**Mapping exercise and status update of eight national registries within the TREatment of ATopic eczema (TREAT) Registry Taskforce**

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**PS** has done consultancies in the past for Sanofi 111017 and AbbVie 041217 (unpaid), received a departmental independent research grants for TREAT NL registry from Pharma since December 2019 for the TREAT NL registry, is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis, for which financial compensation is paid to the department/hospital and, is Chief Investigator (CI) of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children and one of the main investigators of the SECURE-AD registry.

**LG** is one of the main investigators of the TREAT NL registry. She has no further conflicts of interest.

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**Introduction**

Atopic eczema (AE), i.e. atopic dermatitis, is a chronic inflammatory skin condition that affects up to 10% of adults and up to 20% of children and adolescents.1, 2 Patients with moderate-to-severe AE may require systemic immunomodulating medication or photo(chemo)therapy, when topical treatments including corticosteroids and emollients are insufficient. A recent survey among 238 dermatologists from 30 European countries conducted by the TREatment of ATopic eczema (TREAT) Registry Taskforce has shown that these therapies are frequently prescribed off-label in both children and adults.3 At this moment, only ciclosporin and baricitinib, for adults, and dupilumab, for both adults and children from the age of 6 years, are approved for the treatment of AE by the European Medicines Agency. Although there is some evidence on the short-term effectiveness of phototherapy and conventional systemic immunomodulating therapies prescribed in patients with moderate-to-severe AE, a clear knowledge gap for long-term safety, effectiveness and cost-effectiveness remains to exist.

The TREAT Registry Taskforce is a collaborative international network of national registries for AE patients receiving systemic therapy (and phototherapy).4 Patients, both children and adults, receiving phototherapy and/or systemic therapies are included and followed during treatment and after treatment discontinuation. The registries established within the TREAT Registry Taskforce have the common goal to provide long-term comparative and real-life data on effectiveness, safety and cost-effectiveness of therapies for AE. These data are currently lacking.5, 6 Previous work of the taskforce has been to develop a core dataset, consisting of domains and domain items with corresponding measurement instruments, to be captured in AE research registries, to harmonize data collection.7, 8

The aim of developing this core dataset was to increase interoperability, direct comparability and pooling of data, and to reduce heterogeneity in data collection across country borders. Heterogeneity of outcomes used in disease registries has been demonstrated to hinder comparing results and pooling of data between centers and countries. A need to harmonize outcomes has been identified within similar collaborative initiatives for other diseases. Within for example the Psonet initiative (European surveillance network to monitor the long term effectiveness and safety of systemic agents in the treatment of psoriasis) it was observed that heterogeneity between registries results in challenges regarding the conduction of comparative and pooled analyses.9

The TREAT core dataset consists of 19 core domains and 69 domain items, counting 49 baseline items and 20 follow-up items (defining ‘what to measure’).7 As a final step in the harmonization process, the outcome measurement instruments and follow-up frequency and visit window used were determined (defining ‘how to measure’ and ‘when to measure’).8 All affiliated TREAT registries are encouraged to collect data in accordance with this core dataset.

Several registries from different countries have joined the TREAT Registry Taskforce over the past years, currently including A-STAR registry (The UK-Irish Atopic Eczema Systemic Therapy Register; United Kingdom and Ireland), Biobadatop registry (Spain), TREATgermany registry (Germany), TREAT NL registry (the Netherlands and Belgium), SCRATCH registry (Denmark), FIRST registry (French atopIc deRmatitiS cohorT, France), AtopyReg registry (Italy) and SwedAD registry (Sweden). These registries concern prospective observational cohorts and offer a platform to conduct cross-border research. A framework to conduct studies within the taskforce has been published previously.10

Despite the common use of a core dataset, differences in data collection still exist. Between-country differences in data collection include the use of different data entry platforms. Potential differences may also arise due to variability in interpretation of the core dataset and the selection of (optional) core dataset items (in the context of feasibility). Furthermore, patient in- and exclusion criteria may differ per country, for example due to discrepancies in treatment reimbursement and differences in prescribing practices.

