



# LA RECHERCHE COLLABORATIVE AU SERVICE DES PATIENTS

LIVRET 2021





Chers amis,

C'est un plaisir de partager avec vous le livret du GEM Reso 2021. Cette année, notre dynamisme collectif a permis 27 communications à des congrès et 12 publications, et ce malgré la pandémie qui a continué à perturber notre quotidien.

En plus des communications sur le psoriasis, la dermatite atopique, la maladie de Verneuil, l'urticaire, nous avons mené une enquête de pratiques sur la prise en charge de la pelade, ouvrant la voie au sein du GEM Reso à de nouvelles dermatoses inflammatoires chroniques.

Nos études ont à nouveau permis de répondre à des questions pratiques: Peut-on prescrire en toute sécurité des biothérapies chez des patients avec un antécédent d'hémopathie ou de cancer? Comment sont utilisés les traitements systémiques pour le psoriasis, la dermatite atopique ou la maladie de Verneuil?

Même si nous n'aurons pas l'occasion de nous retrouver cette année lors des JDP, je vous invite à prendre connaissance des études à venir, et à me solliciter pour vos projets de recherche au sein du GEM.

Merci encore pour votre mobilisation.

Amitiés à tous et rendez-vous aux JDP 2022!

Anne-Claire Fougousse  
Coordinatrice scientifique Reso

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# ETUDES EN COURS

## RELEVÉ : RECIDIVE LOCALE APRÈS EXCISION CHIRURGICALE DE LA MALADIE DE VERNEUIL



### Investigateurs principaux :

Drs Anne- Cécile Ezanno et Philippe Guillem

Nombre de patients inclus : 95

Nombre de centres participants : 5

### Communications

#### SHSA 2021

##### EVALUATION OF PERIOPERATIVE QUALITY OF LIFE IN HIDRADENITIS SUPPURATIVA

Anne- Cécile EZANNO , Anne- Claire Fougrousse, Manuela Perez , Pierre- André Becherel , Juliette Delaunay, Christelle Perat , Philippe Guillem and GEM RésoVerneuil

##### PROFILE OF PATIENTS OPERATED FOR HIDRADENITIS SUPPURATIVA IN FRANCE: RESULTS OF A MULTICENTER OBSERVATIONAL STUDY

Anne- Cécile EZANNO , Anne- Claire Fougrousse, Pierre- André Becherel , Philippe Guillem and GEM RésoVerneuil

#### Journées Dermatologiques de Paris 2021

##### Évaluation de la qualité de vie péri opératoire dans la maladie de Verneuil

Anne- Claire Fougrousse , Manuela Perez, Pierre- André Becherel, Juliette Delaunay, Christelle Perat, Philippe Guillem et GEM ResoVerneuil

##### Profil des patients opérés pour une maladie de Verneuil en France en 2021 : résultats d'une étude observationnelle multicentrique.

Anne- Cecile Ezanno, Anne- Claire Fougrousse , Manuela Perez, Pierre- André Becherel, Juliette Delaunay, Christelle Perat, Philippe Guillem et GEM ResoVerneuil

## ENQUÊTE DE PRATIQUES CONCERNANT LA PRISE EN CHARGE DE LA PELADE



### Investigateurs principaux :

Drs Pierre- André Bécherel , Anne- Claire Fougrousse , François Maccari, Ines Zaraa

### ENQUETE DE PRATIQUES

95 dermatologues ayant déjà répondu au questionnaire

**Objectif :** Décrire les pratiques de prise en charge des patients atteints de pelade auprès des dermatologues exerçant en ville, à l'hôpital ou en pratique mixte

# ETUDES EN PROJET

## ENQUÊTE DE PRATIQUES CONCERNANT LA PLACE DU TRAITEMENT CHIRURGICAL DE LA MALADIE DE VERNEUIL POUR LES DERMATOLOGUES



### Investigateurs principaux :

Drs Anne- Cécile Ezanno, Philippe Guillem

### ENQUETE DE PRATIQUES

Prévue début 2022

**Objectif :** Décrire les pratiques des dermatologues concernant l'adressage au chirurgien de patients atteints de maladie de Verneuil, identifier les éventuelles difficultés.

## ENQUÊTE DE PRATIQUES CONCERNANT L'UTILISATION DES RÉTINOÏDES DANS LA MALADIE DE VERNEUIL



### Investigateurs principaux :

Drs Anne- Claire Fougrousse, Germaine Gabison

### ENQUETE DE PRATIQUES

Prévue début 2022

**Objectif :** Décrire les modalités de prescription des rétinoïdes dans la maladie de Verneuil.

## PSORIASIS

- SKIN CAT



**Investigateur principal :** Dr Edouard Begon

**Objectif :** Création d'un questionnaire patient à type d'échelle de quantification visant à évaluer le fardeau du traitement (Treatment burden) / les contraintes liées au traitement (CAT ou Contraintes Associées aux Traitements) chez les patients psoriasiques en France.

### Communications

#### Journées Dermatologiques de Paris 2019

Première échelle d'évaluation des contraintes associées aux traitements dans le psoriasis : le questionnaire SKIN-CAT (SKIN- Contraintes Associées aux Traitements).

