 DOI: 10.1515/acm-2016-0005

CENTRALISED BIOLOGICAL THERAPY REGISTRY FOR MODERATE TO SEVERE PLAQUE PSORIASIS – OVERVIEW AND METHODOLOGY

Sutka R, Pec J, Pecova T

Dermatovenereology Clinic of Martin University Hospital, Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia

Abstract

The introduction of new pharmacotherapy entities in the last decade accentuate the necessity to set up treatment guidelines based on real life evidence. Randomized controlled trials remain golden standard of a research. Data derived from studies aiming on daily clinical practice should bring needed, added value. Disease prevalence growth, due to increased life expectancy, better diagnostic procedures and earlier medical intervention, as well as ever growing demand for highly priced, sophistically produced drugs put stress on healthcare budgets even in developed countries. Large databases commonly called - therapy registries are implemented to collect data on therapy effectivity in terms of effectiveness, safety and patient long-term on therapy survival. Registries importance rose together with biological therapies introduction. New in class molecules entered the market conditionally being obliged to provide additional e.g. safety data. Such procedures require involvement of many different professionals, e.g. physicians, professional medical bodies, IT experts, database administrators, statisticians and government institutions. Paper based, followed by computer based forms were distributed among physicians to collect these data. eHealth technologies provide physicians with centralized, more intuitive applications. The particularities of different diagnosis caused great variations within each specific registry launched. Important information was missing since they were pointed out as optional and many were redundant causing frustration among physicians due to inadequate administrative workload. The main objective of this work was to set up the therapy registry standards and procedures. Methodology of „ideal" moderate to severe plaque psoriasis biology therapy registry development, introduction, administration and evaluation was prepared to assist any government institution or professional body when planning registry deployment. Electronic application based on widely used MS Excel platform was developed and installed in the biological therapy centers as a standalone application for the pilot use.

Keywords: therapy registry, patient register, plaque psoriasis, biological therapy, effectiveness, safety, eHealth

INTRODUCTION

Psoriasis is primarily an inflammatory skin disease with acute exanthematous or chronic stationary course. It is based on genetic predisposition with polygenic or multifactorial heritability, influencing every age and sex group with important external triggering risk factors influence [1].

New molecules introduced in the last decade to psoriasis treatment portfolio play important role in influencing different levels of inflammation processes. Better efficacy and improved safety profile is expected in comparison to former topical and systemic therapy [2]. Biological medicines (biologics) are very complex drugs with higher price reflecting raised production costs and in final put more stress on healthcare system budget. Sophisticated models (patient registries) for therapy efficacy, long term safety and cost effectiveness monitoring were launched in the clinical practice in many developed countries.

The situation as of March 2014

European national projects

Netherland (AMC Psoriasis Registry) – 2005 first register of psoriasis; [3];
http://www.amc.nl/web/Research/ResearchAMC/AMC-a-glance.htm
CAPTURE – 2005; an analogy of pediatric registry CHILD-CAPTURE [4, 5, 6]

Address for correspondence:
Prof. Péč J., MD, PhD, Dermatovenereology Clinic, Jessenius Faculty of Medicine and University Hospital, 036 01 Martin, Kollarova str. 2, 03601 Martin, Slovakia, e-mail: juraj.pec@jfmed.uniba.sk,

Italy (PSOCARE renamed to PSODIT) – 2005; [7, 3, 8]; http://www.centrostudigised.it/psodit.html
Sweden (PSOREG) – 2006; [9, 10, 3]; http://www.psoreg.com
Denmark (DERMBIO) – 2007; [11]; https://dermbio.dk
United Kingdom (BADBIR) – 2007; [12]; http://www.badbir.org
Spain (BIOBADADERM) – 2008; [13, 14]; https://biobadaser.ser.es/biobadaderm
Germany (PSOBEST) – 2008; [15]; http://www.psobest.de
Czech Republic (BIOREP) – 2005; [16, 17, 18, 19]; https://www.biorep.cz/Login.aspx?ReturnUrl=%2f
Switzerland (SDNTT) – 2011; [20]; http://www.derma.ch/spec/SDNTT.html
France (PSOBIOTEQ) – 2012; [21] [22]; *no web link available*
Austria (PSORA) – 2010; [23]; http://www.meduni-graz.at/13818

European multinational projects
PSONET – 2007; European surveillance network to monitor the long term effectiveness and safety of systemic agents in the treatment of psoriasis [3]; http://www.psonet.eu/cms

National projects outside Europe
Israel (Clalit Health Services medical database) – 1997; [24]; http://www.clalit-global.co.il/en
Australia (APR) – 2008; [25]; https://www.psoriasis.asn.au
Malaysia (DERMREG) – 2007; [26, 27]; http://www.acrm.org.my/dermreg
Egypt (Egyptian Psoriasis Network) – 2012; http://egyptianpsoriasisnetwork.com
USA (CORRONA) – 2014; [28]; http://www.psoriasis.org

International multinational projects
PSOLAR – 2007; Psoriasis Longitudinal Assessment and Registry; [29, 30]; *no web link available*

Slovakia similarly as many other European countries is missing data on biologics long term treatment outcomes. The aim of this study was to create, set up and launch pilot phase of biological therapy registry for patients suffering from moderate to severe plaque psoriasis in specialized treatment centers in Slovakia.

