Supplementary Material – Supplementary File S1

Title

Immunobiological therapy in moderate to severe psoriasis: A retrospective cohort study investigating the effects of inadequate therapeutic compliance on drug survival

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Supplementary File: S1 – Study Protocol

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Observational Study Protocol IM011-1306

IMMUNOBIOLOGICAL TREATMENT IN MODERATE TO SEVERE PSORIASIS: A RETROSPECTIVE COHORT STUDY TO INVESTIGATE INADEQUATE THERAPEUTIC COMPLIANCE EFFECTS ON DRUG SURVIVAL

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DOCUMENT HISTORY

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Original Protocol	29-JUL-2025	Not Applicable

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SYNOPSIS

Observational Study Protocol IM011-1306

Protocol Title: Immunobiological treatment in moderate to severe psoriasis: a retrospective cohort study to investigate inadequate therapeutic compliance effects on drug survival

Department: Medical Affairs

Objective(s):

Primary Objective: To test whether distribution problems, low adherence, and inadequate storage of immunobiologicals are important risk factors for a lower drug survival in the therapy of moderate to severe psoriasis

Secondary Objective: To analyze the specific reasons for discontinuation of the immunobiologicals in a subgroup analysis, including treatment failure, adverse events, or low-adherence

Study Design: Anonymized study data will be acquired from a real-life ongoing registry for the institutional follow-up of patients with psoriasis (Registry Name: *Doenças autoimunes na vida real no Brasil: um estudo de coorte multicêntrico com base na avaliação da epidemiologia clínica e molecular* (Autoimmune Diseases in Real Life in Brazil); Registry number: CAAE: 68068323.3.1001.5558). Additionally, this registry contains a comprehensive questionnaire that assesses patient adherence to all storage and administration recommendations for immunobiologicals as per label instructions, including questions related to the delivery of the medications (distance and time), transport during travel, and inadequate cooling of the medications. This registry complies with all current legislation, has institutional research ethics committee approval, and the collected data is only entered after the informed consent form was previously signed. The registry will be accessed, after anonymization, 4 times by our study team at intervals of 2 months between each access or until the desired sample size is reached. Since this protocol consists solely of accessing previously approved and ongoing registry data, no patients will be directly included or accessed for this study. The included longitudinal data will be analysed using a retrospective cohort methodology, where groups will be divided based on the main risk factor, which consists of the correct or incorrect use of injectable immunobiologicals (distribution problems, low adherence, or inadequate storage of injectable immunobiologicals). The primary outcome will be drug survival, measured by the time until discontinuation or continuation of the immunobiologicals in use or previously used.

Study Population:

The study will include patients with moderate-to-severe psoriasis (PASI or DLQI >10) who initiated immunobiological treatment prior to June 2025 and are followed in the Specialized Psoriasis Ambulatory, University of Brasília, Brasília, Brazil.

Inclusion Criteria:

- Diagnosed with PsO by a dermatologist
- Previous informed consent form signed for participation in the registry (Registry number: CAAE: 68068323.3.1001.5558).

- Started on or switched to an eligible systemic PsO treatment at enrollment or within the previous 12 months of the date of enrollment (Eligible medications: adalimumab, adalimumab biosimilar, infliximab, infliximab biosimilar, ustekinumab, risankizumab, secukinumab, guselkumab, brodalumab, bimekizumab, certolizumab pegol)

Exclusion Criteria:

- Participating in or planning to participate in an interventional clinical trial with a nonmarketed or marketed investigational drug (i.e., phase I-IV drug trial)

Data Collection Methods: Anonymized registry data comprising of a comprehensive questionnaire administered to patients during specialized clinical consultations will be included. The questionnaire will assess patient adherence to storage and administration recommendations for immunobiologicals, as well as questions related to medication delivery, transport, and cooling.

