Psoriasis: implications of biologics
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Citation for published version (APA):

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Dermatology 2009; 218:347–356
Abstract

About 11 million people suffer from psoriasis in Europe. This chronic condition may have a dramatic impact on quality of life. About 20% of patients may need systemic treatment to effectively control their disease activity. The introduction of biologics greatly increased the options of systemic therapies for psoriasis. However, clinical experience with newer systemic therapies is relatively limited and available data are mostly derived from short-term phase III trials. Except for PUVA and cyclosporine, long-term safety data from formal postmarketing studies are also largely lacking for conventional treatment options. Registries provide one mechanism to monitor the long-term safety and effectiveness of treatment in the ‘natural environment’. Several European countries have established registries to collect data on systemic psoriasis treatment. Even though different in some aspects of study design and monitoring, the registries share a number of common features: they include all the biological drugs and sometimes all the licensed systemic agents for psoriasis, and they observe the patients for a defined period of time irrespective of the drug given. Combining the results from these registries would increase their power and impact. We are developing an international collaboration called ‘Psonet,’ that will perform a joint analysis of data from 9 individual national psoriasis registries.
Introduction and Rationale

The prevalence of psoriasis in Europe is about 1.5%. It is estimated that in Europe (year 2000), about 11 million people suffer from psoriasis, a condition that has a dramatic impact on the health-related quality of life. About 10-20% of affected patients suffer from severe or complicated disease requiring phototherapy or systemic treatment for adequate control.

No single treatment is completely safe, and most conventional therapies, like methotrexate, cyclosporine and photo(chemo)therapy, are associated with specific short- and long-term adverse effects. In general, the likelihood of serious adverse events such as liver or renal toxicity and cancer development is dose dependent; moreover, some adverse effects such as cancer may appear after a long latency period.

In recent years, a number of molecules which specifically target steps deemed to play a crucial role in the inflammatory process of psoriasis have been developed with the hope that they will be more effective and less toxic treatments for psoriasis. At present, the molecules which are often referred to as ‘biologics’, include agents that modulate T cell functions by acting on costimulatory molecules, e.g. efalizumab or alefacept, and antagonists of the pro-inflammatory cytokine tumour necrosis factor α, e.g. infliximab, adalimumab and etanercept. These drugs have entered the European market registered by the European Medicines Agency (EMEA) for the ‘treatment of moderate to severe plaque psoriasis in adults who do not respond or present contra-indications or intolerance to other systemic therapies, including cyclosporine, methotrexate and/or PUVA therapy’.

Quite paradoxically, such an indication is not supported by firm evidence from available preregistration randomized clinical trials, where patients with moderate to severe psoriatic patients were included without any consideration of previous responses to conventional systemic agents. Such an indication may translate into patients treated with biological agents in Europe, who have a higher co-morbidity rate or are clinically more complex than patients studied in preregistration trials. In addition, most randomized clinical trials of biologicals last for no longer than 24 weeks. Besides that the limitations of randomized clinical trials to rule out safety issues are well known, spontaneous notification of adverse events is not an efficient way to assess safety either, since it is charged with significant underreporting of events and lacks any opportunity to relate the events to the number of treated patients.
New therapeutic options for the treatment of psoriasis create an increasing need for long-term observational studies and comparative trials in real-life situations.\textsuperscript{6} The need for long-term data on biologics could not be covered with ‘extension studies’ that usually follow specialized populations and are not lasting for the long term. In view of the problems mentioned above, regulatory agencies, such as the Food and Drug Administration, mandate the conduct of postmarketing phase IV studies for newly registered drugs.\textsuperscript{7} Although pharmaceutical companies have made commitments to initiate such long-term safety studies, these commitments are rarely accomplished in a satisfactory way. It has been documented that only 37\% of the postmarketing commitments taken with the Food and Drug Administration were completed in due time.\textsuperscript{8} This unsatisfactory situation has been the subject of substantial debate and has resulted in legal changes in the USA.\textsuperscript{8}