METHODS

New trends in modern medicine require innovative approach. The methodology of patient registry comes primarily from clinical practice requirements. Almost every register suffered from low acceptance by physicians in its pilot phase. Higher workload and non-compliance due to workplace stereotypes were among the most frequent reasons. The obstacles can be avoided by implementing set of rules before starting registry preparation [31].

Each workgroup should prepare patient registry in line with, The Agency for Healthcare Research and Quality, guidance (AHRQ 2010) [32].

Registry planning

The differences in particular healthcare systems across the continent, in terms of provided services and the reimbursement, are limiting possibility to share data between the countries by analogy. Patient registry in Slovak environment should be utilized as follows

– directly

to help dermatology clinicians evaluate efficacy and safety within large patient sample to simplify future therapy intervention decisions

– **indirectly**
to secure better control over resources utilization by health insurance companies
to evaluate physician adherence to national treatment guidelines by professional society
to support demand for innovative treatment methods availability by patient groups
to confirm the claims on therapy quality by pharmaceutical companies

Main purpose of the patient registry is a prospective observation of limited parameters to be able to reach preset objectives and evaluate the outcomes while avoiding inadequate workload.

– **Primary objectives**
1) long-term efficacy
2) long-term safety

– **Secondary objectives**
1) efficacy and safety in relation to the comorbidities
2) patient quality of life
3) predictors of treatment outcomes
4) disease severity progress and therapeutic modality sequence since first diagnosis

The cost effectiveness analysis in terms of quality adjusted life year (QALY) parameter is not in a scope, but in case of need Dermatology Life Quality Index (DLQI) questionnaire data can be extrapolated to Health-related quality of life questionnaire (EQ-5D) [33, 34, 35].

Registry design

The proposed type of patient registry is multi-product, longitudinal research in the real life setting. The registry partially meets criteria of non-interventional cohort clinical study when health insurance company approval is required. Biomedical research and patient registries are regulated by many national and EU healthcare directives as well as ethical norms to secure transparency and protection of patient rights and wellbeing.

Ownership

Scientific Advisory Board (SAB), constituted under supervision of Slovak Dermatovenereology Society (SDS) is considered an idea holder and is responsible for the registry design, regular data quality control, major financial, ethical and scientific decisions. The members of the SAB are heads of 8 biology therapy centers where the pilot offline version is running and statutory body is the Main specialist for Dermatovenereology within Ministry of Health. IT technology supplier is database software developer co-operating with Slovak medical chamber. The funding is covered from the sources of nonprofit organization committed to the support of projects for patients suffering from rheumatoid arthritis and psoriasis. The registry will run under umbrella of National Center for Healthcare Information (NCZI) after its pilot phase. It will be included in the online system called – National Medical Registries. The data collection and processing will be performed directly in NCZI or through procurer. The registry will be closed down when the costs of data collection will exceed the informative value gained in the future. Ultimate decision will be made by NCZI. All the electronic data will be archived in NCZI. The paper forms will be stored in the therapy centers according to the law.

Inclusion criteria

The inclusion criteria are defined by Indication limitations stated by Ministry of health for each biologic. They are in line with approved therapeutic indications in the official Summary of product characteristics. All the patients who were ever prescribed biology therapy based on the actual European treatment guidelines S3 (except off label use), either once or repeatedly will classify themselves [36]. The therapy is administered in 8 specialized dermatovenereology centers that are equally distributed throughout the country. The data collection should become obligatory after launch of official phase. Patient participation in the registry is terminated as soon as biology therapy was permanently discontinued.

The hypothesis set, in case of efficacy and safety registries is usually simple, specific and verifiable, if the primary objectives clearly define the target population.

1) Target population are all the patients suffering from moderate to severe plaque psoriasis
2) Observed population are all the patients who meet inclusion criteria
3) Treated population are all randomly selected patients from observed population who were offered treatment and they agreed
4) Actual population covers all the patients who are treated and agreed their personal details to be processed electronically (being part of the registry)
5) Analyzed population are those patients from actual population whose data will be submitted for final analysis

Database security

The access rights are granted in the two levels. Administrator – SAB member, NCZI representative, nonrestrictive use. User – physician or project coordinator at the biology therapy center, limited access. Regular updates and patches are issued based on feedbacks from pilot phase trial use. All the patient details are anonymous - software encrypted. The data for scientific and publication purposes will be available upon request and approval of SAB. The authorship rights and responsibilities will be regulated by ICMJE standards [37].

Patient recruitment plan and visit schedule

The visit schedule plan is obligatory to secure continuous treatment and register data uniformity. Paper form, so called - Protocol on the beginning and continuation of psoriasis treatment, mandatory requirement from Health insurance company, is being filled at every patient visit. The protocol design and review was done by SAB. Unscheduled visit should be recorded only if an adverse event, change to therapy course or treatment failure is the reason.

Visit schedule

Visit No. 1 (day 0) – dermatovenereology specialist collects the following
- a) informed consent
- b) data on anamnesis (family and personal history)
- c) basic physical examination including laboratory parameters
- d) psoriasis area severity index (PASI), physician global assessment (PGA), DLQI values
- e) blood sample for pulmonology Interferon Gamma release assay (IGRA) testing
- f) Protocol on the beginning and continuation of psoriasis treatment

Visit No. 2 (usually day 30) – If the patient meets the inclusion criteria. No apparent contraindication. Health insurance company approves biology therapy. Physician enters paper based Protocol data into the registry. Biologic is prescribed.