Data Analyses: Unadjusted relative risks (RRs) and hazard ratios (HRs) will be calculated, and log-rank tests and survival evaluations by the Kaplan-Meier method will be performed to assess the relationship of the main risk factors with the main outcome. For the main risk factors, a multivariate model using a Cox proportional hazards model will be conducted. The Cox proportional hazards model will be adjusted using covariates, demographic data and clinical data. Variables deemed clinically relevant by the study's team of specialists will be selected following an analysis of unadjusted data. For all covariates, a post hoc exploratory strategy will be used. Statistical significance will be defined by a p-value <0.05 and an appropriate 95% confidence interval (CI). Statistical analysis was performed via the survival and survminer packages in R version 4.4.2 (R Core Team (2021); R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria; URL https://www.R-project.org/).

Sample Size/Power: The study is based on the assumption that 25% of patients who followed immunobiological therapeutic procedures correctly will have to stop the medication, while 50% of patients who did not follow them correctly will have to stop the drug in five years. To achieve a 1-alpha = 95 and a power of 80%, 66 patients in each group (those who discontinued the last biologic drug and those who are still using it) are needed for this analysis.

Limitations/Strengths: Like all observational studies, this work may suffer from confounders that will be addressed through adjusted analysis. Due to the detailed nature of the questionnaire, some data may be missing, resulting in incompleteness. This is an innovative research question, and the retrospective longitudinal methodology can associate therapeutic habits and social problems with the outcome of advanced psoriasis treatment..

1 INTRODUCTION

1.1 Background and Study Rationale

Psoriasis (PsO) is a common, chronic, noncommunicable skin disease with no clear cause or cure [1]. The most common type, plaque PsO, is characterized by raised red lesions with silvery scales; additional symptoms include rash, erythema, itch, flacking, burning, bleeding, skin pain, joint pain, and fatigue [1]. PsO lesions are most commonly located in the knees, elbows, scalp, and lumbosacral region, with nail involvement also common [2]. PsO affecting the scalp, face, genitals, nails, and palms of the hand or feet is often difficult to treat, and further, patients with PsO in these special areas are disproportionately affected by physical impairment and emotional distress [3]

PsO is associated with significant comorbidities, including arthritis, cardiovascular disease (CVD), diabetes, obesity, and depression [1]; [4]. In addition, up to a third of patients with PsO also have psoriatic arthritis (PsA), which can involve the musculoskeletal system, nails, eyes, and gut [1]; [5]. While PsA can lead to disfigurement and disability, PsO also confers a significant patient burden, as physical, mental, and social well-being may all be impacted [1].

Access to adequate psoriasis treatment has been studied through extensive registries conducted in North America and Europe.[6-12] The Global South is populated by developing countries with large populations and notable social inequalities. The impact and access to high-performance medications in these populations, especially the most vulnerable, remain uncertain.[13] Brazil is South America's biggest country with over 215 million people and the prevalence of PsO has been estimated to be 1,3% [14,15]. It has one of the largest health systems called the Brazilian Unified Health System (SUS), which mainly combines the public sector with health insurance and private healthcare [16]. Since 2020, the Brazilian Ministry of Health has offered all patients with moderate to severe psoriasis, who cannot use systemic treatments, the option of using four kinds of immunobiologicals: Adalimumab (1st line), Ustekinumab, Secukinumab, and Rizankizumab (2nd line) [17]. However, recent national surveys have shown a lower drug survival rate of immunobiologicals for psoriasis than international data [18,19]. Other drugs such as infliximab, infliximab biosimilar, guselkumab, brodalumab, bimekizumab, and certolizumab pegol are only available for patients with private health insurance, which constitutes about 25% of the Brazilian population [17].

The Brazilian SUS is known as one of the largest purchasers of health supplies globally [14,15] . This includes immunobiological medications and other immunosuppressants. The system's goal is to provide health services to the entire population of Brazil, which consists of over 200 million people [14,15] . While the system is decentralized across municipalities, it ensures centralized

distribution of critical inputs, especially high-cost medications. This adherence results in reduced prices, making the system economically sustainable [14,15] .

The centralized supply chain is responsible for distributing biologics for treating psoriasis [17]. While centralization brings advantages, it can also jeopardize important aspects of the system, such as pharmacovigilance. For subcutaneous biologics, many barriers contribute to reduced drug survival in psoriasis treatment. These barriers include distribution issues, low adherence, and poor compliance with proper storage and use of the drugs, as most patients receive medications via syringes at home.[20-22], This research will provide insights as to whether these socioeconomics barriers lead to a poor prognostic outcome related to biologics drug-survival.