Edouard BEGON, Nathalie Beneton, Emmanuel MAHE, Anne- Claire FOUGEROUSSE, Jean Luc PERROT, Domitille THOMAS BEAULIEU, Josiane PARIER, Marc Perrussel, Laure Mery Bossard, Diane Pourchot, Catherine Goujon, Caroline Jacobzone, Anne Caroline Cottencin, Juliette Delaunay, Helene Aubert, Anne Benedicte Duval Modeste, Nathalie Quiles, Claire Boulard, Annie Vermersch Langlin, Pierre Pfister, Michele Zeitoun, François Maccari, Laurent Wagner, Bruno Halioua, Chantal Rousseaux, Marc Marty, Hugues Barthelemy, Alain Beauchet et GEM RESOPSO

ETUDE TERMINÉE

Nombre de patients inclus : 241

Nombre de centres participants : 23

- SWITCH ANTI IL17



**Investigateur principal :** Dr Anne- Claire Fougousse

**Objectif :** Analyser la réponse terme (efficacité et tolérance) à court (3 mois) et long (12 mois) chez les patients ayant reçu plusieurs anti IL- 17, en switch immédiat ou « décalé ».

### Communications

#### World Congress of Dermatology 2019 Milan

Switch between interleukine-17A antagonists for psoriasis : a french multicentric retrospective experience.

A.- C. Fougousse, C Boulard, Z Reguiat, L Mery- Bossard, H Barthelemy, E Begon, F Maccari, C Girard, C . Jacobzone, J Parier, J- B Monfort, D Lons- Danic, , N Sultan, A- C Cottencin, E. Mahé , for the GEM Resopso

ETUDE TERMINÉE

Nombre de patients inclus : 100

Nombre de centres participants : 21

## Journées Dermatologiques de Paris 2019

### Switch entre anti IL17 pour du psoriasis: étude rétrospective multicentrique

Anne- Claire Fougerousse, Ziad Reguiat, Claire Boulard, Edouard Begon, Nathalie Beneton, Guillaume Chaby, Juliette Delaunay, Hughes Barthelemy, Josiane Parier, Laure Mery Bossard, François Maccari, Marie Bastien, Dominique Lons Danic, Jean- Luc Perrot, Caroline Jacobzone, Nathalie Sultan, Anne- Caroline Cottencin, Mahtab Samimi, Jean- Benoit Monfort, Emanuele Trovato, Emmanuel Mahe et pour le GEM Resopso

- APREPSO



**Investigateur principal :** Dr Anne- Claire Fougerousse

**Objectif :** Evaluer la tolérance du traitement par Otezla® après sa prescription initiale chez des patients adultes atteints de psoriasis en plaques chronique modéré à sévère, en conditions réelles de prescription en France

## Communications

### World Congress of Dermatology 2019 Milan

Profile of the patients treated by apremilast in a prospective non interventional, descriptive, multicenter study in France: first results.

A.- C. Fougerousse , D. Bouilly- Auvray, M. Bastien, R. Safar, C. Girard, E. Begon, M. Perrussel, M. Zeitoun, J.- B. Monfort, C. Jacobzone, P. Pfister, E. Mahé, V. Pallure, D. Thomas- Beaulieu, B. Solyga, F Maccari, for the GEM Resopso

### INCLUSIONS TERMINÉES

Nombre de patients inclus : 229

Nombre de centres participants : 27

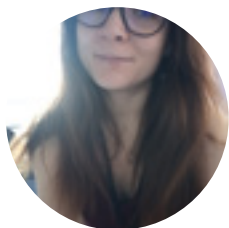
## Journées Dermatologiques de Paris 2019

### Evaluation de l'utilisation de l'apremilast dans la prise en charge du psoriasis en plaques chronique modéré à sévère chez l'adulte en pratique courante en France: résultats à 4 mois d'une étude prospective multicentrique

Anne- Claire Fougerousse, Danielle Bouilly- Auvray, Marie Bastien, Ziad Reguiat, Josiane Parier, Edouard Begon, Valérie Pallure, Nathalie Beneton, Jean- Benoit Monfort, Claire Boulard, Juliette Delaunay, Laure Mery Bossard, Caroline Jacobzone, Emmanuel Mahe, Céline Girard, Catherine Goujon, Mathilde Kemula, Marc Perrussel, Pierre Pfister, Bénédicte Solyga, Michele Zeitoun, Maud Steff, Domitille Thomas- Beaulieu, Nihal Bekkali, Eric Esteve, François Maccari pour le GEM Resopso



## • ENQUÊTE DE PRATIQUES : GESTION DES DIARRHÉES SOUS APREMILAST



### Coordinateurs :

Chloé Venuto (interne en dermatologie au CHU d'Angers) avec le Dr Hervé Maillard

ETUDE TERMINEE

ENQUETE DE PRATIQUES

165 dermatologues ayant participé

**Objectif :** Etablir une conduite à tenir concernant la gestion des diarrhées sous APREMILAST à l'aide d'un questionnaire en ligne à destinée des dermatologues.

Article soumis pour publication

## • CANCER-BIO



### Investigateurs principaux :

Drs Anne-Claire Fougousse,  
Laure Mery-Bossard

**Objectif :** Décrire la tolérance et l'efficacité des biothérapies ou de l'apremilast à partir d'une série de patients atteints de psoriasis ayant des antécédents de cancer solide en rémission ou évolutif.