Visit No. 3 (day 114/128/142) – Minimum PASI 50 improvement must be confirmed in different time intervals, depending on the molecule, for the patient to be able to continue the treatment. All the procedures as during Visit No. 1 are performed except IGRA testing. The protocol on the continuation is being filled up. When insurance company approves the therapy prolongation, all the data from the protocol are entered into the registry.

Visit No. 4 (day 212) – All the procedures are performed according to Visit No. 3 (including IGRA testing). If the protocol on the treatment continuation is approved by insurance company all the data are entered into the registry.

The procedures from visit 4 onward are repeated every 26 weeks, while IGRA testing is performed at every other visit.

Patient should have the treatment up-titrated or treatment intervals shortened or biology therapy combined with other systemic treatment or biology therapy discontinued in case when the formerly reached improvement declines by >50%. All information are entered into the registry, based on the protocol. If the new biology therapy is started then all the procedures according to visit schedule beginning at Visit No. 1 are repeated.

Registry variables

The selection of registry variables was based on the registry primary and secondary objectives. They are divided into three groups: personal, therapy and outcomes related data.

Personal:

1) sex, ethnicity
2) diagnosis including comorbidities
3) age, height / weight, BMI
4) addictions (tobacco, alcohol)
5) anamnesis (family history / personal history)
6) biomarkers – CRP, FW, HBsAg, anti-HIV, TPHA, ASLO, ANA, standard hematology, biochemistry and urine-analysis test
7) special testing
   - obligatory: – pulmonology testing (chest X-ray, IGRA test)
     – stomatology examination
     – ORL examination
     – gynecology and urology examination
     – prostate examination
   - optional: – ultrasonography examination
     – internal medicine examination
     – optional e.g. psychological/psychiatrical examination

Therapy:

1) Drug generic and brand name, ATC code, dosing, route of administration, beginning/discontinuation/termination of the treatment
2) Treatment naïve / treatment continuation
3) Health insurance company therapy approval interval
4) Data on diagnosis according to International Classification of Diseases
5) Concomitant medication

Outcomes:

The observational studies therapy efficacy is defined rather as the therapy effectivity, where benefit is evident only after introduction to real world of heterogenic population. It is usually lower than the one observed in registration phase III trials [7]. PASI and PGA parameters are used to define clinical response. Two additional parameters need to be recorded due to their impact on the treatment outcome:

– disease localization – capillitium, nails, palmoplantar, genitals, facial, others
– psoriasis type – plaque, guttate, inverse, pustulosis, unguium, erythrodermic, arthritica

The therapy safety is evaluated through the adverse event reporting process according to effective Law. All the participants are trained with special aim at opportunistic infections and lymphoproliferative diseases. Medical Dictionary for Regulatory Activities (MedDRA) should be used as unified terminology standard [38].

The patient reported outcomes should reflect patient treatment satisfaction in terms of improved quality of life. DLQI questionnaire for adult and CDLQI for children as well as Visual analogue scale (VAS) are part of the registry [39, 40, 41, 42, 43].

Potential bias avoidance

The bias potential within patient registries is the main reason for observational studies to be only the tools to generate hypothesis, being afterwards confirmed under stringent conditions of clinical trials. The biases are classified based on the process phase when they appear:

– Process of patient selection:
– Physician low adherence to inclusion criteria during patient recruitment
– Number of patients on therapy limited by insurance company, due to rising costs
– Prescription not performed inline with S3 guidelines

Process of data recording and summarization

– Not 100% of treated patients have their data recorded

– Incomplete or missing data in the database
– Subjective treatment outcome assessment
– Limited patient adherence to the long-term therapy course

Analytical methods

The plan of statistical analysis should be prepared by renowned Institute of Biostatistics and Analysis, Masaryk university, Brno, Czech Republic, having expertise in medical registries management – ATTRA (rheumatology register), CAMELIA (Chronic myelogenous leukemia), register (gastrointestinal stromal tumor) [15, 44, 45]. Regular intervals since the treatment initiation (in years) are suggested for patient data analysis to detect early and long-term events - 0.25; 0.5; 1; 2; 3; 5; 10 years.

RESULTS

The electronic application was prepared based on the actual findings, trends and methodology in the area of creation, management and evaluation of phase IV clinical studies (population-observational studies). It is fulfilling the highest standards required by applicable legislation and taking into account stringent criteria of patient privacy data protection.

It was built on standardized, generally widely used platform MS Office 2003/2007. The system is user friendly and intuitive. The inputs are done based on the requirements of the Protocol on the beginning and continuation of psoriasis treatment. The application itself consists of three modules:

1) administrator – to administer, update/upgrade and synchronize
2) patient – to manage patient data
3) visit – to record patient visit details

The system was successfully launched for the pilot training use into almost all biology therapy centers. The updates and patches are being developed to avoid errors reported by study center coordinators.

Administrator module

This module is to provide service and maintenance capability. The installation module is integral part. The system (in terms of PC performance) requirements are minimal, but approval and assistance of IT infrastructure administrator at the study center is needed. The replication module helps to connect to the server and download updates or synchronize database in real time. Remote access for service purposes is also available through secure channel.