It has been proposed that registries involving a long-term follow-up of registered patients could provide long-term safety and effectiveness data of systemic psoriasis treatment in routine practice.\textsuperscript{9} In spite of their likely benefits, remarkably little is available in terms of extended administrative or clinical registries specific for psoriasis.\textsuperscript{7} Objectives that can be addressed by registries are:

\begin{itemize}
  \item investigation of the clinical effectiveness of systemic treatments for psoriasis in a population context;
  \item identification of prognostic factors that can help in predict the response to systemic treatments as well as in predict adverse events;
  \item monitoring of adverse effects of systemic treatments, with particular attention to long-term and rare adverse events, including infections, lymphomas and other cancers;
  \item creating benchmark data for quality assurance of the medical service;
  \item in a chronic disease, such as psoriasis, to provide an evidence base for the trade-off between risks and benefits of interventions in ‘real world’ practice over the longer term.
\end{itemize}

A major advantage of registries over industry-driven observational postmarketing studies is that registries follow patients irrespective of treatment continuation with a specific drug. Patients are enrolled when a certain drug is started, but the follow-up does not end when the drug is discontinued.\textsuperscript{10}
There are several local and national registries in Europe which collect data on systemic treatment for psoriasis; these efforts are particularly advanced in Sweden and Italy. Even though different in some aspects of study design and monitoring, the registries share a number of common features: they include all the biologicals and in several instances all the licensed systemic agents for psoriasis, and they observe the patients for a defined period of time irrespective of the drug given. The merging of data from these registries across several countries could be a powerful source of robust information on systemic drugs for psoriasis. For this purpose, an international collaboration has been established in Europe, under the label of ‘PSONET’. It will combine data from individual registries of several countries.

We will first summarize the national initiatives participating in the Psonet collaboration and their stages of development (Table 1). Then we will present the details of the Psonet initiative.
<table>
<thead>
<tr>
<th>Status</th>
<th>Italy</th>
<th>Sweden</th>
<th>Germany</th>
<th>Israel</th>
<th>United Kingdom</th>
<th>The Netherlands</th>
<th>Spain</th>
<th>Portugal</th>
<th>France</th>
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<td>running</td>
<td>running</td>
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<td>start-up phase</td>
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<td>prosp. cohort</td>
<td>prosp. cohort</td>
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<td>prosp. cohort, biological vs conventional drugs</td>
<td>prosp. cohort, retro- and prosp. cohort with controls</td>
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<td>biologicals, conventional drugs</td>
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<td>biologicals versus conventional drugs</td>
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<td>&lt; 2,000</td>
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<td>500-1,999</td>
<td>500-1,999</td>
<td>100-499</td>
<td>100-499</td>
<td>&lt;100</td>
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<td></td>
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<td>Geographical area covered</td>
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<td>80% of publicly funded dermatological services</td>
<td>459 hospital- and office-based centres</td>
<td>14 hospitals</td>
<td>all centres prescribing biologicals</td>
<td>2 academic centres</td>
<td>9 centres</td>
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<td>connected to internal network</td>
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<td>reversibly anonymized</td>
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</table>

Table 1. Overview of the 9 national registries for systemic therapies for psoriasis
Table set-up loosely based on Black et al.21
NATIONAL INITIATIVES

Italy
In Italy a national registry, called ‘Psocare’, has been established by the Italian Drug Agency in collaboration with the Italian Dermatological Societies and the Study Centre of the Italian Group for Epidemiologic Research in Dermatology. The registry has already collected data from over 12,000 psoriasis patients (March 2008).11,12 Almost half of these patients were treated with a biological, the others with conventional systemic treatments. One of the major advantages of the Italian system is the establishment of a country-wide network involving all the reference psoriasis centres and the compulsory registration of patients within the network, which minimizes selection bias.

The patients are assigned a unique code and provided with a card (psocard) needed to fill in prescriptions for the treatments under study. The follow-up process consists of visits at week 8, 16, 32, 52, 78, 104 and 208 subsequent to therapy commencement. All consecutive patients receiving a first prescription for any of the systemic treatments for psoriasis- photochemotherapy, cyclosporine, acitretin, methotrexate, efalizumab, etanercept, infliximab - or any other new systemic treatment approved for psoriasis are enrolled. Enrolled patients are followed, even if a patient discontinues the initial systemic therapy. Data collected are demographic data, comorbidities, clinical dermatological history, previous treatments undergone by the patient, the severity of psoriasis at entry baseline, the tests undergone by the patient and dosage of the drug prescribed for the treatment of the psoriasis. Updates are made at regular time intervals on current treatment and on the course of the psoriasis, as well as any other event, hospitalizations or specialist visits undergone by the patient and (possibly) associated with the treatment. The logistical part of the registry is carried out using a web-based program which can be filled in online by the dermatologists.