1.2 Research Question

Do distribution problems, low adherence, and inadequate storage of injectable immunobiologicals reduce drug survival in the therapy of psoriasis?.

2 OBJECTIVES

2.1 Primary Objective

To test whether distribution problems, low adherence, and inadequate storage of immunobiologicals are important risk factors for a lower drug survival in the therapy of moderate to severe psoriasis

2.2 Secondary Objective:

To analyze the specific reasons for discontinuation of the drug in a subgroup analysis, including treatment failure (PASI ≥10 or DLQI ≥ 10 or BSA ≥ 10), adverse events, or low-adherence.

3 STUDY DESIGN

3.1 Overview of Study Design

This is a retrospective cohort study. The registry of patients with moderate to severe psoriasis (PASI or DLQI >10) recruited at the Specialised Psoriasis Ambulatory, University of Brasília, Brasília, Brazil will be assessed. A comprehensive questionnaire was previously included in the registry to assess the patient's adherence to all recommendations of storage and administration

of immunobiologicals as per label instructions. Questions related to the delivery of the medications (including distance and time), transport during travel, and inadequate cooling of the medications will also be included.

3.2 Study Population

The study population includes adult patients diagnosed with severe plaque psoriasis (PASI > 10) who initiated immunobiological treatment before May 2025 and are included in a real-life ongoing registry for the institutional follow-up of patients with psoriasis (Registry Name: *Doenças autoimunes na vida real no Brasil: um estudo de coorte multicêntrico com base na avaliação da epidemiologia clínica e molecular* (Autoimmune Diseases in Real Life in Brazil); Registry number: CAAE: 68068323.3.1001.5558). Additionally, this registry contains a comprehensive questionnaire that assesses patient adherence to all storage and administration recommendations for immunobiologicals as per label instructions, including questions related to the delivery of the medications (distance and time), transport during travel, and inadequate cooling of the medications. This registry complies with all current legislation, has institutional research ethics committee approval, and the collected data is only entered after the informed consent form was previously signed. The registry will be accessed, after anonymization, 4 times by our study team at intervals of 2 months between each access or until the desired sample size is reached. Since this protocol consists solely of accessing previously approved and ongoing registry data, no patients will be directly included or accessed for this study.

3.2.1 Inclusion Criteria

The patient must:

- Have been diagnosed with PsO by a dermatologist;
- Have a previous informed consent form signed for participation in the registry (Registry number: CAAE: 68068323.3.1001.5558).
- Started on or switched to an eligible systemic PsO treatment at enrollment or within the previous 12 months of the date of enrollment (Eligible medications: adalimumab, adalimumab biosimilar, infliximab, infliximab biosimilar, ustekinumab, risankizumab, secukinumab, guselkumab, brodalumab, bimekizumab, certolizumab pegol).

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3.2.2 Exclusion Criteria

Patient is participating in or planning to participate in an interventional clinical trial with a nonmarketed or marketed investigational drug (i.e., phase I-IV drug trial).

3.3 Data Source/Data Collection Process

The study data will be collected from a longitudinal national registry database titled: Autoimmune Diseases in Real Life in Brazil: a Multicenter Cohort Study Based on the Evaluation of Clinical and Molecular Epidemiology, (Registry Name: *Doenças autoimunes na vida real no Brasil: um estudo de coorte multicêntrico com base na avaliação da epidemiologia clínica e molecular* (Autoimmune Diseases in Real Life in Brazil); Registry number: CAAE: 68068323.3.1001.5558). approved by the national research ethics regulatory body, the National Research Ethics Commission (CONEP).