Patient module

Back up option is the first part of this module. It provides bidirectional data flow to back up and to recover the database. The file can be saved to local workstation or to the portable media. No real time database synchronization with server is possible when the system is running offline. If more than one computer is used at the study center then all the partial backups are centralized in the study coordinator workstation for synchronization.

This module serves to collect all the primary information on therapy center contact details (center name, address, coordinator name, prescribing physician name)

The various reports can be printed out according to the physician needs. Official paper forms, e.g. questionnaires, patient informed consent form is contained within the application ready for printout.

The sheet - Patient list is the first screen of the entire module. The physician has clear overview of patient database. Predefined visual data (patient name, drug brand name, Health insurance company name, date of therapy approval expiration) can be modified based on physician preference. The traffic light like color scheme of the rows helps physician to evaluate patient compliance to proposed visit schedule. Search option is available.

Addition of new or modification of existing patient data is performed here. Yellow fields are mandatory. The rest is optional. The physician has an option to see how the main variables develop overtime in the graphic design (Fig. 1).

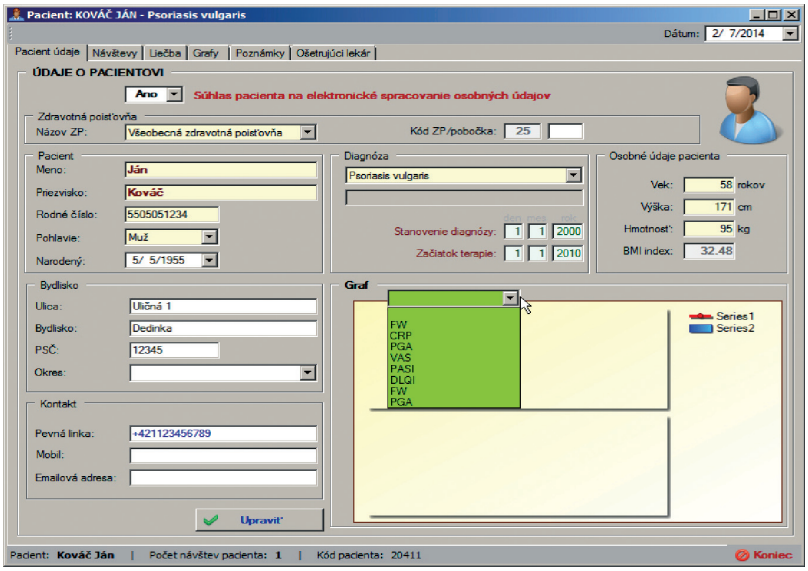

Fig. 1 Patient list sheet

The sheet - Therapy allows physician to get complex overview of prior and actual concomitant medication (type, brand name, therapy duration and discontinuation reason). No data are entered here. No information about biology therapy is present either.

Visit module

This module is entered via the sheet - Visits. It is the core part of the database consisting of 11 partitions collecting information on the main parameters of an efficacy and safety.

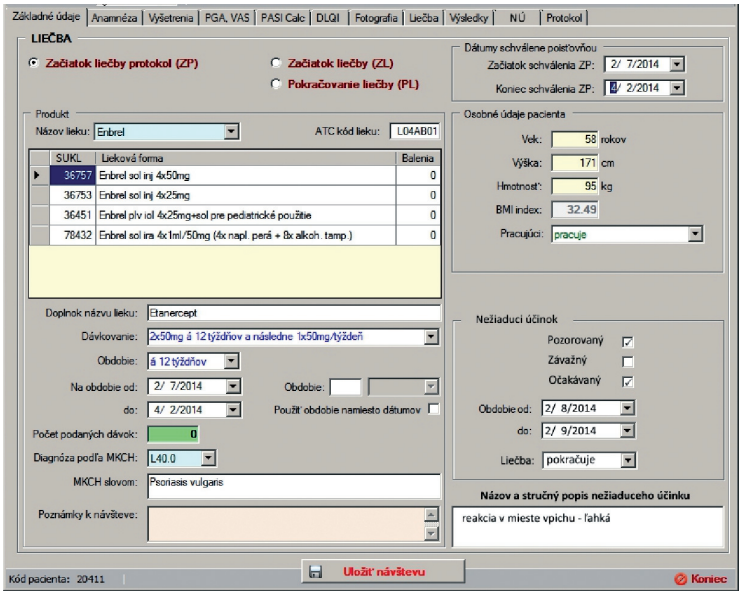

Fig. 2 Basic data sheet

A sheet - Basic data identifies visit type (first time prescription, continuation). Biology therapy details: drug name, application form and dosing interval are entered only once and then confirmed if no change occurs. Physical examination results are recorded from each visit. Adverse events irrespective of the ype are entered when ever noticed (Fig. 2.).

The sheet - Anamnesis contains data on family and personal history. Very similar sheet - Variables shows 52 parameters not recorded on every visit. The parameters are divided into three parts: biochemistry, immunochemistry, hematology, urine. Due to special status of pulmonology examination there is separate section for IGRA test results (Fig. 3).