Sweden
Sweden also has an already fully functioning web-based registry, called ‘PsoReg’, which collects data on systemic treatment for psoriasis.13 This registry is based on voluntary participation of dermatologists.

The program can offer both real-time pharmacovigilance and support to clinicians in their day-to-day management of psoriasis patients. The idea of the developers is that to succeed, a register needs to provide benefits to the user: time invested in the registration
needs a pay-back. At this point, PsoReg provides a structured electronic medical record for psoriasis care, and statistical, reporting, and search functionality will follow shortly. The first page of the register ‘Admission’ needs to be filled in on the first visit only, containing the age of onset and its circumstances and former psoriasis treatments as well as former (not ongoing) morbidities of special interest, such as lymphoma, skin cancers, and severe infectious diseases. The next 4 pages ‘Status,’ ‘Treatment,’ ‘Patient,’ and ‘Lab values’ are filled in on every consecutive visit. The side effect report incorporated in PsoReg can be forwarded digitally to the authorities by the push of a button. This is not only active pharmacosurveillance, but also a usability incentive which helps to integrate PsoReg into everyday care.

Spain
The Academia Española de Dermatología y Venereología in agreement with the Agencia Española de Medicamentos y Productos Sanitarios will soon launch a registry (Biobadaderm) in Spain. It has already received ethical approval, and the electronic form that will be used for data collection is completely developed (it is a modified version of the database already in use by rheumatologists in the Biobadaser initiative). At the moment, 9 hospitals will voluntarily participate. All of them are already including patients receiving systemic therapy. A start in 2008 is aimed at. It is designed as a retrospective as well as prospective cohort study with the main aim of assessing the safety of biological drugs. Patients that have started therapy with biologicals in each centre since January 2005 will be included. The control cohort will be formed by a random sample of patients starting phototherapy in the same centre (for retrospective controls), and a systematic sample of those starting other systemic therapy (for prospectively collected controls). It is estimated that data on 5,700 person-years in each group will be collected at the end of the 5th year. Funding will come from the Academia Española de Dermatología y Venereología, the government and pharmaceutical companies.

United Kingdom
Partnered to the established and successful BSRBR register of biologicals in rheumatoid arthritis, the UK has established a nationwide registry, called ‘BADBIR’, that collects data on biological treatments and conventional treatments including PUVA. The register is web based and is currently running with active data collection and being rolled out to all centres in the UK that prescribe biologicals. The register is a prospective cohort study, it
concerns two cohorts and compares patients treated with biologicals to a control group with similar disease characteristics but exposed only to non-biological systemic therapies. The comparison group would include patients treated with PUVA, methotrexate, cyclosporine and acitretin. Aims are to quantify long-term safety as well as effectiveness. Primary endpoints include cancer, especially lymphoma, melanoma, non-melanoma skin cancer, especially squamous-cell carcinoma, demyelinating disease and tuberculosis. A number of subsidiary questions will also be addressed; they include differences between these agents, multiple agents used concurrently or in sequence in terms of serious adverse effects. Further, it is proposed that the register will seek to identify all available data on patients who become pregnant on treatment and to follow up the outcome of those pregnancies. Subject to prescribing patterns, the goal is to recruit 4,000 patients under conventional treatments and 2,000-4,000 on each biological intervention (depending on the uptake of these drugs in clinical practice). This registry is supported by the British Association of Dermatologists and sponsored by pharmaceutical companies.

France
France currently lacks any official network devoted to pharmacosurveillance of biologicals. However, there is a system of spontaneous notification of severe events during anti-tumour-necrosis-factor-therapies, e.g. *Legionella* infections, called ‘RATIO’. This is supported by both government and industry. There are also several initiatives in this area, like Club Psoriasis, a new study group instituted in 2006. A postapproval study is requested by the French ‘Commission de la transparence’, and some pharmaceutical companies agreed to cooperate. In fact, 2 directions are still debated in France. One is a prospective national psoriasis longitudinal closed cohort study devoted to surveillance of skin cancers (non-melanoma skin cancer and melanoma). The aims of this project are to gain information on the incidence of skin cancers in patients exposed to any biological agent or cyclosporine versus non-exposed patients (the duration of prior exposition to methotrexate will be taken into consideration), predictive factors and the natural history. The study duration will be 6 years, and the number of patients needs to be calculated. Visits will be every 6 months during 3 years and then every year for 3 years. Participating dermatologists will be paid per included patient. The second is a retrospective cohort, followed by the prospective one. Potential grants will come from the French drug agency, cancer leagues and the French Society of Dermatology.
Israel
In Israel there is a psoriasis surveillance system, which was started on January 1, 2007. Since then, 875 patients who started a new systemic medication or phototherapy have been followed prospectively (acitretin n = 199, methotrexate n = 217, etanercept n = 104, infliximab n = 19, alefacept n = 11, adalimumab n = 87, efalizumab n = 17, PUVA n = 48). The cohort also includes patients with psoriasis who started a biological treatment for co-existent arthritis.

