Protocol Title:

Pustular psoriasis, eLucidating Underlying Mechanisms (PLUM)

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1. Study synopsis

Title of study (acronym)	**P**ustular psoriasis, e**L**ucidating **U**nderlying **M**echanisms (PLUM)
Sponsor name	Guy's and St. Thomas' NHS Foundation Trust
Chief Investigator	Prof. Catherine Smith
IRAS Identifier	201357
Disease under investigation	Pustular Psoriasis
Purpose of study	Elucidate the pathogenic mechanisms underlying pustular psoriasis, through genetic and functional studies.
Primary objectives	1. To identify novel genetic determinants for pustular psoriasis. 2. To determine the biological impact of pustular psoriasis mutations on IL-1 signalling and innate immune function 3. To establish a case-control bio-resource (including DNA, RNA and tissue) for future research studies of pustular psoriasis and other autoinflammatory/neutrophilic dermatoses
Secondary objectives	1. To establish correlations between genotype and clinical phenotype. 2. To establish correlation between genotype and response to systemic treatment.
Sample Size	Affected cases: n≥300 Healthy controls: n≥250 Disease controls: n≥250
Summary of eligibility criteria	<u>Pustular psoriasis cases</u> Patients with pustular psoriasis (including

	generalised pustular psoriasis, acrodermatitis continua of Hallopeau and palmar plantar pustulosis) diagnosed by a trained dermatologist Healthy Controls Healthy individuals who do not have a family history of plaque psoriasis or inflammatory skin disease Disease controls Patients affected by other autoinflammatory syndromes or neutrophilic dermatoses, diagnosed by a trained specialist (e.g. a nephrologist, rheumatologist or dermatologist as appropriate).
Version and date of protocol amendments	Version 1.0_05/10/2016 Version 1.1_03/04/2017

2. Disease definitions and Glossary of Terms

2.1 Disease definitions

The European Rare And Severe Psoriasis Expert Network (ERASPEN http://eraspen.eu/home.html) have recently sought to harmonise phenotypic descriptions of pustular psoriasis, and these criteria will be used in this study as follows:

i. Acrodermatitis Continua of Hallopeau.
   Primary, persistent (> 3 months), sterile, macroscopically visible pustules affecting the nail apparatus
ii. Palmoplantar Pustulosis.
   Primary, persistent (> 3 months), sterile, macroscopically visible epidermal pustules on palms and/or soles
iii. Generalised Pustular Psoriasis
   Primary, sterile, macroscopically visible epidermal pustules on non-acral skin (excluding cases where pustulation is restricted to psoriatic plaques)
   a. With / without plaque psoriasis
   b. With / without systemic inflammation
   c. Relapsing (>1 episode) or persistent (> 3months)
iv. Acral Pustular Psoriasis
   Forms of pustular psoriasis affecting the hands and / or feet

2.2 Glossary of Terms

APP	Acral Pustular Psoriasis
APRICOT	Anakinra for Pustular psoriasis: Response in a Controlled Trial
CAPS	Cryopyrin-Associated Periodic Syndromes
GPP	Generalised Pustular Psoriasis

SAE Serious Adverse Event

3. Background and rationale

Pustular psoriasis presents with the eruption of monomorphic, sterile, neutrophilic pustules on painful, intensely inflamed, red skin. The disease may be chronic and localised, typically involving the hands and feet (Acral Pustular Psoriasis; APP), or, more rarely, generalised, episodic and potentially life-threatening (generalised pustular psoriasis; GPP). Although pustular psoriasis accounts for less than 10% of psoriasis cases, it consistently ranks highest among all disease variants in terms of symptoms and functional impairment[1].
Management of plaque-type disease has been revolutionised in the last 10 years with the advent of biological therapies, driven in great part by the discovery of underlying pathogenic pathways[2]. In contrast, treatment options for pustular psoriasis remain profoundly limited. There is therefore a significant unmet need in this patient group[3].

The poor response in pustular psoriasis to therapies used to great effect in plaque type disease may be explained by genetic evidence that has emerged in recent years. This indicates that the molecular pathways underlying pustular psoriasis are distinct and involve the interleukin (IL)-36/IL-1 axis. In fact, we and others have identified deleterious *IL36RN* mutations in both GPP and APP[4].
IL36RN encodes the IL-36 receptor antagonist (IL-36Ra), which contrasts the pro-inflammatory activity of IL-36 cytokines. Disease mutations disrupt the inhibitory function of IL-36Ra, causing enhanced production of inflammatory molecules, including IL-1[5, 6].