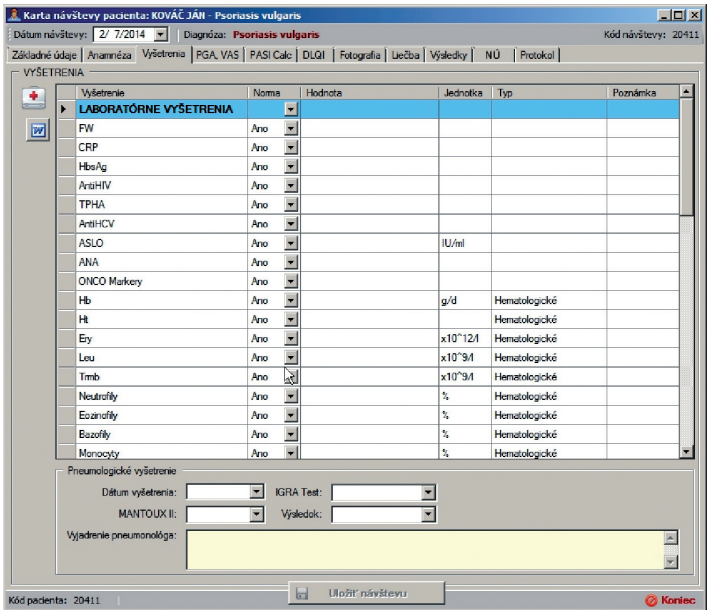

Fig. 3 Lab variables sheet

Fig. 4 PASI calculator sheet

The sheets – PGA/VAS; PASI and DLQI are the platforms for treatment efficacy evaluation in relation to the clinical symptoms appearance and other related factors (alcohol and nicotine consumption, type and localization of the disease). PASI calculator is present to determine severity of the disease at the particular location and for the physician to compare the value variation within certain time period (Fig. 4.).

Additional sheets – Photography, Therapy, Results, Adverse events and Protocol have informative and supportive function as the source of optional data and summaries of collected variables. Especially Protocol serves for the revision and last check before printing out official Request and final protocol for Health insurance company purposes.

DISCUSSION

The randomized clinical trial publications revealed short term benefit of biologics for the moderate to severe plaque psoriasis treatment. Although some articles indicate that the therapy effect should be more robust than it is in the real clinical practice within first 12 weeks. There is a clear benefit for the patient when switching regular systemic therapy for biologics as shown in the analysis of Swedish registry PsoReg [46, 47]. Long-term information on efficacy and safety are inconsistent in real life settings. It is usually impossible to extrapolate to general population from the results gained under different randomized clinical trials conditions since head to head comparisons are very rare. Primarily long-term safety was the main reason for the introduction of national registries in dermatovenereology. The one of the Italian registry Psocare outcomes was that patient can benefit from the change of one anti-TNF biologic for another when inadequate treatment response or adverse event was observed [48].

The working groups were established in the EU, consisting of the experts among various areas, based on the initiatives coming from the professional bodies reflecting similar situation in rheumatology. The collaboration delivered the database tools for monitoring of biology therapy long-term benefit. The differences in the social-economic and political principles of healthcare system functioning, set substantial argument for launching the registry in each country. However the variables and other monitored parameters should be similar across the whole continent to enable future comparison [49].

The first “dermatology” registry in Slovakia was officially mentioned in 2008, when the pharmaceutical company Janssen-Cilag offered a monitoring of patients treated with their drug ustekinumab [50]. Corresponding software application development was started in 2011 according to the Ministry of health request [51]. The core structure of the registry was based on Protocol on the beginning and continuation of psoriasis treatment. The protocol offers complex information on the patient and the treatment, required by Health insurance company to issue a therapy approval. Even complete retrospective data can be acquired from archived copies of the first biology therapy treated patients back to 2006. Additional registry variables are derived from international project on psoriasis epidemiology survey in biologics naïve population [52]. The registry was installed in 7 out of the total 8 therapy centers for the pilot evaluation phase by the end of 2014. The monitoring of the whole country is secured.

The recruitment is performed inline with inclusion criteria. The registry fulfills European Medical Agency (EMA) standards, Agency for Healthcare Research and Quality (AHRQ) and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative recommendations. The therapy efficacy is evaluated based on the criteria used in the clinical trials - PASI and PGA. The therapy safety assessment follows the rules set by Good Clinical Practice [53]. Patient quality of life is quantified by DLQI and VAS.

The database collects the data on comorbidities and monitors psoriasis major risk factors (elevated BMI, excessive alcohol and nicotine consumption). The hypothesis on the relationship between pursued parameter and the disease can be drawn from the data entered.

The registry parameters, in terms of spectrum and extent are in line with the majority of currently running psoriasis registries. Database reflects all the recent trends in plaque psoriasis diagnostics and treatment. It has the potential to improve dermatovenereology clinical practice in Slovakia when launched in real life setting.

Registry application as an innovative solution was prepared inline with Slovak Republic strategy of eHealth – electronic healthcare system. Its main objective is to provide right information, at the right time, in the right place in every phase of patient care to ensure substantial cost savings [54].

The need for the registry in Slovakia is indisputable despite late introduction. Although the benefit of retrospectively acquired data might be questioned when facing physician expertise. The demand for the comparison of currently available biologics portfolio to the new drug candidates (secukinumab, brodalumab or tildrakizumab), will escalate registry importance, in terms of new data that might accelerate the launch and drug availability to the patients [55] [56].