Nombre de patients inclus : 112

Nombre de centres participants : 22

## Communications

### Journées Dermatologiques de Paris 2021

**Tolérance des biothérapies et de l'apremilast pour un psoriasis chez des patients avec antécédent de cancer solide : étude rétrospective multicentrique**

Anne-Claire Fougousse, Valérie Failla, Emmanuel Mahé, Guillaume Chaby, François Maccari, Jean-Luc Perrot, Claire Boulard, Emilie Brenaut, Pierre-Dominique Ghislain, Céline Girard, Pierre-André Becherel, Charlotte Lepelley-Dupont, Josiane Parier, Nathalie Quiles, Edouard Begon, Anne-Sophie Dillies, Valérie Florin, Caroline Jacobzone, Sophie Osdoit, Mahtab Samimi, Hervé Maillard, Laure Mery-Bossard et Pour le GEM Resopso



### • ENQUÊTE DE PRATIQUES SUR L'ANTIBIOTHÉRAPIE DANS LA MALADIE DE VERNEUIL



#### Investigateurs principaux :

Drs Anne-Claire Fougrousse, Ziad Reguiai

**Objectif :** Décrire les modalités de traitement par antibiotiques au cours de la maladie de Verneuil selon le stade de Hurley

#### Communications

##### EHSF 2021

Antibiotic use in Hidradenitis suppurativa: a practice survey

Anne-Claire Fougrousse, Ziad Reguiai, for the GEM ResoVerneuil

##### Journées Dermatologiques de Paris 2021

Antibiothérapie dans l'hidradénite suppurée: enquête de pratiques.

Anne-Claire Fougrousse, Ziad Reguiai et Pour le GEM ResoVerneuil

108 réponses au questionnaire

### • EPIVER



#### Investigateur principal :

Pr Jean-Luc Perrot

**Objectif :** Permettre une meilleure connaissance des malades français atteints d'une maladie de Verneuil en précisant leurs antécédents inflammatoires et cardiovasculaires personnels et familiaux, leurs expositions aux toxiques, leur profil démographique et phénotypique, l'étude de leur qualité de vie, le ressenti de la douleur

#### Communications

##### Journées dermatologiques de Paris 2017

Données démographiques et biométriques de 882 sujets atteints de maladie de Verneuil : EpiVer étude multicentrique française ville-hôpital

S Allal, P Guillem, AC Fougrousse, N Beneton, F Maccari, B Labeille, E Tisserand, F Vuering, S Vergote-Pelamopurgues, E Cinotti, JL Perrot, ResoVerneuil

Ressenti des patients atteints de maladie de Verneuil à propos de 882 sujets EpiVer étude multicentrique française ville-hôpital

S Allal, P Guillem, AC Fougrousse, N Beneton, F Maccari, C Girard, I Kupfer, V beraud, A Brams, T Bonnefoy, E Cinotti, JL Perrot, ResoVerneuil

Descriptif des sites atteints par la maladie de Verneuil à propos de 882 sujets EpiVer étude multicentrique française ville-hôpital.

JL Perrot, P Zuckervar, M Salavert, J Parier, JL Michel, JP Barrachin, P Guillem, E Cinotti, B Labeille, ResoVerneuil

ETUDE TERMINEE

Nombre de patients inclus : 1428

## **Addictions au tabac et ou au cannabis et maladie de Verneuil EpiVer étude multicentrique française ville- hôpital**

S Allal, P Guillem, AC Fougerousse, C Girard, C Fite, J Gand- Gavanou, N Quiles, E Cinotti, JL Perrot, ResoVerneuil

## **Antécédents personnels et familiaux de 882 sujets atteints de maladie de Verneuil étude Epiver**

P Guillem, S Allal, AC Fougerousse, N Beneton, F Maccari, B Labeille, E Tisserand, F Vuering, S Vergote- Pelamourgues, E Cinotti, JL Perrot, ResoVerneuil

## **Journées dermatologiques de Paris 2018**

### **Influence de l'ancienneté de la maladie de Verneuil sur la qualité de vie et la douleur à propos de 1428 sujets : étude Epiver**

AC Fougerousse, P Guillem, S Allal, F Maccari, N Beneton, R Binois, E Cinotti, F Cambazard, JL Perrot, ResoVerneuil

### **Tabagisme et sévérité de la maladie de Verneuil : à propos de 1428 sujets : étude Epiver**

E Ravni, F Cambazard, AC Biron, C Couzan, E Couty, JL Perrot, ResoVerneuil

### **Modalités de prise en charge thérapeutique de 1428 sujets atteints de maladie de Verneuil : étude Epiver study**

Z Reguiai, C Jacobzone, E Tisserand, E Esteve, A Nassif, A Duval Modeste, P Bravard, T Boyé, N Sultan, E Cinotti, JL Perrot, ResoVerneuil

## **EHSF 2019 Wroclaw : Posters**

### **Influence of the duration of Hidradenitis Suppurativa on the quality of life and pain in 1428 subjects: EpiVer study**

AC Fougerousse, S Allal, G Tonini, Ph Guillem, F Maccari, N Beneton, R Binois, C Fite, E Cinotti, P Rubegni, JL Perrot