3.4 Definitions of Study Variables

3.4.1 Outcomes/Endpoint Variables

Primary endpoint:

Drug survival – Biologic treatment interruption (yes/no)

Secondary endpoints:

PASI > 10 classification after biologic therapy, DLQI > 10 classification after biologic therapy, BSA >10 classification after biologic therapy, occurrence of any adverse event or serious adverse event after biologic therapy, occurrence of any severe adverse event after biologic therapy (only events that led to treatment discontinuation), occurrence of any infection after biologic therapy, occurrence of any MACE after biologic therapy, occurrence of any infusion reaction after biologic therapy.

3.4.2 Main Risk Factors (Exposure/Independent Variables of Interest)

Three key variables were selected to accurately represent the occurrence of distribution problems, low adherence, and inadequate storage as main risk factors respectively:

Distribution problems:

Have you experienced any delays in the delivery of your medication (Yes/No).

Low adherence:

Are you taking your biological on the exact date your doctor prescribed them? (Yes/No).

Inadequate storage:

Do you store your biological product exactly as instructed in the package insert? (Yes/No).

Covariates

Distribution problems:

Is your medication delivered directly to your house, or you receive/apply your medication in a reference center of hospital? (Yes/No), When receiving your medication, have you ever noticed any tampering with the seal or packaging? (Yes/No), Has the type of medication you use been changed without your doctor's knowledge (switched to biosimilars)? (Yes/No), When receiving your medication, have you noticed that it was not transported at the correct temperature? (Yes/No), Has your medication delivered to your home ever been received by third parties when you were not present? (Yes/No), Have you ever received your medication at room temperature, without refrigeration? (Yes/No), Has your medication ever been out of stock, causing a delay in delivery? (Yes/No).

Low adherence:

Do you feel uncomfortable using an injection frequently? (Yes/No), Are you able to personally administer your immunobiological when necessary? (Yes/No), Do you feel dizzy, lightheaded, or unwell when seeing or administering an injection? (Yes/No), Do you feel comfortable in being assisted by a non-healthcare professional in administering your biological medication? (Yes/No),

Do you feel comfortable only with the help of a healthcare professional in administering your biological medication? (Yes/No), Do you properly clean the injection site when administering your biological medication? (Yes/No), Have you ever accidentally pricked yourself while administering your biological medication? (Yes/No), Have you ever discarded the needle from your immunobiological in regular trash? (Yes/No), Have you been properly instructed by a healthcare professional on how to administer your immunobiological? (Yes/No), Have you been properly instructed on the correct disposal of the needle from your immunobiological? (Yes/No), Do you have difficulty renewing the prescription for your immunobiological? (Yes/No).

Inadequate storage:

Do you receive your biological medication at home or go to a clinic for supervised administration? (Home or supervised administration)? Have you always stored your immunobiologicals as recommended? (Yes/No), What is the maximum time you have left your immunobiological out of the refrigerator? (Yes/No), Have you ever stored your immunobiological in the refrigerator door? (Yes/No), During the transport of your immunobiological, has it ever lost cooling and stayed at room temperature? (Yes/No), How many times in the last month has there been a power outage at your home? (Numeric), Do you live on land not regulated by housing regulatory agencies? (Yes/No), Have you ever transported your immunobiological on your car's dashboard? (Yes/No), Have you ever forgotten your immunobiological in your car for more than an hour? (Yes/No), Have you ever had any problems with infusion clinics? (Yes/No), Have you ever lost your immunobiological due to a power outage? (Yes/No), Does your residential area frequently experience power outages? (Yes/No), Have you ever shared your biological medication with someone else or received a donation from another patient? (Yes/No).

Demographic data:

Sex, age, geographical area of residence, comorbidities, smoking habit, alcohol comsumption.

Clinical data:

Type of psoriasis, psoriasis severity (PASI, BSA, DLQI, NAPSI), presence of scalp lesions, presence of nail lesions, presence of genital lesions, association with PsA, immunobiologics in use.

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4 DATA MANAGEMENT

Data from the real-world registry and collected during a clinical interview will be recorded in electronic forms such as restricted RedCap or Google Forms, processed, and tabulated in analysis spreadsheets with xls, CSV, or CSV2 files.