Recent scientific progress in the psoriasis etiopathogenesis and treatment armamentarium answered some, but not all the questions. The biology therapy impact on the healthcare budget requires monitoring of predictive biomarkers. The introduction of new genetic markers to better understand a disease nature and interpersonal differences would contribute to continuous drug development. Substantial effort should be put into the further research in genetics, immunology, angiogenesis, environmental factors, psoriasis in children, elderly and pregnant population, psoriatic arthritis, cardio-metabolic comorbidities, etc. [57].

Every decision made on patient treatment should take into the consideration impact on the quality of life [58]. Validated commonly used life quality questionnaires should be inevitable part of each registry. Their selection is not defined [59].

The loss of physician motivation is the most common problem in the context of information collection. Repeated recording of the same data is challenging in long-term perspective without apparent short-term outcome. Elimination of redundant optional data should be the priority. Therapy center representatives and study center co-ordinators should meet regularly to share experience and best practices.

Every effort should be made to have data compared to other countries. Evaluate similarities and differences among specific parameters depending on population of scope. Registry owners should apply for the membership in the multinational initiative PSONET.

REFERENCES

1. Braun-Falco O, Plewig G, Wolff H. Dermatológia a venerológia. Martin: Osveta; 2001.
2. Stern R. A promising step forward in psoriasis therapy. JAMA 2003; 290, 3133-5.
3. PSONET.eu [Internet], Italy: European surveillance network to monitor the long term effectiveness and safety of systemic agents in the treatment of psoriasis; [updated 2013; cited 2014 Feb 3]. Draft protocol 20 7. Available from: http://www.psonet.eu/cms/.
4. Driessen R, Boezeman J, Van de Kerkhof P, De Jong E. Three-year registry data on biological treatment for psoriasis: the influence of patient characteristics on treatment outcome. Br J Dermatol 2009, 160 (3): 670-5.
5. Van Lumig P, Driessen R, Berends M, Boezeman J, Van de Kerkhof P, De Jong E. Safety of treatment with biologics for psoriasis in daily practice: 5-year data. J Eur Acad Dermatol Venereol 2013; 26 (3): 283-91.
6. Oosteveen A, De Jong E, Evers A, Donders A, Van de Kerkhof P, Seyger M. Reliability, Responsiveness and Validity of Scalpdex in Children with Scalp Psoriasis: The Dutch Study. Acta Derm Venereol 2014; 94 (2): 198-202.
7. Nijsten T, Wakkee M. Psocare: Italy Shows the Way in Postmarketing Studies. Dermatology 2008; 217: 362-4.
8. Naldi L, Cazzaniga S. Dermatology: experience with the disease registry for the treatment of psoriasis. Recenti Prog Med 2013; 104 (6): 236-40.