### **Is severity of Hidradenitis Suppurativa related to hypertension and angina pectoris ? EpiVer study on 1428 subjects**

AC Fougerousse, S Allal, G Tonini, Ph Guillem, F Maccari, N Beneton, R Binois, C Fite, E Cinotti, P Rubegni, JL Perrot

### **Demographic and biometric data of 1428 patients with Hidradenitis suppurativa: EpiVer French multicenter study**

AC Fougerousse, S Allal, G Tonini, Ph Guillem, F Maccari, N Beneton, R Binois, C Fite, E Cinotti, P Rubegni, JL Perrot

### **Personal and family history of 1428 subjects with Hidradenitis Suppurativa: EpiVer study**

Z Reguiai, C Jacobzone, E Tisserand, AB Duval Modeste, P Bravard, T Boyé, N Sultan Bichat, A Nassif, E Cinotti, P Rubegni, JL Perrot

### **Therapeutic management of 1428 subjects suffering from Hidradenitis Suppurativa: EpiVer study**

Z Reguiai, C Jacobzone, E Tisserand, AB Duval Modeste, P Bravard, T Boyé, N Sultan Bichat, A Nassif, E Cinotti, P Rubegni, JL Perrot

## • RESOVERNEUIL.NET



**Investigateur principal :**  
Dr Anne- Claire  
Fougrousse

**Inclusions en cours :**  
**Inclusions terminées**

**Centres sollicités :** tous les membres de  
ResoVerneuil

**Nombre de patients inclus : 501**

**Nombre de centres participant : 28**

### Objectif :

- Décrire les caractéristiques des patients atteints de maladie de Verneuil consultant internet, de décrire le contexte et l'impact de ces recherches sur le comportement des patients
- Analyser les sites les plus visités (critères de qualité des sites, qualité de l'information)

### Communications

#### EHSF 2020 Athenes

Use of internet by hidradenitis suppurativa's patients: an observationnal study, Resoverneuil.net

Anne- Claire Fougrousse, Ziad Reguiai, Germaine Gabison, Nathalie Beneton, Juliette Delaunay, Jean- Luc Perrot, Anne- Cécile Ezanno, Marie Bastien, Valérie Pallure, François Maccari, Philippe Guillem for the GEM ResoVerneuil

#### EADV 2020 Vienne

Use of internet by hidradenitis suppurativa's patients: an observationnal study, Resoverneuil.net

Anne- Claire Fougrousse, Ziad Reguiai, Germaine Gabison, Nathalie Beneton, Juliette Delaunay, Jean- Luc Perrot, Anne- Cécile Ezanno, Marie Bastien, Valérie Pallure, François Maccari, Philippe Guillem for the GEM ResoVerneuil

## URTICAIRE

### • OMALIZUMAB ET GROSSESSE



**Investigateur principal :**  
Dr Antoine Badaoui  
Etude collaborative avec  
le GUS

**APPEL A CAS**

**Nombre de patients inclus : 12**

**Nombre de centres participants : 5**

**Objectif :** Evaluer la tolérance et l'efficacité de l'omalizumab au cours de la grossesse

### Communications

#### 5th GA<sup>2</sup>LEN Global Urticaria Forum 12/2020

Pregnancy outcome following maternal omalizumab use for chronic spontaneous urticaria: a French retrospective cohort

Antoine Badaoui, Emmanuelle Amsler, Anne- Sophie Darrigade, Anne- Claire Fougrousse, Ziad Reguiai, Florence Castelain, Angèle Soria,

## CFA 2021

Prescription d'Omalizumab pendant la grossesse chez des patientes atteintes d'urticaire chronique spontanée : résultats d'une étude rétrospective française.

Antoine Badaoui, Emmanuelle Amsler, Anne- Sophie Darrigade, Anne- Claire Fougerousse, Ziad Reguiat, Florence Castelain, Angèle Soria et Groupe Urticaire de la SFD et du GEM Reso

## GERDA 2021

Prescription d'Omalizumab pendant la grossesse chez des patientes atteintes d'urticaire chronique spontanée : résultats d'une étude rétrospective française.

Antoine Badaoui, Emmanuelle Amsler, Anne- Sophie Darrigade, Anne- Claire Fougerousse, Ziad Reguiat, Florence Castelain, Angèle Soria et Groupe Urticaire de la SFD et du GEM Reso

## Journées Dermatologiques de Paris 2021

Prescription d'Omalizumab pendant la grossesse chez des patientes atteintes d'urticaire chronique spontanée : résultats d'une étude rétrospective française.

Antoine Badaoui, Emmanuelle Amsler, Anne- Sophie Darrigade, Anne- Claire Fougerousse, Ziad Reguiat, Florence Castelain, Angèle Soria et Groupe Urticaire de la SFD et du GEM Reso

### • MODIFICATION DE L'EQUILIBRE THYROIDIEN SOUS OMALIZUMAB



#### Investigateurs principaux :

Drs Anne- Claire Fougerousse,  
Angèle Soria

Etude collaborative avec le GUS

**Objectif :** Colliger les cas de patients ayant vu leurs besoins en hormones thyroïdiennes diminuer après l'introduction de L'omalizumab.