Underscoring the success of our pustular psoriasis gene identification programme, we have also been able to uncover disease associated mutations in *AP1S3*, a gene that contributes to the regulation of innate immune homeostasis[7]. Thus, genetic studies suggest that APP may be an autoinflammatory condition caused by abnormal activation of innate immune cells and enhanced IL-1 production.

On this basis, a clinical trial of the IL-1 antagonist anakinra (**A**nakinra for **P**ustular psoriasis: **R**esponse in a **Co**ntrolled **T**rial; APRICOT) will be shortly initiated by Prof Catherine Smith and collaborators across the UK. Dr Capon will be leading associated mechanistic studies, which will aim to validate the pathogenic role of IL-1, by integrating the results of genetic analysis, transcription profiling and immune phenotyping experiments. A number of these investigations will be undertaken prior to treatment initiation, so that their power would be substantially enhanced by the recruitment of further patients outside the trial.

The ascertainment of extended patient resources would also enable the discovery of further disease genes and pathways, allowing us to investigate whether the processes underlying the pathogenesis of pustular psoriasis overlap with those that cause other IL-1 mediated autoinflammatory conditions.

In this context, the recruitment drive initiated by APRICOT can be leveraged to boost the power of gene identification studies through the ascertainment of individuals who may be unwilling or ineligible to take part into a formal interventional study but would nevertheless be happy to contribute to research. The availability of these subjects will in turn benefit the mechanistic studies associated with APRICOT. Thus, the synergy between the two companion investigations will facilitate gene discovery and enable rigorous clinical research.

4. Study objectives

4.1. Primary objectives

1. To identify novel genetic determinants for pustular psoriasis.
2. To determine the biological impact of pustular psoriasis mutations on IL-1 signalling and innate immune function
3. To establish a case-control bio-resource (including DNA, RNA and tissue) for future research studies of pustular psoriasis and other autoinflammatory/neutrophilic dermatoses.

4.2 Secondary objectives

1. To establish correlations between genotype and clinical phenotype.
2. To establish correlation between genotype and response to systemic treatment.

5. Study design

PLUM is an observational multi-cohort multi-centred research study. Participants are required to attend one study visit, and possibly some recall visits, at which clinical data and blood samples are collected for the research aims below.

5.1 Discovery of disease associated mutations

DNA analysis

Patient DNA will be examined by whole-exome/whole-genome sequencing or by targeted screening of candidate genes, with a view to identifying disease associated mutations.

RNA analysis

If a mutation is identified in a known or novel gene, its effect on gene expression will be assessed by examining RNA levels in the relevant cases and by comparing them to those observed in healthy controls and in individuals affected by other neutrophilic dermatoses or IL-1 mediated autoinflammatory syndromes (disease controls).

Plasma analysis

The effect of pustular psoriasis mutations will be further assessed by measuring plasma cytokine levels in the relevant cases and by comparing them to those observed in healthy and diseased controls.

5.2 Functional characterisation of disease-associated mutations

Functional assays

To determine the biological impact of disease mutations, the samples obtained from cases and controls will be compared in functional studies. These may include measurements of RNA levels, immune phenotyping and/or stimulation of keratinocyte cultures. To facilitate the latter experiments, the patient and control cells may be immortalised.

Genotype-phenotype correlations

In the final stage of the study the genotype of the patients will be correlated to the clinical presentation of the disease and to the response to treatment with systemic agents, using the information collected in the case report forms.

6. Selection and withdrawal of participants

6.1 Inclusion criteria

Pustular psoriasis cases

- Patients with pustular psoriasis (including generalised pustular psoriasis, acrodermatitis continua of Hallopeau and palmar plantar pustulosis) diagnosed by a trained dermatologist, based on the diagnostic criteria set up by the European Rare And Severe Psoriasis Expert Network (http://eraspen.eu/home/rfp/diagnostic-criteria.html)
- Affected relatives of patients with pustular psoriasis

Healthy Controls

- Healthy individuals who do not have a family history of plaque psoriasis or inflammatory skin disease
- Unaffected relatives of patients with pustular psoriasis

Disease controls

- Patients affected by other autoinflammatory syndromes or neutrophilic dermatoses, diagnosed by a trained specialist (e.g. a nephrologist, rheumatologist or dermatologist as appropriate).