Therefore, we aimed to give an overview of the status and characteristics of the established TREAT registries and to perform a mapping exercise. The objective of this mapping exercise was to examine the degree of overlap between the TREAT core dataset and the registries that are currently participating within the TREAT Registry Taskforce and, consequently, the pooling ability between the registries. Ultimately, this will allow us to determine which research questions can be answered in the future by pooling data and how these future analyses can be approached.

**Methods**

The following established registries in the TREAT registry Taskforce were included in this study: the A-STAR registry (the United Kingdom and Ireland), TREAT NL registry (the Netherlands and Belgium), TREATgermany registry (Germany) Biobadatop registry (Spain), SCRATCH registry (Denmark), FIRST registry (France), SwedAD registry (Sweden) and AtopyReg registry (Italy) (n=8).

*Status and characteristics of the registries*

To present a current status update and a description of the characteristics of the registries, we requested the following information of each registry via the contact person as per March 1, 2021: status of recruitment, (planned) month and year of first inclusion, number of included patients, number of participating centers that commenced recruitment, website, data capture platform/modality, language of the database, in- and exclusion criteria of the registry, included therapies and funding sources. In addition, information was collected on the follow-up frequency and visit window applied within the registries, to allow comparison with the defined ‘when to measure’. The results were compiled descriptively in a table.

*Mapping exercise*

All eight established registries were asked to share their dataset (e.g. the (electronic) case report forms ((e)CRFs) used) for the purpose of the mapping exercise. If more than one CRF was used for different timepoints within one registry, multiple CRFs were received. The use of the core dataset and the actual overlap between the core dataset and the registry dataset was identified according to the domains (n=19), domain items (n=69; ‘what to measure’) and measurement instruments (n=118; ‘how to measure’) of the TREAT core dataset.8 We scored positive (+; plus) if the dataset item was completely in accordance with the core dataset, negative (-; minus) if the item was not captured and partially positive (±; plus-minus) if the item was partly corresponding. The degree of overlap was assessed on four predefined levels:

1. Core dataset domain items: we scored the presence of core dataset domain items in each registry dataset.
2. Core dataset measurement instruments: we scored the use of core dataset instruments in each registry dataset, of which usually more are included within one domain item. We considered an instrument partially positive (±) if at least one part or category of the core dataset instrument was used. For example, if the answer categories for topical treatment in a registry were: <30 gr | 30-60 gr | > 60 gr; instead of the predefined categories in the core dataset: <30 gr | 30-60 gr | 60-100 gr | >100 gr, this instrument would be scored partially positive (±).
3. Ability to pool instrument outcomes: the pooling ability of instrument outcomes was scored positive (+) if the outcome of an instrument could be pooled with the outcome of the core dataset instrument. For example, when a national dataset registers age of AE onset, pooling ability of the core dataset domain “year of onset of AE” was scored positive, because we are able to translate age into year of onset.
4. Ability to pool domain item outcomes: the ability to pool outcomes of the domain items was scored positive (+) if pooling of at least one instrument was deemed possible. Otherwise, pooling ability of the domain items was scored negative (-). We considered this the main level of interest.

Uncertainties in data collection were resolved through discussion or per e-mail correspondence. Analyses were performed by using descriptive statistics to summarize the results, using Microsoft Excel.

**Results**

*Status and characteristics of the registries*

The status and characteristics of the registries are summarized in Table 1. All eight registries are currently recruiting. In total, to date, 2356 participants have been recruited to the eight registries, ranging from 20 to 1115 participants per registry. Therapies included in the registries are methotrexate (in 6 of the registries (n=6)), ciclosporin (n=6), azathioprine (n=6), mycophenolate mofetil/mycophenolic acid (n=6), systemic corticosteroids (n=4), dupilumab (n=7), omalizumab (n=5), baricitinib (n=7) and phototherapy (n=3). Three registries also include patients on investigational drugs like tralokinumab, upadacitinib and abrocitinib. Each national registry is a separate entity. Due to local restrictions data is collected in each registry independently, instead of a central collection in one central data entry platform. Funding sources comprise governmental support, pharmaceutical support, charity support, academic support or a combination of these. The in- and exclusion criteria of each national registry are displayed in Table 2.