5 STATISTICAL ANALYSIS

5.1 Statistical Analysis Methods

Approach to Variable Transformation for Statistical Analysis

The main risk factors—distribution problems, low adherence, and inadequate storage—previously identified in the protocol as the three primary concerns, will be operationalized as dichotomous variables, indicating the presence or absence of each factor (yes/no).

The covariates previously identified in this protocol—those related to distribution problems, low adherence, inadequate storage, as well as demographic and clinical data—will be plotted and adapted for analysis as follows:

Key Exposure-Related Covariates

(Additional questions addressing distribution problems, low adherence, and inadequate storage):

Medication delivery method (home vs. clinic). History of delivery issues, including delays, temperature deviations, drug substitutions (e.g., biosimilars), stock-outs. Adherence-related behaviors, such as difficulty with injection, need for assistance, site cleaning practices, and disposal methods. Storage-related behaviors, including refrigerator use, power outages, and improper transport or storage conditions

Demographic Covariates:

Age (continuous; potential non-linear effects). Sex. Geographical area of residence (urban/rural or regional classification). Socioeconomic status (if available; often proxied by education level). Smoking status (yes/no/current). Alcohol consumption (yes/no or frequency-based)

Clinical Covariates:

Psoriasis severity scores (PASI, BSA, DLQI). Presence of specific lesion sites (scalp, nails, genital area – yes/no). Presence of psoriatic arthritis (PsA). Comorbidities (e.g., cardiovascular disease, diabetes, obesity, depression). Type of immunobiologic in use (categorical: e.g., TNF inhibitor, IL-23 inhibitor). Duration of disease prior to biologic initiation.

Treatment and System-Related Covariates:

Number of previous biologics used (biologic-naïve vs. experienced). Mode of drug administration (self-injection vs. healthcare professional-administered). Class of biologics used. Distance to healthcare center (if available). Health insurance status (public vs. private, when relevant to access). Year of treatment initiation (to account for temporal trends in clinical practice or drug availability)

Descriptive and unadjusted analysis

The frequency of occurrences of the collected variables (main risk factors and covariates) will be addressed descriptively. Measures of central tendency and dispersion will be evaluated for numerical variables. Unadjusted relative risks (RRs) and hazard ratios (HRs) will be calculated, and log-rank tests and survival evaluations by the Kaplan-Meier method will be performed to assess the relationship of the main risk factors with the main outcome. For all covariates, a post hoc exploratory strategy will be used.

Multivariate adjusted model

For the main risk factors, a multivariate model using a Cox proportional hazards model will be conducted. The Cox proportional hazards model will be adjusted using covariates, demographic data and clinical data. Variables deemed clinically relevant by the study's team of specialists will be selected following an analysis of unadjusted data.

Experts agreed to develop a hierarchical model composed of three blocks. Variables reaching a univariate statistical threshold of $p < 0.1000$ would be carried forward to the next block for adjusted analysis. The variables included in the three hierarchical blocks were selected by the experts in ascending order of relevance and were distributed as follows:

- **Block 1: Demographic and Clinical Covariates** – Age, sex, PASI score
- **Block 2: Therapeutic Covariates** – Number of previous biologics used (biologic-naïve vs. experienced), Class of biologics used (ANTI-TNF, ANTI-IL17, ANTI-IL12/23, or ANTI-IL23), Mode of drug administration (self-injection vs. healthcare professional-administered)
- **Block 3: Main Risk Factors** – Distribution problems (yes/no), low adherence (yes/no), and inadequate storage (yes/no)"

Statistical significance will be defined by a p-value <0.05 and an appropriate 95% confidence interval (CI). Statistical analysis was performed via the survival and survminer packages in R version 4.4.2 (R Core Team (2021); R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria; URL https://www.R-project.org/).

5.1.1 Analysis Plan for Primary Objective

For the main outcome and risk factors, unadjusted relative risks (RRs) and hazard ratios (HRs) will be calculated, and log-rank tests and survival evaluations by the Kaplan-Meier method will be performed. Statistical significance will be defined by a p-value <0.05 and an appropriate 95% confidence interval (CI). For the main risk factors, a multivariate model using a Cox proportional hazards model will also be conducted.