6.2 Exclusion criteria

1. Individuals who are unable to give written informed consent
2. Individuals who have received a blood transfusion within 4 weeks
3. Individuals who are known to be infected with HIV, HBV or other blood-borne viruses

6.3 Recruitment strategies and procedures

Participating centres will recruit to the patients with pustular psoriasis cohort only unless otherwise agreed with the central study team at set up.

Ascertainment of patients with pustular psoriasis

Pustular psoriasis patients (n>300, see calculations in 9.1) will be ascertained as follows:

(i) In clinic at participating sites

Potentially eligible patients will be identified in clinics and approached initially by a member of the direct clinical care team. The study will be explained and the patient (and/or their parents, if the patient is younger than 16) will be provided with an appropriate information leaflet. Patients will be given as much time as they require to come to a decision regarding their participation or at least 24hrs.

(ii) Via existing databases

Local study teams will identify potentially eligible patients through searching local clinic and pharmacy lists, electronic patient records, referral lists, research databases and other lists as appropriate. Potential participants (and/or their parents, if the patient is younger than 16) may be contacted by their consultant and the research team by letter/email to invite them to participate and provide them with the patient information leaflet.

(iii) Self-referral

Potential study participants (including individuals living overseas) may identify themselves or contact us through their clinician after becoming aware of our research work and this particular study. The latter will be publicised with REC approved material via posters in clinic waiting rooms, on the Psoriasis Association website, other relevant patient organisations, social media and via the study specific website page.

These individuals will be provided with an appropriate information leaflet and will be given as much time as they require to come to a decision regarding their participation.

Ascertainment of healthy controls

Unrelated control subjects (n>250) will be recruited through advertisements on the KCL website. As partners or spouses of patients enrolled in APRICOT/PLUM may be recruited as controls, adverts will also be placed on the trial web page and associated sites on social media. Potential volunteers responding to our adverts will be sent the participant information sheet by a member of the clinical team.

Ascertainment of patients with other neutrophilic or autoinflammatory conditions (disease controls)

Potentially eligible individuals affected by autoinflammatory syndromes or neutrophilic dermatoses (n>250) will be identified through clinics, existing databases and self-referrals, as detailed above. They may be contacted by the direct clinical team in person or by letter/email to invite them to participate.

Recruitment of pustular psoriasis patients' family members

If a patient reports a family history of psoriasis or harbours a deleterious mutation in a known or novel disease-associated gene, they will be asked to deliver study invitations and participant information sheets to relevant family members. Alternatively, if it is more convenient, the patient may be asked to grant permission (in writing) to contact their relatives. If the latter complete the reply slip on the participant invitation letter, they will be contacted by a member of the study team and invited to clinic to provide biological samples and clinical data, as dictated by the protocol.

Recall of patients and controls

If a known or novel mutation is detected in a patient or we run out of DNA/RNA, we may wish to recall them for further clinical phenotyping and collection of biological samples for functional studies. Patients who are about to start a new treatment or are experiencing a disease flare may also be recalled, to further investigate the molecular changes (e.g. variation in RNA levels) that underlie response to therapy or disease recurrence. In every case, age and sex-matched healthy and diseased controls will be recalled at the same time, to provide biological samples for comparison. No subject will recalled more than 4 times. This recall is entirely voluntary as stated in the patient and participant information sheets. If it is necessary to recall the subject, a member of the study team will contact them by telephone, letter or approach them at their next clinic visit (patients only).

6.4 Withdrawal of subjects

A participant may voluntarily discontinue participation in this study at any time and for any reason. This will not affect his/her current or future treatment. A withdrawal of consent form

will then be completed and kept in the study file. The chief investigator or co-investigators may also, at their discretion, exclude a subject from this study at any time. In either case, the biological material collected so far can be retained as part of the bio-resource.

6.5 Expected duration of study

Given that enrolment into APRICOT may continue until the end of 2019, this study is expected to continue until the end of 2021.

7. Study procedures

7.1 Participant pathway

The participant pathway will involve a discovery and (an optional) recall visit, as shown below. Recall visits will be determined by the central site on a participant by participant basis.

Sites are asked to collect DNA samples from all participants (child and adult) at the discovery visit. If other samples (as listed below) are required this will be confirmed by the central study team.

