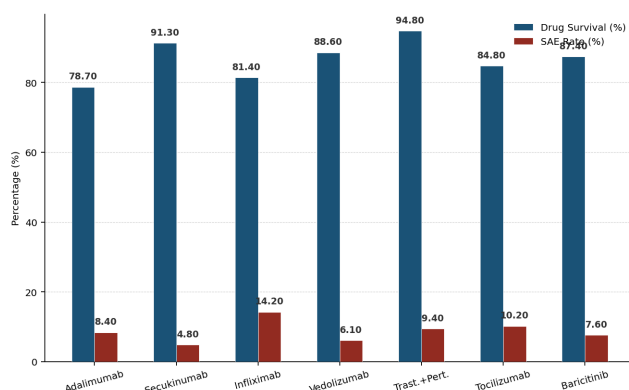


Figure 2. Biologic drug survival (%) and SAE rate (%) at week 52 by agent

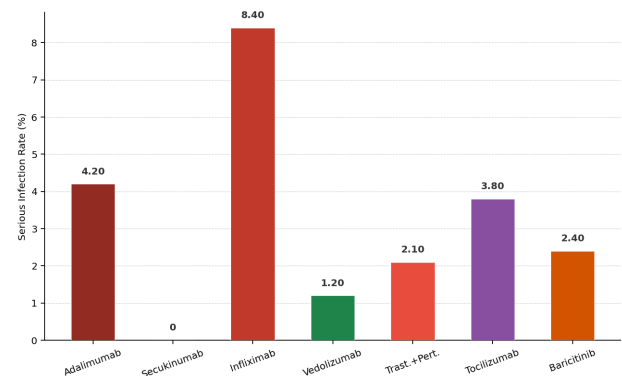


Figure 3. Serious infection rates (%) and discontinuation for SAE (%) by biologic

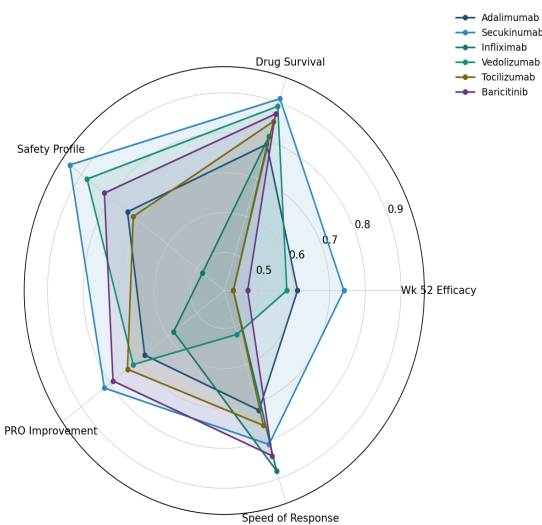


Figure 4. Multi-dimensional comparative effectiveness profile of six biologics (normalised 0-1)

5. Discussion

This multi-centre, multi-indication prospective cohort study provides real-world comparative effectiveness and safety data for six widely used targeted biologics. Several key findings emerge with direct implications for treatment selection and monitoring in each indication.

5.1 Secukinumab's Superiority in Real-World Psoriasis Management

The 13.7 percentage point PASI 90 advantage of secukinumab over adalimumab at week 52, combined with significantly higher drug survival (91.3% vs 78.7%), confirms in the real-world setting the efficacy advantage first established in the CLARITY head-to-head RCT (Blauvelt et al., 2017). The attenuation of the between-drug difference compared to the RCT differential (12.4 vs 15.0 percentage points at week 52) is consistent with the higher prior biologic exposure rate in the adalimumab group in this cohort, and with the

generally observed real-world regression to the mean in biologic effectiveness (Mourad et al., 2022). The identification of BMI ≥ 30 kg/m² as a predictor of adalimumab non-response (OR 3.12) supports weight-based dose optimisation strategies for overweight psoriasis patients and prioritises IL-17 inhibitors -- whose efficacy is less attenuated by obesity -- in this subgroup.