5.1.2 Analysis Plan for Secondary Objectives

For secondary outcomes and covariates, unadjusted relative risks (RRs) and hazard ratios (HRs) will be calculated, and log-rank tests and survival evaluations by the Kaplan-Meier method will be performed. Statistical significance will be defined by a p-value <0.05 and an appropriate 95% confidence interval (CI).

5.2 Power/Sample Size

Previous survival data for the drugs are highly variable, reaching up to 95% at 5 years for IL-23 inhibitors and less than 50% for TNF inhibitors.[23,24,25,26,27,28,29,30] In addition to the much superior effectiveness of IL-23 inhibitors, the team of specialists assessed that the main anti-TNF used in Brazil has a less convenient and more frequent dosage, which may affect drug survival, not only biologically but also in terms of patient compliance. For this reason, the specialists responsible for this protocol defined arbitrary survival values for the evaluation of the outcome. Sample size calculation was based on the assumption that 25% of patients who followed

immunobiological therapeutic procedures correctly will have to stop the medication, while 50% of patients who did not follow them correctly will have to stop the drug in five years. To achieve a 1-alpha = 95 and a power of 80%, 66 patients in each group (those who discontinued the last biologic drug and those who are still using it) are needed for this analysis. A minimum increase of 20% will be anticipated to avoid the detrimental effects of losses.

6 STUDY LIMITATIONS/STRENGTHS

Like all observational studies, this work may suffer from confounders that will be addressed through adjusted analysis. Due to the detailed nature of the questionnaire, some data may be missing, resulting in incompleteness. This is an innovative research question, and the retrospective longitudinal methodology can associate therapeutic habits and social problems with the outcome of advanced psoriasis treatment.

7 PROTECTION OF STUDY PARTICIPANTS

This study will be conducted in accordance with International Society for Pharmacoepidemiology (ISPE) Guidelines for Good Pharmacoepidemiology Practices (GPP) and applicable regulatory requirements. All data, once collected, will be anonymized to ensure confidentiality.

7.1 Ethics Committee Review and Informed Consent

This study does not require review and approval by an Ethics Committees or informed consent. The study data will be collected from a longitudinal national registry database titled: Autoimmune Diseases in Real Life in Brazil: a Multicenter Cohort Study Based on the Evaluation of Clinical and Molecular Epidemiology, approved by the national research ethics regulatory body, the National Research Ethics Commission (CONEP), under protocol number: CAAE: 68068323.3.1001.5558.

7.1.1 Ethics Committee Review

To comply with local regulations, this study will obtain all necessary approvals from Ethics Committees, Independent Review Committees, Regulatory Authorities, and/or other local governance bodies prior to beginning the research, as applicable.

7.1.2 Informed Consent

This registry complies with all current legislation, has institutional research ethics committee approval, and the collected data is only entered after the informed consent form is signed. The real-world registration is approved by the research ethics committee of the Faculty of Medicine at the University of Brasília (UnB) under the registration number CAAE: 68068323.3.1001.5558.

7.2 Confidentiality of Study Data

This study uses anonymized data, ensuring the privacy of data. No personally identifying data will be included in the database used for this study.

8 STUDY CONDUCT

8.1 Responsibilities within the Study

The study shall be conducted as described in this approved protocol. All revisions to the protocol must be approved by BMS.

8.1.1 Sponsor Roles and Responsibilities

BMS employees will be responsible of reviewing and approving the protocol, reviewing the results, manuscripts and further approvals.

8.1.2 CRO Roles and Responsibilities

IDEPEA will be responsible for ensuring protocol development storage and maintenance of the dataset, data collection, data analysis, results reporting, and manuscript writing.

8.1.3 External Investigator/External Advisory/Steering Committee Roles and Responsibilities

Provide insight into the study design, conduct and interpretation of data, defining publication strategy.

8.2 Quality Control

Procedures for the careful and complete collection of data will be implemented by IDEPEA, including consistency checks, format checks, cross-referencing, error correction, duplicate removal and standardization.

CRO and investigators will collect data which may be reviewed by the study team throughout the data collection process and after data collection.

BMS and study director can assess anonymized data.