In context of the defined ‘when to measure’, the follow-up frequency and visit windows of all TREAT registries are shown in Table 3. Although the taskforce has reached consensus on the follow-up frequency and visit window to be applied, differences exist between the registries. A baseline visit is conducted in all registries, but not all registries have specified a follow-up frequency and visit window. When specified, the first follow-up visit after inclusion ranges from 4 weeks to 12 months after baseline. The next follow-up visits during treatment are scheduled ranging from every 3 to (at least) every 12 months. The follow-up frequency after treatment discontinuation varies from no follow-up at all to (at least) every 6 months. Five registries have the option for extra visits, for example in case of switch of therapy or disease flares. The specified visit windows range from 2 weeks to 1 month.

*Mapping exercise*

The assessment and scoring for all four levels per registry can be found in Supplementary Table 1. Briefly, of the 69 core dataset domain items (level 1), 69 items were captured in TREAT NL (the Netherlands), 56 items in A-STAR (UK and Ireland), 40 items in FIRST (France), 33 items in Biobadatop (Spain), 29 items in TREATgermany (Germany), 29 items in SCRATCH (Denmark), 29 items in AtopyReg (Italy) and 20 items in SwedAD (Sweden). Nine out of 118 core dataset instruments (7.6%) were scored positive on instrument overlap in all 8 registry datasets (level 2). Fifteen out of 118 core dataset instruments (12.7%) were scored positive on pooling ability in all 8 registry datasets (level 3). The main level of interest was the ability to pool outcomes within the domain items (level 4) and these results are displayed in Table 4. Of the 69 core dataset domain items, data pooling was possible for 69 items in TREAT NL (the Netherlands), 53 domain items in A-STAR (UK and Ireland), 36 items in TREATgermany (Germany), 36 items in FIRST (France), 29 items in Biobadatop (Spain), 28 items in SCRATCH (Denmark), 28 items in AtopyReg (Italy) and 19 items in SwedAD (Sweden). The number of domain items that scored positive for pooling ability according to the number of registries (level 4) can be found in Figure 1.

**Figure 1. Pooling ability of domain items according to the number of registries**

No. = number; As an example, the red part represents 12 of out 69 (17%) domain items that were deemed possible to pool across 3 registries.

**Discussion**

Since its inception the TREAT Registry Taskforce has aimed to develop an international platform to uniformly collect long-term data on the effectiveness and safety of systemic immunomodulating therapies and/or phototherapy in patients with AE. Currently, the national registries participating within the TREAT Registry Taskforce are jointly collecting data of over 2300 patients. National TREAT registries have successfully been publishing their first results on various data on patient characteristics, treatment aspects and effectiveness and safety individually over the previous years.11, 12 The next step is to increase the power of the data of individual countries by pooling data across registries. As described, the TREAT Registry Taskforce has developed a core dataset to be used in all national registries and a protocol to enable this cross-border data pooling.8, 10 The current study has revealed both similarities and differences regarding the degree of core dataset use and pooling ability between national registries within the TREAT Registry Taskforce.

As for similarities, dataset domain items with the ability to pool data from all eight registry datasets include ‘systemic therapy’ (domain: current AE treatments), ‘physician-assessed clinical signs’ (domains: baseline physician- and patient-reported domains and follow-up physician- and patient-reported domains), ‘patient-reported symptoms’ (domains: baseline physician- and patient-reported domains and follow up physician- and patient-reported domains) and ‘skin-specific quality of life score’ (domains: baseline physician- and patient-reported domains and follow-up physician- and patient-reported domains) (table 4). These examples of overlapping dataset items can be used to perform pooled analyses across all registries.