Ascertainment visit (Discovery)*	**Recall visit (Functional characterisation**)**
Consent; Collect clinical data	Update clinical data
	and/or any of the following for a maximum 35ml blood
DNA: Blood (2 x 6ml EDTA tubes)	DNA: Blood (1 x 6ml EDTA tube)
Plasma: Blood (1 x 5ml)	Plasma: blood (1 x 5ml)
RNA from whole blood (1 x 3ml Tempus tube) + (1 x 5ml EDTA tube for FBC) RNA from selected cell types (Central site only) (2 x 5ml EDTA tubes)	RNA from whole blood (1 x 3ml Tempus tube) + (1 x 5ml EDTA tube for FBC) RNA from selected cell types (Central site only) (2 x 5ml EDTA tubes)
Optional skin biopsy*** (2mm, non-lesional)	Optional skin biopsy*** (2mm, non-lesional)
	Immuno-phenotyping: Blood (1 x 20ml)
	Hair plucks (6-10 from occipital scalp)

*All cases and controls >16 year old; **Individuals who have consented to a recall visit (cases, matched controls, patient relatives; see also 6.3). No participant will be contacted for recall more than 4 times. *** Skin biopsies may not be required. The central study team will confirm at set up if they are applicable.

For patients who are younger than 16, the pathway will be modified as shown below

Ascertainment visit (Discovery)	**Recall visit (Functional characterisation)^**
Consent; Collect clinical data	Update clinical data
	and/or any of the following for a maximum 10ml blood
DNA: Blood (1 x 3ml EDTA tubes)	DNA: Blood (1 x3ml EDTA tubes)
RNA from selected cell types (1 x 5ml blood in EDTA tubes) **or** Plasma (1 x 5ml blood)	RNA from selected cell types (1 x 5ml blood in EDTA tubes) **or** Plasma (1 x 5ml blood)
	and/or Hair plucks (6-10 form occipital scalp)

^ Individuals who have consented to a recall visit (cases, matched controls; see also 6.3). Children who have turned 16 since the discovery visit will be consented again using the adult informed consent form.

7.2 Study schedule by visit

7.2.1 Ascertainment visit

All potential participants will be provided with an information sheet (simplified versions will be available for individuals who are younger than 16 at the time of recruitment). This will explain that DNA will be examined solely for the purposes of the current research and that the analysis will not provide any information on the risk of developing other diseases. The information sheet will also state that a full blood count will be performed and that participants will be promptly informed of any abnormalities this may reveal by the direct clinical care team.

The individuals that wish to enrol in the study will be asked to give their written informed consent to i) participate in the research; ii) be contacted again for an optional recall visit. If a participant is younger than 16 at the time of recruitment, their parents or guardians will be asked to grant written informed consent on his/her behalf. Participants aged 12-16, deemed competent, in Scotland ONLY may provide their own consent using the young person consent form. Parental agreement will be captured on the same form in these cases.

The following clinical data, assessments and samples will then be collected:

Patients with pustular psoriasis (including family members of affected individuals)

1. Demographics (date of birth, sex, ethnicity, country of origin)
2. Pustular psoriasis subtype
3. Presence of psoriatic arthritis and other co-morbidities
4. Past history of pustular psoriasis (age of onset, clinical course, details of disease flares including possible triggers and markers of systemic inflammation)
5. Date, dose, effectiveness and reason for discontinuation of previous therapies

6. Current medications
7. Family history and parental relatedness
8. Clinical assessments: disease severity (psoriasis area severity index (PASI) for concurrent plaque psoriasis and palmoplantar pustulosis PASI (ppPASI) for localised disease), physician's global assessment (PGA)
9. Blood samples for DNA and RNA isolation (see flowchart in 7.1 for details) and an optional skin biopsy (adult patients only)
10. An optional 2mm punch biopsy taken from non-lesional skin (adults only; the site of the biopsy will be recorded).
11. Height and weight

Disease controls

1. Demographics (date of birth, sex, ethnicity, country of origin)
2. Clinical diagnosis
3. Presence of arthritis and other co-morbidities
4. Past disease history (age of onset, clinical course, details of disease flares including possible triggers and markers of systemic inflammation)
5. Current and past medications
6. Family history and parental relatedness
7. Clinical assessments: relevant disease severity score
8. Blood samples for DNA and RNA isolation (see flowchart in 7.1 for details)
9. An optional 2mm punch biopsy taken from non-lesional skin (adults only; the site of the biopsy will be recorded).
10. Height and weight

Healthy controls (including family members of affected individuals)