9. Schmitt-Egenolf M. PsoReg – The Swedish Registry for Systemic Psoriasis Treatment. Dermatology 2007; 214: 112-17.
10. Hägg D, Eriksson M, Sundstrom A, Schmitt-Egenolf M. The higher proportion of men with psoriasis treated with biologics may be explained by more severe disease in men. PLoS ONE 2013; 8 (5): e63619. doi:10.1371/journal.pone.0063619.
11. Gniadecki R, Kragballe K, Dam T, Skov L. Comparison of drug survival rates for adalimumab, etanercept and infliximab in patients with psoriasis vulgaris. BJD 2011; 164: 1091-6.
12. Burden A, Warren R, Kleyn C, McElhone K, Smith C, Reynolds N, Ormerod A, Griffiths C. The British Association of Dermatologists' Biologic Interventions Register (BADBIR): design, methodology and objectives. British Journal of Dermatology 2012; 166: 545-54.
13. Rivera R, Garcia-Doval I, Carretero G, Daudén E, Sánchez-Carazo J, Ferrándiz C, Harrera E, Alsina M, Ferrán M, López-Estebaranz J, Goméz F, Herranz J, Carrascosa J, Vanaclocha F. BIOBADADERM, the Spanish Registry of Adverse Events Associated With Biologic Drugs in Dermatology: First Report. Actas Dermosifiliogr 2011; 102 (2): 132-41.
14. Biobadaser.ser.es [Internet], Spain: Fundacion Academia Espanola de Dermatologia. Protocol registration receipt; 2013 [cited 2014 Feb 4]. Available from: https://biobadaser.ser.es/biobadaderm/cgi-bin/upload/archivo.aspx?id=21.
15. Augustin M, Spehr C, Radtke M, Boehncke W, Luger T, Mrowietz U, Reusch M, Stromer K, Wozel G, Kiedrowski R, Rustenbach S, Purwins S, Reich K. German psoriasis registry PsoBest: objectives, methodology and baseline data. J Dtsch Dermatol Ges 2014; 12 (1): 48-57.
16. Arenberger P. Zápis ze schúze výboru ČDS konané dne 1. dubna 2010 v Praze. Česká a slovenská dermatovenerologie 2010; 85 (4): 241-2.
17. Dermanet.cz [Internet], Czech Republic: Česká akademie dermatovenerologie - Centra biologické léčby; [updated 2013; cited 2014 Feb 5]. Available from: http://www.dermanet.cz/cs/kozni-ordinace/centra-biologicke-lecby/.
18. Ordinace.cz [Internet], Czech Republic: Vyšínová R. „Nejsme spokojeni s výsledky léčby," říkají pacienti s lupénkou; 4 6 2012 [updated 2012 Jun 4; cited 2014 Feb 5]. Available from: http://www.ordinace.cz/clanek/nejsme-spokojeni-rikaji-pacienti-s-lupenkou/?chapter=1.
19. Prolekare.cz [Internet], Czech Republic: Arenberger P. Česko-slovenská dermatologie; [updated 2011 Jan; cited 2014 Feb 5]. Available from: web.lfhk.cuni.cz/dermat/data/zapis_13_01_2011.doc.
20. Clinicaltrials.gov [Internet], United States: Swiss Dermatology Network for Targeted Therapies; [updated 2012 Oct 12; cited 2014 Feb 5]. Available from: http://clinicaltrials.gov/show/NCT01706692.
21. Clinicaltrials.gov [Internet], United States: Assistance Publique - Hôpitaux de Paris; Study record detail; [updated 2012 Jun 8; cited 2014 Feb 5]. Available from: http://clinicaltrials.gov/show/NCT01617018.
22. Ormerod A, Augustin M, Baker C, Chosidow O, Cohen A, Dam T, Garcia-Doval I, Lecluse L, Schmitt-Egenolf M, Spuls P, Watson K, Naldi L. Challenges for Synthesising Data in a Network of Registries for Systemic Psoriasis Therapies. Dermatology 2012; 224: 236-43.
23. Meduni-graz.at [Internet], Austria: Medizinische Universität Graz; Bioimmuntherapie: Register & Datenbanken; [updated 2013; cited 2014 Feb 6]. Available from: http://www.meduni-graz.at/13818.
24. Cohen A, Weitzman D, Dreiher J. Psoriasis and Hypertension: A Case-Control Study. Acta Derm Venereol 2010; 90: 23-6.
25. Psoriasis.asn.au [Internet], Australia: Australasian psoriasis registry; [updated 2008; cited 2015 Feb 12]. Available from: https://www.psoriasis.asn.au/default.aspx?Logout=Refresh.
26. Chang C, Gangaram H, Hussein S. Malaysian Psoriasis Registry - preliminary report of a pilot study using a newly revised registry form. Med J Malaysian 2008; 63: 68-71.
27. Acrm.org.my [Internet], Malaysia: Mohd Affandi A, Alias F, Johar A, Baba R. Annual Report of the Malaysian Psoriasis Registry 2007-2012; [updated 2014; cited 2015 Feb 12]. Available from: http://www.acrm.org.my/dermreg/documents/MPR_Annual_Report_2007-2012_Final.pdf
28. Psoriasis.org [Internet], United States: National psoriasis foundation; [updated 2014 Jan 8; cited 2014 Feb 6]. Available from: http://www.psoriasis.org/news/press-releases/2014/01/08/npf-and-coronna-co-develop-first-nonprofit-psoriasis-registry.
29. Clinicaltrials.gov [Internet], United States: Centocor Ortho Biotech Services, L.L.C.; [updated 2014 Jan 16; cited 2014 Feb 6]. Available from: http://clinicaltrials.gov/ct2/show/record/NCT00508547?term=psolar&rank=1.
30. Papp K., Strober B, Augustin M, Calabro S, Londhe A, Chevrier M. PSOLAR: design, utility, and preliminary results of a prospective, international, disease-based registry of patients with psoria-