The Psoriasis surveillance system in Israel is based on a health maintenance organization, Clalit Health Services (CHS). CHS is Israel's largest health management organization and insures 3.8 million persons, which represent 54% of the total Israeli population. CHS has a comprehensive computerized database that has continuous real-time input from pharmaceutical, medical and administrative computerized operating systems.

In the current study, data are collected using datamining techniques utilizing the CHS database. The Psoriasis study in Israel was approved by a hospital-based ethical committee, which granted the access to the electronic data set.

A cohort of 15,403 patients with psoriasis has been identified in CHS. In this cohort each patient who is prescribed for the first time during his/her illness one of the biological agents, acitretin or methotrexate, or who starts phototherapy is entered into the study.

A longitudinal follow-up of the patient is performed every 6 months to monitor serious adverse events, especially opportunistic infections, diagnosis of cancer, autoantibody production and organ involvement or failure (liver, kidney, heart, haematological, musculoskeletal, lung) requiring hospitalization.

Portugal
Portugal is also prepared to start a registry. It will begin in a first phase within 3 centres localized one each in the south, the centre and another in the north of Portugal. The registry will be based on a comprehensive computerized database that also supports the Pharmacy and Therapeutic Committee of the main and bigger Portuguese hospitals. The mentioned computerized database is under the supervision of the Clinical Director of those hospitals. In this way, any change in the prescription of biologicals (withdrawal, changes in therapeutics or treatment of adverse effects) both for psoriasis and rheumatic diseases will be detected and registered, and therefore pharmacists and clinicians have all the information needed to study and do the follow-up of these cases. With this methodology, all the adverse effects of biologicals that occur in hospitals can be traced.
This model can easily be implemented in the majority of Portuguese hospitals. Support will be given by the Portuguese Government using a grant for that purpose.

**Germany**

In Germany, a national psoriasis registry, ‘PsoBest’, has been established in December 2007, which will document the long-term course of patients administered a defined biological or conventional systemic drug for the first time (fumaric acid, methotrexate, cyclosporine A, efalizumab, etanercept, infliximab and adalimumab). Four hundred and fifty-nine psoriasis centres (clinics and office-based dermatologists) are included, and 3,500 psoriasis patients with and without arthritis will be followed for 5 years after starting biological or other systemic therapies for psoriasis. A patient will be included at the first initiation of the treatment and will remain in the registry for 5 years, regardless of the subsequent therapy. Major outcome criteria include effectiveness in the long term, that of combined/alternating treatments and under comorbidity conditions, patient-defined benefits and quality of life, maintenance doses, prediction of response and safety. Follow-ups will be every 3 months, comprising patient and treatment characteristics, clinical parameters, patient-defined benefit, quality of life and adverse events. Standardized questionnaires will be administered to the patient and to the dermatologist 12 times at the dermatology centres. At interim intervals, patients are directly contacted another 9 times by mail. Requirements of EMEA guidance volume 9a and of relevant international guidelines on outcome research in observational studies are incorporated. Scientific quality is assured by an advisory board, by the AWMF (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften), EMEA and BfArM (Bundesinstitut für Arzneimittel und Medizinprodukte) consultation and by DIN ISO 9001:2000 certification. Descriptive reports will be generated regularly, hypotheses will be tested e.g. by MAN(C)OVA, multiple/logistic/survival regression and multilevel modelling. Comparisons between cohorts will be achieved by propensity score matching.