Differences in data collection were identified on both the domain item and instrument level, affecting the pooling ability of dataset items. Differences may have arisen as the result of various factors. Heterogeneity resulted from an absence of complete overlap in core dataset items, either by absence of the core dataset item or deviation from the predefined core dataset item. After the mapping exercise was finalized, the results were shared among TREAT Registry Taskforce members and a subsequent survey was held to clarify the use of the core dataset in their national registries. Participating members (n=23) mentioned feasibility as the main reason for not including all core dataset items in the registry dataset. The majority of the participants said they are willing to adapt their registry dataset after taking knowledge of the mapping exercise results. Despite the fact that feasibility aspects were considered in the TREAT core dataset consensus seeking process, the high number of domains and domain items included in the core dataset have compromised its feasibility. In addition, countries may have given their own interpretation to core dataset items. Another factor to consider is that, due to national regulations and preferences, different modalities for data collection (e.g. the data entry platform) and languages are used across countries.

Differences in data collection may pose challenges in data pooling and synthesis. The independent collection of data in separate databases allows the introduction of potential differences in registry datasets. If possible, the use of one centralized data entry platform across registries and across countries is strongly recommended, to avoid heterogeneity as much as possible. The present study can inform researchers worldwide who are engaged in similar data harmonization processes in international research groups studying other diseases and who are aiming to perform pooled and comparative analyses in the future. Moreover, we encourage researchers working with AD patients that are treated with systemic treatments and/or phototherapy to join the taskforce. Contact details are found on our website treat-registry-taskforce.org. To every dataset item applies that only the data from registries that scored positive for pooling ability can contribute to pooled analyses. Besides differences in registry datasets, when analyzing data from different countries, one should take into consideration differences in prescribing practices (e.g. patient indications) and reimbursement restrictions, which underlie potential variations in patient populations across the registries. Challenges for synthesizing data in a network of registries are not always avoidable and could result from heterogeneity in both dataset items and populations, leading to potential methodological difficulties.

*Future perspectives*

The overview of the status and characteristics presented here provides insight into all established registries within the TREAT Registry Taskforce. The results of the mapping exercise inform on which data from which registries can be used to answer specific research questions and therefore will facilitate comparative or joint analyses across country borders in the future. For example, the intention to perform inter-country analyses will aid in answering research questions regarding safety as large numbers of patients are needed to detect rare events like malignancies. Studies within the TREAT Registry Taskforce will run as investigator-led projects but we are open to project proposals requested by others. This way researchers, clinicians and other stakeholders can request the investigation of specific research questions within the taskforce. Financial support will be needed for this, for example from charities, governments and pharmaceutical companies. As a next step, the technical compatibility of the registry data will be assessed in a separate pooling exercise. In addition, we are currently performing an analysis on baseline demographic and clinical characteristics of patients included in all registries.

*Conclusion*

Despite the aspired use of a predefined core dataset, differences exist in data collection within the TREAT Registry Taskforce that pose potential challenges in data pooling and synthesis. Differences in data collection can result from various factors, including the use of different data entry platforms per registry, the use of different inclusion and exclusion criteria and potential differences in patient populations. When performing inter-country analyses, these differences in data collection should be taken into consideration in the analyses and interpretation of results.

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**Table 1**. Description and status of the TREAT registries, as of 1st of March 2021