sis who are receiving, or are candidates for, conventional systemic treatments or biologic agents. J Drugs Dermatol 2012; 11 (10): 1210-7.
31. Gliklich R, Bertagna M. The emerging role of the patient registry. Good Clinical Practice journal 2006; 14-7.
32. Gliklich R, Dreyer N, Registries for evaluating patient outcomes: User s guide, 2 ed. Rockville: Agency for Healthcare Research and quality; 2010.
33. Norlin J, Steen Carlsson K, Persson U, Schmitt-Egenolf M. Analysis of three outcome measures in moderate to severe psoriasis: a registry-based study of 2450 patients. Br J Dermatol 2012; 165 (4): 797-802.
34. Blom C, Beikert F, Rustenbach S, Augustin M. Mapping DLQI on EQ-5D in psoriasis: transformation of skin-specific health-related quality of life into utilities. Arch Dermatol Res 2013; 305 (3): 197-204.
35. Shikiar R, Willian N, Okun M, Thompson C, Revicki D. The validity and responsiveness of three quality of life measures in the assessment of psoriasis patients: results of a phase II study. Health Qual Life Outcomes 2006; 4 (71): 1-12.
36. Nast A, Boehncke W, Mrowietz U, Ockenfels H, Philipp S. S3 - Guidelines on the treatment of psoriasis vulgaris (English version). Update. JDDG 2012; 10 (2): 51-595.
37. Icmje.org [Internet], United States: International committee of Medical journal editor; [updated 2013 Dec; cited 2014 Feb 9]. Available from: http://www.icmje.org/icmje-recommendations.pdf.
38. Meddra.org [Internet], United States: International conference on harmnisation; [updated 2013 Sep; cited 2014 Feb 14]. Available from: http://www.meddra.org/.
39. Flytstrom I, Stenberg B, Svenson A, Bergbrant I. Patients' Visual Analogue Scale: A Useful Method for Assessing Psoriasis Severity. Acta Derm Venereol 2012; 92: 339-409.
40. Hjortsberg C, Bergman A, Bjarnason A, Heikkilä H, Hjelmgren J, Svensson A, Tennvall G. Are treatment satisfaction, quality of life, and self-assessed disease severity relevant parameters for patient registries? Experiences from Finnish and Swedish patients with psoriasis. Acta Derm Venereol 2011; 91 (4): 409-14.
41. McInnes I, Combe B, Burmester G. Understanding the patient perspective - results of the Rheumatoid Arthritis: Insights, Strategies & Expectations (RAISE) patient needs survey. Clin Exp Rheumatol 2013; 31 (3): 350-57.
42. Dougados M, Nataf H, Steinberg G, Rouanet S, Falissard B. Relative importance of doctor-reported outcomes vs patient-reported outcomes in DMARD intensification for rheumatoid arthritis: the DUO study. Rheumatology (Oxford) 2013; 52 (2): 391-9.
43. Finlay A, Basra M. DLQI and CDLQI scores should not be combined. Br J Dermatol 2012; 167 (2): 453-4.
44. Attra.registry.cz [Internet], Czech Republic: Česká revmatologická společnost - ATTRA clinical register; [updated 2014; cited 2014 Feb 26]. Available from: http://attra.registry.cz/.
45. Iba. muni.cz [Internet], Czech republic: IBA Masarykova univerzita; [updated 2013; cited 2014 Feb 26]. Available from: http://www.iba.muni.cz/index.php?pg=vyzkum.
46. Weller R. U.S. experience of immunomodulators in the treatment of psoriasis. Br J Dermatol 2005; 152 (4): 817-818; author reply 818-819.
47. Norlin J, Steen Carlsson K, Persson U, Schmitt-Egenolf M. Switch to biological agent in psoriasis significantly improved clinical and patient-reported outcomes in real-world practice. Dermatology 2012; 225 (4): 326-32.
48. Piaserico S, Cazzaniga S, Chimenti S, Giannetti A, Maccarone M, Picardo M, Piaserico A, Naldi L. Efficacy of switching between tumor necrosis factor-alfa inhibitors in psoriasis: Results from the Italian Psocare Registry. J Am Acad Dermatol 2014; 70 (2): 257-62; e3. doi: 10.1016/j.jaad.2013.10.019.
49. Garcia-Doval I, Rustenbach S, Stern R, Dam T, Cohen A, Baker C, Spuls P, Naldi L. Systemic psoriasis therapy shows high between-country variation: a sign of unwarranted variation? Cross-sectional analysis of baseline data from the PSONET registries. Br J Dermatol 2013; 169 (3): 710-4.
50. SDS-sk.sk [Internet], Slovak Republic: Slovenská dermatovenerologická spoločnosť - Zápisnice zo zasadnutia výboru Slovenskej dermatovenerologickej spoločnosti - rok 2008; [updated 2008 Mar 14; cited 2014 Mar 16]. Available from: http://www.sds-sk.sk/2008.htm.
51. SDS-sk.sk [Internet], Slovak Republic: Slovenská dermatovenerologická spoločnosť - Zápisnice zo zasadnutia výboru Slovenskej dermatovenerologickej spoločnosti - rok 2011; [updated 2011 May 20; cited 2014 Mar 16]. Available from: http://www.sds-sk.sk/2011_05_20%20Zapisnica%20zo%20zasadnutia%20vyboru%20SDVS%20Martin.pdf.
52. Péč J, Palotai T, Šimaljaková M, Zaujec L, Polák I, Psotová M, Vrtíková E, Šalkovská J, Hemza M, Vojtáš I, Urbanček S, Ševc J, Chríbiková I, Martinásková K jr, Péčová K jr, Tindirová M,

Martinásková K, Surňáková K, Jautová J, Baloghová J, Linkeschová E. Epidemiologická štúdia psoriázy v skupine biologicky naivných pacientov v podmienkach Slovenska. Biologická léčba 2011; 4 (1): 15-22.
53. ICH Expert Working Group. GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R1) Current Step 4 version. Rockville: U.S. Department of Health and Human Services; 1996.
54. Ezdravotnictvo.sk [Internet], Slovak Republic: Národné centrum zdravotníckych informácií; [updated 2011; cited 2014 Mar 6]. Available from: http://www.ezdravotnictvo.sk/Elektronicke-zdravotnictvo/Stranky/default.aspx.
55. Sonnenreich P. Advances in psoriasis treatment: experts comment on recent developments. P T 2013; 38 (12): 776-9.
56. Levy L, Solomon S, Emer J. Biologics in the treatment of psoriasis and emerging new therapies in the pipeline. Dove Press Journal: Psoriasis: Targets and Therapy 2012; 29-43.
57. Ryan C, Korman N, Gelfand J, Lim H, Elmets C, Feldman S, Gottlieb A, Koo J, Lebwohl M, Leonardi C, Van Voorhees A, Bhushan R, Menter A. Research gaps in psoriasis: opportunities for future studies. J Am Acad Dermatol 2014; 70 (1): 146-67.
58. Ahn C, Gustafson C, Sandoval L, Davis S, Feldman S. Cost effectiveness of biologic therapies for plaque psoriasis. Am J Clin Dermatol 2013; 14 (4): 315-26.
59. Tan X, Feldman S, Balkrishnan R. Quality of life issues and measurement in patients with psoriasis. Psoriasis: Targets and Therapy 2012; 2: 13-23.

Received: September, 22, 2015
Accepted: April, 4, 2016