1. Demographics (date of birth, sex, ethnicity, country of origin).
2. Clinical assessment to confirm the absence of other skin/inflammatory diseases and family history thereof (does not apply to family member of affected individuals)
3. Blood samples for DNA and RNA isolation (see flowchart in 7.1 for details)
4. An optional 2mm punch biopsy taken from non-lesional skin (adults only; the site of the biopsy will be recorded).
5. Height and weight

7.2.2 Recall visit

The following clinical data, assessments and samples will be collected from participating subjects as follows:

Pustular psoriasis cases, healthy and disease controls in whom recall for further phenotyping / sample collection are indicated (see 6.3)

The clinical information relating to patients with pustular psoriasis and disease controls will be updated with details of recent changes to disease activity and/or treatment regimen.

If the individual who is being recalled is older than 16, blood will be collected for further RNA isolation and/or immune phenotyping (see 7.1). An optional non-lesional skin biopsy may also be requested and/or 6-10 hairs will be taken from the occipital scalp. Matching biological samples will be obtained from healthy and diseased controls.

If the individual who is being recalled is younger than 16, a single blood sample will be requested and/or 6-10 hairs will be taken from the occipital scalp. Matching biological samples will be obtained from healthy and diseased controls.

Family members of patients with pustular psoriasis
If a mutation is identified in a pustular psoriasis patient, clinical data (see above) and biological samples (see 7.1 for details) will also be collected from affected and unaffected family members (including children, in which case the provisions outlined above apply) who have agreed to take part in the study.

In exceptional circumstances where a family member is not able to attend clinic, they may be asked to provide a 2 ml saliva sample via post. In that case they will then be sent a consent form and an Oragene®-DNA self-collection kit (DNA Genotek). They will be asked to sign and return the consent form and sample pack to the Division of Genetics and Molecular Medicine (King's College London), Guy's Hospital, London via Royal Mail Freepost service.

7.3 Laboratory tests

DNA will be extracted from blood samples (or saliva, in exceptional cases) and genetic studies will be undertaken by next generation sequencing or mutational screening of candidate genes. RNA will be isolated from blood or skin and gene expression will be measured by real-time PCR, array based hybridisation methods or RNAseq. Serum will be isolated from blood samples and cytokine levels will be determined by ELISA.

If a known or novel mutation is identified in a participant, the individual in question will be invited to clinic to donate biological samples for functional analyses, which will seek to determine the consequences of disease-associated variants on cell function. This work will utilise RNA extracted from blood or skin, as well as keratinocyte cultures derived from hair plucks. Immortalised cell lines may be established for cell-based functional assays. It is specified in the patient/participant information sheet that the participant will not have any financial benefits or rights over these cell lines.

7.4 Sample management

All samples will be taken, processed, stored and then transported to Francesca Capon's lab (King's College, London) according to Standard Operating Procedures already established within our research network. All samples will be sent to King's College and will be curated and stored in line with GCP and statutory requirements for clinical and sample storage and patient confidentiality. The site and/or laboratory performing the functional studies will depend on where the relevant expertise exists. This will primarily be within the lab of Francesca Capon, King's College, London. Anonymised results and samples may be shared with collaborating partners outside King's College, London, including the ERASPEN network and potential future collaborators that may include industry partnerships if appropriate

8. Assessment of safety

This non-CTIMP, observational study does not impact patient treatment and has a low risk of causing adverse events. The possible adverse effects for the subjects are related to the procedures. When taking blood samples, discomfort, bruising and infection may occur. Skin

biopsy carries the risk of bleeding, discomfort, infection and scarring. After injection of local anaesthesia, intolerance reactions might also very rarely occur. When taking hair plucks, the study participant may experience slight discomfort. Based on our long lasting experience with the described routine procedures we consider the risks of all adverse effects as low.

If a serious adverse event (SAE) directly caused by the study procedure occurs, it will be reported to the research ethics committee, in line with the National Research Ethics Service standard operating procedure on reporting of SAEs, as defined in the 'standard operating procedure for safety reporting for non-CTIMP studies'.

9. Statistics

9.1 Sample size

For the discovery of novel genetic variants in pustular psoriasis-associated genes by exome sequencing, power calculations indicate that a sample of 278 patients will have 80% power to detect a disease-associated mutation with a minor allele frequency of 0.5% and odds ratio of 4.5 (threshold P value is $2.5x10^{-6,}$ corresponding to an exome-wide significance level). We therefore plan to recruit at least 300 patients.