#### APPEL A CAS

Nombre de patients inclus : 2

Nombre de centres participants : 2

#### Communication EADV 2020

Decrease thyroid hormones needs after introduction of omalizumab in patients with chronic spontaneous urticaria and non auto-immune hypothyroidism

Anne- Claire Fougerousse, Angèle Soria

• DAPHNE



**Investigateurs principaux :**

Drs Caroline Jacobzone et Sébastien Barbarot

**Objectif :** Etudier la répartition des formes phénotypiques de dermatite atopique de l'adulte en recueillant les données cliniques et épidémiologiques chez tous les patients adultes vus en consultation.

Décrire les modalités d'utilisation des traitements systémiques chez ces patients.

**Communications**

**Journées Dermatologiques de Paris 2019**

**REPARTITION DES FORMES PHENOTYPIQUES DE LA DERMATITE ATOPIQUE CHEZ L'ADULTE PREMIERS RESULTATS DE L'ETUDE DAPHNE**

Caroline Jacobzone, Ziad Reguiai, Anne Claire Fougrousse, Emmanuel Mahé, Francois Maccari, Antoine Badaoui, Jean- Luc Perrot, Eric Esteve, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Marie Jachiet, Nicole Jouan , Valérie Pallure , Jeffrey Loget , Magali Bourrel, Nathalie Beneton, Maud Steff, Paul Bilan, Flavien Huet, Josiane Parier, Claire Alice de Salins, Josiane Parier, Claire Alice de Salins, Sophie Osdoit, Germaine Gabison, Marc Perrussel, Charlotte Lepelley- Dupont, Nathalie Sultan, Charles Taieb, Sébastien Barbarot et Resoeczema

**INCLUSIONS TERMINEES**

**Nombre de patients inclus : 809**

**Nombre de centres participants : 28**

**Journées Dermatologiques de Paris 2021**

**DERMATITE ATOPIQUE DU SUJET AGE. Cohorte Daphné.**

Caroline Jacobzone Leveque, Ziad Reguiai, Anne Claire Fougrousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Charlotte Fite, Laure Mery, Claire Abasq, Emmanuel Mahe et GEM RESO

**Dermatite atopique de l'adulte à type de prurigo – Données de la cohorte Daphné.**

Caroline Jacobzone Leveque, Ziad Reguiai, Anne Claire Fougrousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Catherine Goujon Henry, Dominique Lons Danic, Emmanuel Mahe et GEM RESO

**Description de la dermatite atopique de l'adulte, résultats de la cohorte DAPHNE.**

Caroline Jacobzone Leveque , Ziad Reguiai, Anne Claire Fougrousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Catherine Goujon Henry, Dominique Lons Danic, Magali Bourrel, Laure Mery, Claire Abasq, Claire Alice de Salins., Charlotte Lepelley, Emmanuel Mahe et GEM RESO

**Recours aux médecines alternatives chez les patients adultes atteints de dermatite atopique – Cohorte Daphné.**

Caroline Jacobzone Leveque, Ziad Reguiai, Anne Claire Fougrousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Emmanuel Mahe et GEM RESO

## PSORIASIS

- ENQUÊTE DE PRATIQUES SUR L'UTILISATION DU MÉTHOTREXATE DANS LE TRAITEMENT DU PSORIASIS EN PLAQUES MODÉRÉ À SÉVÈRE



### Investigateurs principaux :

Drs Anne-Claire Fougerousse, François Maccari, Laure Mery-Bossard, Josiane Parier

### ENQUÊTE DE PRATIQUES

204 dermatologues ayant participé

**Objectif :** Décrire les pratiques de prise en charge des patients adultes traités par MTX pour un psoriasis en plaque modéré à sévère auprès des dermatologues exerçant en ville, à l'hôpital ou en pratique mixte.

### Communications

#### Journées Dermatologiques de Paris 2021

Utilisation du méthotrexate dans le psoriasis modéré à sévère en France: résultats d'une enquête de pratiques.

Anne-Claire Fougerousse\*, Laure Mery-Bossard, Josiane Parier, Charles Taieb, Antoine Bertolotti, François Maccari et Pour le GEM Resopso

### Publication

Fougerousse AC, Mery-Bossard L, Parier J, Taieb C, Bertolotti A, Maccari F; GEM ResoPso. Use of Methotrexate in the Treatment of Moderate to Severe Plaque Psoriasis in France: A Practice Survey. Clin Cosmet Investig Dermatol. 2021 Apr 23;14:389-393

- E BIP



**Investigateur principal :** Dr Hélène Aubert

**Objectif :** Evaluer les stratégies d'adaptation des doses des biothérapies lors de l'obtention de la rémission du psoriasis

### Communications

#### Journées dermatologiques de Paris 2019

Stratégie d'espacement et de diminution des doses de traitement par biothérapie dans le psoriasis cutané en rémission ou avec une faible activité : enquête de pratique

Helene Aubert, Emmanuel MAHE, Anne- Claire FOUGEROUSSE, François Maccari, Nathalie BENETON

ETUDE TERMINEE

ENQUETE DE PRATIQUE

54 dermatologues ayant participé

Accepté pour publication dans les Annales de Dermatologie et de Vénérologie.