|  |  |
| --- | --- |
|  | **Registry name, country** |
|  | **A-STAR,****UK and Ireland** | **TREAT NL,****the Netherlands** | **TREATgermany,****Germany** | **Biobadatop,****Spain** | **SCRATCH,****Denmark** | **FIRST,****France** | **SwedAD,****Sweden** | **AtopyReg,****Italy** |
| **Status** | Recruiting | Recruiting | Recruiting | Recruiting | Recruiting | Recruiting | Recruiting | *No answer yet* |
| **(Planned) month and year of first inclusion** | October 2018 | November 2017 | June 2016 | April 2020 |  | October 2020 | September 2019 |  |
| **N included patients (March 1, 2021)** | 136 | 490 | 1.115 | 56 | 250 | 20 | 289 |  |
| **N participating centers**  | 13 | 5 | 38 | 8 | 5 | 1 | 17 |  |
| **Countries involved** | UK and Ireland | The Netherlands and Belgium | Germany | Spain | Denmark | France | Sweden |  |
| **Website** | [https://astar-register.org](https://eur04.safelinks.protection.outlook.com/?url=https%3A%2F%2Fastar-register.org%2F&data=04%7C01%7Ca.h.musters%40amsterdamumc.nl%7C9326afbff82240c276fe08d8ee96dcfd%7C68dfab1a11bb4cc6beb528d756984fb6%7C0%7C0%7C637521679038840298%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=T2JjI3BG9fuVk4fkEH9M4KmZ%2FtPa7iYylr9ij3JguFw%3D&reserved=0) | [www.treatregister.nl](http://www.treatregister.nl)  | [www.treatgermany.org](http://www.treatgermany.org)  | <https://aedv.es/investigacion/proyectos-de-investigacion/>  | - | - | [www.swedAd.nu](https://eur04.safelinks.protection.outlook.com/?url=http%3A%2F%2Fwww.swedad.nu%2F&data=04%7C01%7Ca.h.musters%40amsterdamumc.nl%7C37efd5021eba4108000b08d8de3b1e2f%7C68dfab1a11bb4cc6beb528d756984fb6%7C0%7C0%7C637503692794637907%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=SnpVdgvYBrFFmQUWz%2Bmd%2FKAbxgAQk7OMHreCShzSCwY%3D&reserved=0) |  |
| **Data capture modality** | A-STAR eCRF.Data transribed from paper CRF. | Castor (eCRF) | REDCap Database (eCRF) | RedCap (eCRF) | Zitelabs own software and platform | Epiconcept (Healthcare data host), Voozanoo 4 Software | Carmona, dermareg |  |
| **Language of database** | English | English | German | Spanish | Danish | French | Swedish |  |
| **Funding** | Governmental support, pharmaceutical support, charity support | Governmental support, pharmaceutical support, academic support | Pharmaceutical support | Pharmaceutical support | Pharmaceutical support | Academic support  | Governmental support, pharmaceutical support |  |
| **Conventional systemic therapies included:** |
| **Methotrexate** | Yes | Yes | Yes | Yes | No | Yes | Yes |  |
| **Ciclosporin** | Yes | Yes | Yes | Yes | No | Yes | Yes |  |
| **Azathioprine** | Yes | Yes | Yes | Yes | No | Yes | Yes |  |
| **Mycophenolate mofetil/acid** | Yes | Yes | Yes | Yes | No | Yes | Yes |  |
| **Systemic corticosteroids** | Yes | Yes | Yes | Yes | No | No | No |  |
| **Biologicals included:** |
| **Dupilumab** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |  |
| **Omalizumab** | Yes | Yes | Yes | Yes | No | Yes | No |  |
| **Baricitinib** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |  |
| **Phototherapy included:** |
| **BB-UVB** | No | Yes | Yes | Yes | No | No | No |  |
| **NB-UVB** | No | Yes | Yes | Yes | No | No | No |  |
| **UVA** | No | Yes | Yes | Yes | No | No | No |  |
| **UVA1** | No | Yes | Yes | Yes | No | No | No |  |
| **UVAB** | No | Yes | Yes | Yes | No | No | No |  |
| **PUVA** | No | Yes | Yes | Yes | No | No | No |  |
| **Other therapies included:** |
|  | TralokinumabUpadacitinibAbrocitinib |   | Tralokinumab, Upadacitinib, Abrocitinib,Pimecrolimus, Tacrolimus |  |  | Tralokinumab,Upadacitinib |  |  |

A-STAR, The UK-Irish Atopic Eczema Systemic Therapy Register; FIRST, French atopIc deRmatitiS cohort; TREAT, TREatment of ATopic eczema.