All documents will be labelled, version-controlled, and restricted via administrator control and be held separately from any personally identifiable information. Upon completion of data collection, IDEPEA will provide BMS with a clean, fully documented set of the data collected via the registry through a secure SharePoint site. IDEPEA will be responsible for all data management and statistical analyses.

8.3 Database Retention and Archiving of Study Documents

IDEPEA must retain all study records and source documents for the maximum period required by applicable regulations and guidelines, or organization procedures, or for the period specified by the sponsor, whichever is longer. IDEPEA must contact BMS prior to destroying any records associated with the study. Location of database and supporting documentation will be outlined in the final observational study report.

8.4 Registration of Study on Public Website

This study will be registered on Plataforma Brasil and/OR The Brazilian Registry of Clinical Trials (ReBEC).

9 ADVERSE EVENT REPORTING

This study is not designed to capture data on participants taking a BMS product and therefore, AE collection and reporting is not required as part of the study. However, healthcare professionals should follow local requirements for product(s) in consideration for safety reporting (spontaneous).

10 GLOSSARY OF TERMS AND LIST OF ABBREVIATIONS

10.1 List of Abbreviations

Term	Definition
AE	Adverse event
BSA	Body surface area
CI	Confidence interval
CL	Conditional logit
CVD	Cardiovascular disease
DCE	Discrete choice experiment

DLQI	Dermatology Life Quality Index
GPP	Good Pharmacoepidemiology
IEC	Independent Ethics Committee
HR	Hazard ratio
IL	Interleukin
ISPE	International Society for Pharmacoepidemiology
MACE	Major Adverse Cardiovascular Event
MNL	Multinomial logit
NAPSI	Nail Psoriasis Severity Index
PASI	Psoriasis Area and Severity Index
PGA	Physician's Global Assessment
PsA	Psoriatic arthritis
PsO	Psoriasis
RR	Relative Risk
SAE	Serious adverse event
SAP	Statistical analysis plan
SUS	Brazilian Unified Health System
TNFi	Tumor Necrosis Factor inhibitors

11 SCIENTIFIC PUBLICATIONS

Scientific Publications (such as abstracts, congress podium presentations and posters, and manuscripts) of the study results will be a collaborative effort between the study Sponsor and the external authors. No public presentation or publication of any interim results may be made by any principal investigator, sub-investigator, or any other member of the study staff without the prior written consent of the Sponsor.

Authorship of publications at BMS is aligned with the criteria of the International Committee of Medical Journal Editors (ICMJE, www.icmje.org). Authorship selection is based upon significant contributions to the study (ie, ICMJE criterion #1). Authors must meet all 4 ICMJE criteria for authorship:

1) Substantial intellectual contribution to the conception or design of the work; or the acquisition of data (eg, evaluable participants with quality data or data generation), analysis, or interpretation of data for the work (eg, problem solving, advice, evaluation, insights and conclusion)
2) Drafting the work or revising it critically for important intellectual content

3) Final approval of the version to be published
4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Those who make the most significant contributions, as defined above, will be considered for authorship of the publication.

12 REFERENCES

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Supplementary Table S1.

Number of patients included in the study, the frequency of use of each type of injectable biologic, and the median time to relapse in months.

Biologic	Number of patients included	Median time to relapse, months (interquartile range)
Adalimumab	77	39 (62)
Bimekizumab	1	NA
Brodalumab	1	NA
Certolizumab Pegol	1	NA
Etanercept	4	43 (NA)
Guselkumab	8	56 (NA)
Infliximab	6	180 (140)
Risankizumab	9	48 (NA)
Secukinumab	40	48 (NA)

Ustekinumab	19	48 (30)

Legend: NA = not estimable.

Supplementary Table S2.

Frequency and relationship of the main risk factors to the occurrence of adverse events.

	Adverse Events		
	Yes (n = 15)	No (n = 151)	P value
Distribution problems	4 (26.67%)	60 (39.74%)	0.411
Low adherence	1 (6.67%)	13 (8.61%)	1.000
Inadequate storage	0	21 (13.91%)	0.221