- HÉMOPATHIES ET BIOTHÉRAPIE



**Investigateur principal :**  
Dr Guillaume Chaby

ETUDE TERMINÉE

Nombre de patients inclus : 21

Nombre de centres participants : 8

**Objectif :** Décrire de l'efficacité et de la tolérance des biothérapies ou de l'apremilast à partir d'une série de patients atteints de psoriasis ayant des antécédents d'hémopathie maligne en rémission ou évolutive

### Communications

#### Journées Dermatologiques de Paris 2021

Tolérance et efficacité du traitement du psoriasis par biothérapies ou apremilast en cas d'antécédent d'hémopathie maligne : étude multicentrique rétrospective.

Raphaella Cohen- Sors, Guillaume Chaby, Anne- Claire Fougrousse, François Maccari, Aude Roussel, Ziad Reguiat, Emmanuel Mahe, Maud Amy de la Breteque, Juliette Delaunay, Anne- Caroline Cottencin, Antoine Bertolotti, Helene Kemp et Groupe RESOPSO

### Publication

Cohen- Sors R, Fougrousse AC, Reguiat Z, Maccari F, Mahé E, Delaunay J, Roussel A, de la Breteque MA, Cottencin C, Bertolotti A, Kemp H, Chaby G. Biological Therapies or Apremilast in the Treatment of Psoriasis in Patients with a History of Hematologic Malignancy: Results from a Retrospective Study in 21 Patients. Clin Cosmet Investig Dermatol. 2021 Jul 8;14:845- 854.



- **DATE : UTILISATION DES TRAITEMENTS SYSTÉMIQUES DANS LA DERMATITE ATOPIQUE DE L'ADULTE**



ETUDE TERMINEE  
ENQUETE DE PRATIQUES

305 dermatologues ayant participé

### Investigateurs principaux :

Drs Anne- Claire Fougrousse, Caroline Jacobzone, François Maccari

**Objectif :** Décrire l'utilisation des traitements systémiques dans la dermatite atopique de l'adulte en France

### Publication

Fougrousse AC, Jacobzone C, Mery- Bossard L, Reguici Z, Droitcourt C, Taieb C, Maccari F; GEM ResoEczema Group. Use of Systemic Medications for Treating Adult Atopic Dermatitis in France: Results of a Practice Survey. Clin Cosmet Investig Dermatol. 2021 Feb 25;14:179-183.

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## MALADIE DE VERNEUIL

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- **RÔLE DE LA THÉRAPIE À PRESSION NÉGATIVE DANS LA PRISE EN CHARGE DE LA MALADIE DE VERNEUIL AXILLAIRE**

### Communication

EHSF 2021

The role of negative pressure wound therapy in the management of axillary hidradenitis suppurativa

AC. Ezanno, M. Perez, A. C. Fougrousse, P. Guillem, For the GEM Reso verneuil

### Publication

Ezanno AC, Fougrousse AC, Guillem P; GEM Resoverneuil. The role of negative- pressure wound therapy in the management of axillary hidradenitis suppurativa. Int Wound J. 2021 Sep 29. doi: 10.1111/iwj.13678. Epub ahead of print. PMID: 34590422.

### Autres communications

EHSF 2021

Do men and women have different clinical characteristics in hidradenitis suppurativa?

Benhadou F, Villani A, Mintoff D, Guillem P

Pain in hidradenitis suppurativa correlates with disease severity but also with gender and smoking.

Benhadou F, Villani AP, Guillem P

## Stigmatization feeling in patients with hidradenitis suppurativa.

Guillem P, Vlaeminck- Guillem V

## An educational film to explain hidradenitis suppurativa to patients and non physician careproviders – A nurse initiative.

Perat C, Guillem P

## Therapeutic use of Cicaderma® in the management of surgical wounds

Perat C, Raspado O, Al Samman Zouaghi S, Ghizzo T, Lagrange V, Guillem P

## The first affected site in hidradenitis suppurativa both suggests specific disease- triggering factors and predicts disease outcome.

Villani A, Benhadou F, Guillem P

## The dose- response relationship between tobacco smoking and hidradenitis suppurativa.

Guillem P

## What does/ can the surgeon expect from the association of surgery with hidradenitis suppurativa- targeted medical treatments? A systematic review ( invited lecture)

Guillem P

## SHSA 2021

## Association of Hidradenitis Suppurativa and Mevalonate Kinase Deficiency – Report of Two Cases.

Benhadou F, Vlaeminck- Guillem V, Duquesne A, Mintoff D, Guillem P

## The first affected site in hidradenitis suppurativa both suggests specific disease- triggering factors and predicts disease outcome.

Villani A, Benhadou F, Guillem P

## Stigmatization feeling in patients with hidradenitis suppurativa

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 Open Access Full Text Article

ORIGINAL RESEARCH

# Use of Systemic Medications for Treating Adult Atopic Dermatitis in France: Results of a Practice Survey

This article was published in the following Dove Press journal:  
Clinical, Cosmetic and Investigational Dermatology

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**Purpose:** Recent studies have illustrated that systemic medications are underused for treating adult atopic dermatitis (AD) and that dermatologists have concerns regarding the safety profile of cyclosporine in AD.