**Table 2**. Inclusion and exclusion criteria of the TREAT registries

|  |  |  |
| --- | --- | --- |
| **Registry name, country** | **Inclusion criteria** | **Exclusion criteria** |
| **A\*STAR, UK and Ireland** | * Paediatric and adult patients with AE who due to the severity of their disease and/or impact on quality of life are commencing on or switching to another systemic immuno-modulatory agent (e.g. CsA, AZA, MTX or biologic treatments);
* Written informed consent for study participation obtained from the patient or parents / legal guardian, with assent as appropriate by the patient, depending on the level of understanding;
* Participants consent to participate in long-term follow up and access to all medical records, including hospital admission records and linkage to data held by NHS bodies or other national providers of healthcare data;
* Diagnosis of AE in keeping with the UK diagnostic criteria;
* Willingness to comply with all study requirements;
* Competent use of English language, according to patient’s age (capable of understanding patient questionnaires).
 | * Insufficient understanding of the study by the patient and/or parent/guardian;
* Patients who are currently participating in a randomised clinical trial.
 |
| **TREAT NL, the Netherlands** | * Patient has a diagnosis of AE, based on the U.K. working party’s diagnostic criteria;
* Starts with any type of phototherapy (e.g. UVB) or systemic immunomodulating therapy (e.g. CsA, systemic glucocorticosteroids, AZA, MTX, MPA, dupilumab);
* Has voluntarily signed and dated an informed consent prior to any study related procedure or has a legal representative to do so and is willing to comply with the requirements of this study protocol.
 | * Patient uses only (systemic) antibiotics or antihistamines;
* Patient starts with systemic immunomodulating therapy for another indication than AE;
* Insufficient understanding of the study by the patient or parent/legal representative.
 |
| **TREATgermany, Germany** | * Age ≥ 18 years;
* AD according to the UK working party diagnostic criteria: moderate-to-severe AE;
* Objective SCORAD > 20 or currently anti-inflammatory systemic treatment for AE or previous anti-inflammatory systemic treatment for AE within past 24 months.
 | Not defined |
| **Biobadatop, Spain** | * Any age;
* First time use of systemic treatment.
 | * Unable to provide consent, current participation in a clinical trial, intention to move in the next three months.
 |
| **SCRATCH, Denmark** | * Moderate to severe AE (EASI>16 and DLQI>10 or POEM>16)
 | Not defined |
| **FIRST, France** | * Age ≥ 18 years;
* Systemic treatment.
 | * No systemic treatment (other than phototherapy)
 |
| **SwedAD, Sweden** | * Age ≥ 5 years;
* Systemic treatment.
 | Not defined |
| **AtopyReg, Italy** | *No answer yet* | *No answer yet* |

**Table 3**. Visit schedule and window of the TREAT registries

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Registry name, country** | **Baseline visit** | **First follow-up visit after baseline** | **Follow-up while on treatment**  | **Follow up after treatment discontinuation**  | **Visit schedule window (aspired maximum deviation (**+/-**) from visit schedule)** | **Extra visits (optional)** |
| **A-STAR, UK and Ireland** | Baseline | 4 weeks | 3 months | 6 months | * Baseline: 28 days
* First follow-up: 2 weeks
* Thereafter: 1 month
 | * Therapy switch (schedule restarts at baseline)
* End of therapy visit
 |
| **TREAT NL, the Netherlands** | Baseline | 4 weeks | 3 months | 6 months | * 1 month
 | * (Re)start/switch of therapy (schedule restarts at baseline)
* Unscheduled visit (e.g. in case of therapy side-effects or disease flare-ups)
 |
| **TREATgermany, Germany** | Baseline | 3 months | 6 months (3 months if new systemic treatment) | 6 months | * 2 weeks
 | * Therapy switch
* Therapy side-effects
* Disease flare-ups
* Extra patient questionnaire (every 2 years)
 |
| **Biobadatop, Spain** | Baseline | 3 months | At least every 12 months | At least every 12 months | * As indicated by standard clinical practice
 | * Second follow-up visit (6 months after baseline)
 |
| **SCRATCH, Denmark** | Baseline | Usually 4 weeks (not specifically defined) | Not defined | None, follow-up ends after treatment discontinuation | Not defined | Not defined |
| **FIRST, France** | Baseline | At least in 12 months | At least every 12 months  | At least every 12 months | 1 month | Not defined |
| **SwedAD, Sweden** | Baseline | Usually 1 month (not specifically defined) | 3-6 months (not specifically defined) | 3-6 months (not specifically defined) | Not defined | * Therapy side-effects
* Therapy switch
 |
| **AtopyReg, Italy** | Baseline | 6 months | 6 months | 6 months | *No answer yet* | Not defined |