**The Netherlands**

In the Netherlands until now, there have been only local initiatives to collect data on systemic therapies for psoriasis. Two academic centres, Radboud University Nijmegen Medical Centre and the Academic Medical Center in Amsterdam, have separately built an electronic database with data on patients who have been treated with biologics, since their registration for psoriasis. Some of these data are published already.17-19 Recently
the set-up of a national registry has been started by adjusting the local registries. The programme is in a very early stage, but fast realization is aimed at. The registry will be on a voluntary base and especially academic centres will participate to start with.

**PSONET, INTERNATIONAL INITIATIVE**

**Purpose**
The ‘Psonet’ initiative is a prospective observational cohort study that integrates data from independent national psoriasis registries of 9 European countries. In 2005, the Study Centre of the Italian Group for Epidemiologic Research in Dermatology obtained a research grant from the Italian Drug Agency to establish this international collaboration. Psonet is designed to perform coordinated postmarketing surveillance studies of systemic psoriasis therapies to monitor the effectiveness and safety of these treatments in clinical practice, for instance to identify factors that predict adverse effects of systemic agents for psoriasis. By combining data from multiple registries, the network will have greater power in assessing safety and effectiveness than a single country’s registry.

**Set-Up**
Countries participating in Psonet are France, Germany, Israel, Italy, the Netherlands, Portugal, Spain, Sweden and the UK. A minimum set of data to be collected by all participating registries as well as recruitment methods and follow-up procedures, are defined by an interactive process among investigators.

Most data integrated in the Psonet registry are primary data (collected for direct purposes of the registry), some are secondary. For instance in the Israeli registry, the data are collected by data-mining from a national health service registry.

Dermatologists at the participating centres will collect data as part of clinical care for included patients. All consecutive eligible patients (those who consent) should be enrolled to minimize selection bias. Eligibility for enrolment in the Psonet cohort requires treatment with systemic therapies for psoriasis. In most registries, data collection will be web based and often in real time.

For Psonet, internal comparison groups, often stratified by type of treatment, will be utilized. For internal comparisons, analyses of event occurrence in groups defined by different dosages/duration of treatment and/or different drugs will be performed. External
comparison of event rates to selected external population samples will also be performed. For rare events such as cancer incidence, only marked increases in incidence (i.e. twice or more) compared to the general population are likely to be detected and considered as robust, particularly given the potential selection biases in our cohort.

**Therapies**
The systemic therapies considered in Psonet are methotrexate, PUVA phototherapy, cyclosporine, fumaric acid, etanercept, efalizumab, infliximab, and adalimumab. Collection may be limited to biological agents in some countries (table 1). To be eligible, patients must receive at least one single dose of one given systemic treatment for the first time. Once enrolled, they will be followed independently of subsequent therapies received.

**Population**
The study population will consist of all subjects with active psoriasis in participating centers who receive a specific systemic agent for the first time for their disease. Only patients enrolled in a national registry will be included in the Psonet cohort. There are no restrictions regarding age, comorbidity and comedication and number of prior systemic treatments.

**Data**
For the proposed common variables to be collected, see table 2. All national registries can collect additional elements for individual analysis if desired. According to adverse event, additional information may be requested from medical records or the patient.

**Follow-Up**
Our goal is to have an active follow-up (at least 2 contacts/year) of all enrolled patients, irrespective of the subsequent therapy. We hope to achieve a follow-up of at least 80% of surviving patients for 5-year. Patient retention is especially important to prevent selective loss to follow-up. Experiences from a European collaboration of rheumatology registries have shown that drop-out rates are low.\(^{10}\)
### Data to be collected at baseline visit

<table>
<thead>
<tr>
<th>Demographics and constitutional variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
</tbody>
</table>

Psoriasis characterization

<table>
<thead>
<tr>
<th>First diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous systemic treatments</td>
</tr>
<tr>
<td>Type of psoriasis at entry</td>
</tr>
<tr>
<td>Articular symptoms</td>
</tr>
</tbody>
</table>

Comorbidity

<table>
<thead>
<tr>
<th>Cardiovascular and metabolic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>Cancer</td>
</tr>
<tr>
<td>Kidney and liver disease</td>
</tr>
</tbody>
</table>

Medical status

<table>
<thead>
<tr>
<th>Current treatment and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comedication</td>
</tr>
</tbody>
</table>

### Data to be collected at follow-up visits

<table>
<thead>
<tr>
<th>Assessment of response to treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. Psoriasis Area and Severity Index, body surface area, Physician Global Assessment</td>
</tr>
</tbody>
</table>