**Patients and Methods:** We performed a national online practice survey between March and April 2020.

**Results:** A total of 305 dermatologists responded, 57% with hospital-based activity and 43% with private practice. Overall, 46.9% prescribed cyclosporine for adult AD. Before initiating treatment, 56.9% did not perform evaluation scoring. Reasons for not prescribing cyclosporine were no eligible patients (24.7%), lack of information (52.6%), need for hospital prescription (31.2%), and lack of experience (79.2%). Fifty-four percent of the dermatologists prescribed methotrexate for adult AD. Before initiating treatment, 50.5% did not perform evaluation scoring. Reasons for not prescribing methotrexate were no eligible patients (46.7%), lack of information (39.3%), lack of experience (25.2%), and not approved for AD (47.4%). A total of 2.1% dermatologists prescribed other systemic treatments for adult AD, 9.8% prescribed corticosteroids and 56.4% prescribed dupilumab.

**Conclusion:** Systemic treatments for AD are used by half of dermatologists, although cyclosporine and dupilumab must be initiated in hospitals in France. Methotrexate is more frequently used than cyclosporine, although it is not approved for this indication in France. A vast majority of dermatologists do not perform any evaluation scoring before initiating systemic treatment for adult AD.

**Keywords:** atopic dermatitis, cyclosporine, methotrexate, practice survey

## Introduction


Adult atopic dermatitis is a frequent chronic inflammatory dermatosis, the prevalence of which is estimated to be 4.65% in France,<sup>1</sup> with 68% of patients having moderate to severe forms.<sup>2</sup> Its treatment is based on local treatments (emollients, dermocorticoids, topical calcineurin inhibitors) and, in moderate to severe forms, in the event of failure, phototherapy, immunosuppressants (cyclosporine (the only systemic treatment with marketing authorisation for this indication in France), methotrexate, azathioprine, mycophenolate mofetil) and dupilumab.<sup>3</sup> We are at the dawn of a therapeutic revolution for AD with new treatments like biotherapies targeting IL 13 (tralokinumab, lebrizikumab) or IL 31 (nemolizumab) and Janus Kinase inhibitors (baricitinib, upadacitinib, abrocitinib ...) being developed.<sup>4</sup>

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In France, only dermatologists with hospital activity can initiate cyclosporine and dupilumab, and private dermatologists can only renew these treatments. In 2017, a French study showed that systemic treatments for atopic dermatitis were underprescribed, since in a cohort of 401 patients, 73% had a moderate to severe form, while only 8% were receiving systemic treatment.<sup>5</sup> Dermatologists have also expressed concerns about the safety profile of cyclosporine for this indication.<sup>6</sup> We evaluated the modalities of the use of systemic treatments for adult atopic dermatitis in France.

## Patients and Methods

We conducted a practice survey among ResoEczema member dermatologists by means of a questionnaire sent by e-mail (with two reminders) between March and April 2020.

## Questionnaire

The questionnaire collected the gender of the dermatologist, the year the thesis was obtained, the mode of practice (hospital, private or mixed), and the prescription of cyclosporine, methotrexate, general corticosteroids, other immunosuppressants and dupilumab for adult atopic dermatitis. The questionnaire collected information on how the treatments were prescribed (severity scores, treatment line, dose and duration of treatment, monitoring methods) and, if necessary, the reasons for not using these treatments. For this type of study, French regulations do not require submission to an ethics committee, as this study does not enter the field of the deliberation n°2018-154 of the 3<sup>rd</sup> of May 2018 (JORF n°0160 of the 13th of July 2018).

## Statistics

Quantitative data are expressed as the average  $\pm$  standard deviation (SD), and qualitative data are expressed as head-count (%). Means were compared using Student's *t*-test, and frequencies were compared with the Chi2 test. A value of  $p < 0.05$  was considered statistically significant. Statistical analyses were performed using R software version 3.5.1.

## Results

### Characteristics of the Dermatologists

Three hundred five dermatologists answered the questionnaire, representing 9% [source JO Sénat du 11/12/2014 - page 2726] of French dermatologists. The average length

of practice since the thesis was 19 years  $\pm$  9.98, 202 (66.2%) were women, 87 (28.5%) practised in hospitals, 131 (42.9%) practised in private practice and 87 (28.5%) had a mixed practice. There was no difference in the length of practice between self-employed dermatologists and dermatologists with hospital activity (hospital and mixed).

### Prescription of Cyclosporin

One hundred thirty-six dermatologists (46.9%/290) prescribed cyclosporine for adult atopic dermatitis. This drug was used as a first-line systemic treatment in 77.2% of cases and as a second-line treatment in 31.6% of cases. A total of 46.3% of dermatologists prescribed it for moderate atopic dermatitis and 99.3% for severe atopic dermatitis. The daily doses prescribed were 3 mg/kg in 42.6% of cases, 5 mg/kg in 36% of cases, 2.5 mg/kg in 16.9% of cases, and other in 4.41% of cases. Biological monitoring was carried out every month (75.7%), every 2 months (9.56%), every 3 months (2.9%), and at other monitoring rates (11.8%). The average durations of treatment were less than 3 months (9.6%), from 3 to 6 months (51.5%), from 6 months to 1 year (36.8%), and more than 1 year (2.2%). A total of 56.9% of dermatologists did not perform any evaluation scoring before the initiation of cyclosporine, 7.9% performed the Investigator Global Assessment (IGA), 23.8% performed the Scoring Atopic Dermatitis (SCORAD), 13.4% performed the Eczema Activity and Severity Index (EASI), 17.2% evaluated the affected body surface area (SCA) and 34.8% performed the Dermatology Life Quality Index (DLQI).