**Table 4**. Pooling ability of the TREAT core dataset domain items for each registry

|  |  |  |
| --- | --- | --- |
|  |  | **Registry name, country** |
| **Domain** | **Domain item** | **A-STAR,****UK and Ireland** | **TREAT NL,****the Netherlands** | **TREATgermany,****Germany** | **Biobadatop,****Spain** | **SCRATCH,****Denmark** | **FIRST,****France** | **SwedAD,****Sweden** | **AtopyReg,****Italy** |
| **Demographics** | Date of birth | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Date of enrolment into registry | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Gender | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |
|  | Ethnicity | ✔ | ✔ |  |  |  |  |  | ✔ |
|  | Educational status | ✔ | ✔ | ✔ |  | ✔ | ✔ | ✔ | ✔ |
|  | Current occupation or education | ✔ | ✔ | ✔ |  |  |  | ✔ |  |
| **AE diagnosis** | How diagnosis AE is established | ✔ | ✔ |  |  | ✔ | ✔ |  |  |
|  | Use of validated diagnostic criteria | ✔ | ✔ | ✔ | ✔ |  | ✔ | ✔ |  |
|  | Date of onset AE | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Past AE treatments** | Phototherapy | ✔ | ✔ | ✔ | ✔ |  | ✔ |  | ✔ |
|  | Systemic therapy  | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |
|  | Topical treatments for AE  | ✔ | ✔ | ✔ | ✔ |  | ✔ |  | ✔ |
|  | Day hospital care treatments for AE (outpatient)  |  | ✔ | ✔ |  |  |  |  |  |
|  | Hospitalisation for AE |  | ✔ | ✔ |  |  |  |  |  |
| **Current AE treatments** | Phototherapy | ✔ | ✔ | ✔ | ✔ |  | ✔ | ✔ | ✔ |
|  | Systemic therapy | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Topical treatments for AE | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |
|  | Amount of topical creams/ointments used per week  |  | ✔ |  |  |  |  |  |  |
| **Family history of AE or allergic diseases** | Family history of AE or allergic diseases | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Allergic co-morbidities** | Asthma | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Allergic rhinoconjunctivitis | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Atopic eye disease | ✔ | ✔ |  | ✔ | ✔ | ✔ |  |  |
|  | Eosinophilic oesophagitis | ✔ | ✔ |  | ✔ |  |  |  | ✔ |
|  | Food allergies | ✔ | ✔ | ✔ |  | ✔ | ✔ |  | ✔ |
|  | Contact allergies | ✔ | ✔ |  | ✔ |  |  |  |  |
| **Other past and current co-morbidities** | Malignancies | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |
|  | Serious infections | ✔ | ✔ | ✔ | ✔ |  | ✔ |  |  |
|  | Other significant illnesses | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |
| **Current concomitant medication (i.e. other than specific AE medication)** | Antihistamines |  | ✔ | ✔ |  |  |  |  |  |
|  | Antibiotics |  | ✔ | ✔ |  |  |  |  |  |
|  | Other medication relevant for AE treatment response |  | ✔ |  |  |  |  |  |  |
|  | Immunosuppressives for other inflammatory diseases |  | ✔ | ✔ |  |  |  |  |  |
| **Baseline general AE questions** | Exposures that trigger disease flares | ✔ | ✔ |  |  | ✔ | ✔ |  |  |