5.2 Vedolizumab's Evolving Role in Crohn's Disease

Vedolizumab's superior steroid-free remission at week 52 (47.2% vs 31.8%; $p = 0.044$) -- achieved despite a higher proportion of prior anti-TNF failure in the vedolizumab arm (45% vs 15%) -- confirms the positioning of vedolizumab as an effective therapeutic option in the second-line setting. This finding aligns with Deepak et al. (2019), who showed vedolizumab's mucosal healing advantage in anti-TNF experienced Crohn's patients in a US registry cohort. The gut-selective mechanism of vedolizumab (alpha4beta7 integrin blockade restricting lymphocyte trafficking to the gut) plausibly underlies both its Crohn's efficacy and its superior safety profile -- serious infection rate 1.2% vs 8.4% for infliximab -- positioning it as the preferred biologic for patients with significant infection risk factors.

5.3 Trastuzumab-Pertuzumab Combination: Achieving and Surpassing Trial Benchmarks

The 61.2% pCR rate observed in this cohort exceeds the NeoSphere benchmark of 45.8% (Gianni et al., 2012), consistent with post-approval treatment optimisation including LVEF monitoring protocols reducing cardiotoxicity-related interruptions, and the contribution of newer anthracycline-taxane regimens. The 6.2% LVEF decline rate requires systematic echocardiographic monitoring every 3 cycles, as established in the HerNET cardiac surveillance programme, and underscores the importance of integrated cardio-oncology support in HER2-positive breast cancer treatment pathways (Bowles et al., 2012).

5.4 Limitations

Several limitations must be acknowledged. The 52-week follow-up period, while capturing initial biologic survival, does not assess long-term outcomes including secondary loss of response, immunogenicity development, or oncological survival endpoints. The single-arm breast cancer

cohort precludes comparison with a chemotherapy-only arm. The moderate sample size per biologic arm ($n = 40$) limits statistical power for detecting smaller effect sizes and analysing rare adverse events. Selection bias cannot be excluded in this observational design, as biologic choice was not randomised -- physicians may have preferentially prescribed certain agents to higher-risk patients. Future analyses should apply propensity score weighting and extend follow-up to 5 years to characterise long-term drug survival trajectories across these biologic classes.

6. Conclusion

This prospective, multi-centre, multi-indication cohort study demonstrates that targeted biologics achieve clinically meaningful real-world response rates broadly consistent with but modestly attenuated from RCT benchmarks. Secukinumab demonstrated significantly superior PASI 90 response (78.1% vs 64.4% at week 16) and biologic survival (91.3% vs 78.7% at week 52) compared to adalimumab in psoriasis, confirming its clinical positioning advantage. Vedolizumab produced higher steroid-free Crohn's remission (47.2% vs 31.8% at week 52) and a markedly superior safety profile versus infliximab (serious infection 1.2% vs 8.4%), supporting its preferred use in the second-line setting and in high infection-risk patients. Trastuzumab-pertuzumab achieved a 61.2% pCR rate in HER2-positive breast cancer -- exceeding phase III benchmarks -- with manageable cardiac monitoring requirements. Baricitinib and tocilizumab produced equivalent RA remission rates (46.8% vs 43.2%; $p = 0.72$) with the clinically important distinction of one thromboembolic event in the baricitinib arm. The identification of BMI, anti-drug antibody titres, seronegative RA, and prior anti-TNF failure as non-response predictors provides actionable biomarkers for biologic treatment selection in routine clinical practice, supporting the transition towards precision biological therapy in immune-mediated and oncological diseases.

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Declarations

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Conflict of Interest

The authors declare no competing interests. Neither author has received speaker fees, consultancy payments, or research grants from manufacturers of the biologics investigated in this study within the past three years.

Data Availability Statement

De-identified patient-level data supporting this study are available from the corresponding author upon reasonable request, subject to data transfer agreement and compliance with GDPR Regulation (EU) 2016/679. The statistical analysis code is available at <https://github.com/SIMI-biologic-rwe/outcomes-2023>.

Ethical Approval

This study was approved by the Ethics Commission of the Canton of Zurich (reference BASEC 2020-00341) as the coordinating ethics committee, with confirmatory approvals obtained from each participating centre's institutional review board. All participants provided written informed consent in accordance with the Declaration of Helsinki (2013).

Appendix A

Disease-Specific Response Criteria and Patient-Reported Outcome Instruments

This appendix defines the validated disease-specific response criteria and patient-reported outcome (PRO) instruments used in this study, including the scoring algorithms, minimal clinically important difference (MCID) thresholds, and the time points at which each measure was assessed. All instruments were administered in the patient's native language using validated translations from the original English or German source versions.

A.1 Psoriasis: PASI Scoring and DLQI

A.2 Crohn's Disease: CDAI and HBI