Safety assessment

<table>
<thead>
<tr>
<th>Relevant adverse events associated with treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations and cause for hospitalizations</td>
</tr>
</tbody>
</table>

New diagnoses of cancer

New diagnosis of infection leading to specialist consultation or hospitalization

Therapies

<table>
<thead>
<tr>
<th>Current treatment and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for discontinuation of therapy if applicable</td>
</tr>
<tr>
<td>Alternative therapy if applicable</td>
</tr>
<tr>
<td>Change in comedication</td>
</tr>
</tbody>
</table>

### Table 2. Common data variables to be collected at baseline and follow-up visits

**Consent**

Patient will be informed that his/her medical records will be anonymously utilized for an international observational study. Informed (written) consent will be obtained. Detailed arrangements concerning data ownership and security are being negotiated.
Data Handling
At regular intervals, common data elements from participating national registries will be transmitted to Psonet for inclusion in a centralized database. The International Coordinating Committee will manage the data and ensure that data confidentiality is maintained. Consistency checks of the data will be performed, and simple descriptive tables of the data collected will be prepared and circulated among participants after each update.

Analyses
Initially, descriptive analyses will be performed. Subsequently, hypothesis-driven analyses will be made using, as appropriate, more advanced analytical methods, e.g. multivariate models.

An overall description of the patient outcomes stratified by age and sex as well as predictors of response and risk for each systemic agent will be regularly prepared. We will compare relative rates of adverse events among systemic treatments. For rare events such as cancer incidence, only marked increases in incidence (i.e. twice or more) compared to the general population are likely to be detected and considered as robust, particularly given potential selection biases in our cohort. In addition, analyses will be aimed at:
- evaluating the safety and efficacy of treatment in patients generally excluded from clinical trials, e.g. patients with multiple diseases, older subjects, etc;
- identifying prognostic factors for response;
- identifying characteristics of patients less likely to respond and more likely to experience complications and adverse events.

Comparisons with data from external source databases may also be considered. In countries/regions covered by cancer registries, standardized incidence ratios for lymphoma and other cancers may be computed (i.e. the ratio between the observed number of cases and the expected number using the sex- and age-specific incidence data from the cancer registry). For severe infections and other possible events of interest, observed and expected hospitalization rates, using hospital admission data, may be useful for comparison. We will consider other data sources to determine expected numbers of adverse events such as the literature, ad hoc surveys and clinical trial results.
Among the factors we will consider to evaluate the likelihood that observed adverse events are related to a therapy, there are the temporal relation between administration, dose-response relationships, biological plausibility, confounding effects of the disease itself and other treatments.

The steering committee has appointed an International Safety Review Board which will be in charge of reviewing safety data and which will help prepare periodic safety reports. This committee will also be in charge of setting up procedures for the prompt identification and investigation of unexpected serious adverse events.

Current status
Although the set-up of Psonet is quite advanced, there are still some major issues to be addressed. For example, mechanisms to maximize patient retention are not yet fully elaborated.
The adequacy of funding by the Study Centre of the Italian Group for Epidemiologic Research in Dermatology for all efforts is not clear. Additional funds from government foundations or a consortium of pharmaceutical companies may be needed.

Conclusion
Registries for psoriasis treatment are very necessary to compile the long-term data that are now missing for the various systemic psoriasis therapies. A comparable international collaboration of rheumatology registries has shown promising results. Rheumatologists prescribing biologic agents are now better informed on the balance of their benefits and risks. Pharmaceutically initiated post-marketing phase IV studies for newly registered drugs are not sufficient to create long-term data since these studies lack the possibilities of comparing the safety and efficacy of alternative therapies and do not compare new treatments to established therapies.
The Psonet initiative fits well the requirement for a pro-active surveillance of drug safety recently promoted by the EMEA. Psonet has been registered as a European contact network within the program recently issued by the EMEA called European Network of Centres of Pharmacovigilance and Pharmacoepidemiology. Psonet is an investigator-initiated effort committee maintaining its independence. To communicate advancement and results a website has been launched, www.psonet.eu.
Acknowledgements:
The infrastructure of the Psonet initiative is supported by a grant for independent research by the Italian Drug Agency (AIFA), contract FARM5SC2J5 2005

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