|  | Episodes of skin infection | ✔ | ✔ | ✔ |  |  | ✔ |  |  |
|  | Days lost from usual activities (e.g. work, study) | ✔ | ✔ | ✔ |  |  |  |  |  |
| **Baseline physical examination** | Fitzpatrick skin type | ✔ | ✔ |  |  |  | ✔ |  |  |
|  | Skin examination  | ✔ | ✔ |  |  |  | ✔ |  | ✔ |
| **Baseline physician- and patient-reported domains** | Physician-assessed clinical signs | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Investigator/physician global assessment  | ✔ | ✔ | ✔ |  |  | ✔ |  |  |
|  | Patient-reported symptoms | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Patient global assessment  |  | ✔ |  |  |  | ✔ |  |  |
|  | Generic quality of life score  | ✔ | ✔ | ✔ |  |  |  |  |  |
|  | Skin-specific quality of life score  | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Patient-reported satisfaction with AE care received |  | ✔ | ✔ |  | ✔ |  |  |  |
|  | Impact of AE on the family  |  | ✔ |  |  |  |  |  |  |
| **Baseline investigations**  | Full blood count | ✔ | ✔ |  |  |  |  |  |  |
|  | Liver function | ✔ | ✔ |  |  |  |  |  |  |
|  | Kidney profile  | ✔ | ✔ |  |  |  |  |  |  |
|  | Evaluating TPMT level prior to azathioprine use  | ✔ | ✔ |  |  |  |  |  |  |
| **Baseline management** | Main reasons for choosing specific treatment (systemic or phototherapy) | ✔ | ✔ | ✔ |  |  |  |  |  |
|  | Relative contraindication(s) for selected treatment |  | ✔ |  |  |  |  |  |  |
| **Follow up general AE questions** | Days lost from usual activities  | ✔ | ✔ | ✔ |  | ✔ |  |  |  |
|  | Change in diagnosis after enrolment | ✔ | ✔ |  |  |  |  |  |  |
|  | Date of death and relation to AE  | ✔ | ✔ | ✔ |  |  |  |  |  |
| **Follow up physical examination** | Skin examination | ✔ | ✔ | ✔ |  |  | ✔ |  | ✔ |
| **Follow up physician- and patient-reported domains** | Physician-assessed clinical signs | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Investigator/physician global assessment  | ✔ | ✔ | ✔ |  |  | ✔ |  |  |
|  | Patient-reported symptoms | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Patient global assessment |  | ✔ | ✔ |  |  | ✔ |  |  |
|  | Generic quality of life score | ✔ | ✔ | ✔ |  |  |  |  |  |
|  | Skin-specific quality of life score | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
|  | Reporting of disease control |  | ✔ | ✔ |  |  |  |  |  |
|  | Adherence to treatment between appointments |  | ✔ |  |  |  |  |  |  |
|  | Patient-reported satisfaction with AE care received |  | ✔ | ✔ |  | ✔ |  |  |  |
|  | Impact of AE on the family |  | ✔ |  |  |  |  |  |  |
| **Follow up investigations**  | Full blood count  | ✔ | ✔ |  |  |  |  |  |  |
|  | Liver function | ✔ | ✔ |  |  |  |  |  |  |
|  | Kidney profile | ✔ | ✔ |  |  |  |  |  |  |
| **Follow up adverse events** | Severe adverse events | ✔ | ✔ | ✔ | ✔ | ✔ |  | ✔ |  |
| **Follow up management** | Reason for switching therapy |  | ✔ | ✔ | ✔ |  |  |  |  |
|  | Reason for discontinuation of therapy |  | ✔ | ✔ | ✔ | ✔ |  | ✔ | ✔ |