To investigate the functional consequences of pustular psoriasis alleles, 16 cases and controls will be examined for each variant under investigation, given that such a sample would have 80% power to detect a 25% difference in functional effect given variability of 25% in results (t-test threshold P value 0.05). We therefore plan to recruit at least 20 cases and 20 controls for the functional characterisation of each disease associated variant.

9.2 Analysis

The combined frequency of rare sequence variants observed in a candidate gene will be compared in cases vs. controls, using Fisher's exact test. P values exceeding the threshold for exome wide significance ($P<2.5 \times 10^{-6}$) will be considered statistically significant.
Gene expression, serum cytokine measurements, leukocyte activation levels and cytokine production by cultured keratinocytes will be compared in pustular psoriasis cases, controls and individuals affected by other autoinflammatory syndromes, using an ANOVA test followed by a Bonferroni post-test. P values <0.05 after correction for multiple testing will be considered statistically significant.

10. Ethics and regulatory approvals

The planning, conduct and reporting of this study will be in accordance with Good Clinical Practice (GCP), the principles stated in the Declaration of Helsinki (1996) and all applicable regulatory requirements, including but not limited to the Research Governance Framework.
This protocol will be submitted for review to a Local Research Ethics Committee (REC). The opinion of the ethics committee will be dated and given in writing. All correspondence with the ethics committee will be filed in the Investigator Site File.

11. Quality assurance

The study will be conducted in accordance with the approved protocol, GCP, relevant regulations and standard operating procedures. The investigator sites will provide direct access to all study related source data/documents and reports for the purpose of monitoring

and auditing by the sponsor and inspection by local and regulatory authorities. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents.

12. Data Management

The Chief Investigator has overall responsibility for the trial data. Data will be handled and stored in accordance with the Data Protection Act, 1998. Participants will be assigned a unique identification number. Each local principal investigator will be responsible for keeping a Subject Identification Log of all individuals enrolled into the study and their corresponding identifier. This information will be kept on secure NHS servers in password protected files and will only be available to the local principal investigator and the study personnel who are collecting clinical data.

Study data will either be collected on paper based case report forms (CRFs) and entered on to a secure research database or entered directly onto a secure research database. The database will be password protected and access restricted to named study individuals only. The database used may be one purpose built, developed and maintained by the NIHR Biomedical Research Centre at Guy's and St Thomas's NHS Foundation Trust (GSTT) and King's College London (KCL)known as CAPTURE (ChArting PaTient outcomes Using an online REsource).

CAPTURE is a web-based forms system used to record clinical research data for use in research studies and clinical trials. CAPTURE sits on the GSTT servers behind the NHS firewall and data stored within CAPTURE is afforded the same security controls as any clinical data held within the GSTT servers. CAPTURE will be used by GSTT and KCL staff members onsite as well as third-party collaborators. External staff will access the system via the public internet, secured with industry standard SSL and SafeNet 2-factor authentication. Further details of the architecture of CAPTURE and additional CAPTURE specific security measures can be found in the CAPTURE Information Governance Policy.

Identifiable information held on the database will only be accessible by the Chief Investigator and approved delegated members of the study team. Paper based CRFs will be stored in a secure locked office at study sites and will be the responsibility of the principal investigator.
Exome sequence data will be securely archived in the high performance computing cluster of Guy's and St Thomas' Hospitals Biomedical Research Centre.

At the end of the study, essential documentation will be archived in accordance with sponsor and local requirements. The retention of study data will be the responsibility of the Chief Investigator. Study data will be kept for as long as this or future studies into pustular psoriasis continue at St John's Institute of Dermatology. All types of records for children and young people will be retained until the patient is 25 (or 26 if they are 17 when treatment ends) or eight years after their death if sooner.
Authorised representatives of the regulatory authorities may require access to those parts of the hospital/practice records relevant to the study, including medical history, for verification of data.

13. Publication policy

We are committed to ensure wide dissemination and uptake of our research findings. We will exploit access to clinical and academic networks nationally (eg: UK Translational Research Network in Dermatology, British Association of Dermatologists) and internationally (European Rare And Severe Psoriasis Expert Network, International Psoriasis Council).
We will also report our findings through presentations at relevant scientific meetings and publication of full papers in high impact scientific journals.

The pustular psoriasis community will be informed of our results via the Psoriasis Association website (40,000 hits/month) and related social media. The Psoriasis Association will also ensure information is disseminated internationally to patient groups.

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