Among the 154 dermatologists who not prescribing cyclosporine for adult atopic dermatitis, the reasons given were the absence of eligible patients ( $n=38$ , 24.7%); the fact that the product is not covered by a marketing authorization,  $n=3$  (1.9%); a lack of knowledge of the recommendations,  $n=15$  (9.7%); a lack of information and training,  $n=81$  (52.6%); the need for an initial hospital prescription,  $n=48$  (31.2%); and a lack of experience,  $n=122$  (79.2%).

### Prescription of Methotrexate

One hundred fifty-eight dermatologists (53.9%/293) prescribed methotrexate for adult atopic dermatitis. This drug was used as a first-line systemic treatment in 47.4% of cases, as a 2nd line or above treatment in 47.4% of cases, and after failure of dupilumab in 26.6% of cases. A total of 1.3% of dermatologists prescribed it for mild atopic



dermatitis, with 50% and 98.8% prescribing it for moderate and severe atopic dermatitis, respectively. The prescribed weekly doses were 15 mg in 48.4% of cases, 20 mg in 41.4% of cases, 25 mg in 4.5%, and other in 5.7% of cases. In the event of an insufficient response, the dosage was increased in 70.2% of cases. Biological monitoring was carried out every month (26%), every 2 months (19%), every 3 months (31.6%), and with other monitoring rhythms (23.4%). A total of 50.5% of dermatologists did not perform any evaluation scoring before methotrexate initiation, 7.8% performed IGA, 28.3% performed SCORAD, 13% performed EASI, 17% performed SCA and 38.9% performed DLQI.

Among the 135 dermatologists not prescribing methotrexate for adult atopic dermatitis, the reasons given were as follows: no eligible patients,  $n=63$  (46.7%); no MA in this indication,  $n=34$  (47.4%); a lack of information and training,  $n=53$  (39.3%); and a lack of experience,  $n=34$  (25.2%).

### Prescription of Other Treatments

A total of 4.8% of dermatologists (14/280) prescribed other systemic treatments for adult atopic dermatitis, such as phototherapy,  $n=10$ ; azathioprine,  $n=5$ ; and mycophenolate mofetil,  $n=3$ .

A total of 9.8% of dermatologists ( $n=28/287$ ) prescribed systemic corticosteroids for adult atopic dermatitis in moderate (17.9%) or severe (96.4%) forms. The dosages were  $<0.5$  mg/kg/day in 21.4% of cases and 0.5 to 1 mg/kg/day in 78.6% of cases. The average durations of treatment were less than 7 days in 32.1% of cases, from 7 to 30 days in 64.3% of cases, more than 1 month in 3.6% of cases, and other in 3.6% of cases.

A total of 56.4% of dermatologists prescribed dupilumab for atopic dermatitis in adults, with initial prescription in 71.4% of cases and exclusive renewal in 28.6% of cases.

Table 1 presents the results according to the mode of practice (hospital/mixed and private practice).

### Discussion

Systemic treatments for atopic dermatitis are used by half of the dermatologists who responded to this practice survey. Methotrexate is more commonly used than cyclosporine, although it does not have marketing authorisation for this indication. This illustrates a certain reluctance to use cyclosporine due to fear of side effects, the lack of experience of dermatologists with this medication, and the need

for an initial hospital prescription, among other factors. The greater familiarity with the prescription of methotrexate may also explain its extensive use.

There are differences in practice between private and hospital/mixed practice dermatologists, the latter prescribing more cyclosporine and dupilumab in the expected manner since they require an initial hospital prescription and more methotrexate. Similarly, the scores were used much less by private dermatologists than by hospital/mixed dermatologists before the initiation of systemic treatment, probably due to a lack of habit and lack of time.

This underuse of cyclosporine is also found in other countries.

In a practice survey conducted in 2013 in the United Kingdom, cyclosporine was less commonly used (37.4% of dermatologists) than other oral systemic treatments, such as azathioprine (51.2%) and general corticosteroid therapy (42.9%), whereas only cyclosporine had marketing authorisation for this indication in the United Kingdom at the time. According to the authors, the maximum recommended duration of treatment of one year for cyclosporine explained the choice of azathioprine, which can be used for longer periods.<sup>7</sup>

In a recent Australian survey, 22% of dermatologists surveyed had never used cyclosporine. Phototherapy (72%) and methotrexate (15%) were preferred to cyclosporine (9%) in the event of topical treatment failure. The durations of prescription of cyclosporine were less than 6 months in 7% of cases, 6 to 12 months in 24% of cases and more than 12 months in 69% of cases. The dose used was more than 5 mg/kg/day in 1% of cases, from 3.5 to 5 mg/kg/day in 42% of cases and less than 3.5 mg/kg/day in 56% of cases.<sup>6</sup>

In our study, almost 10% of dermatologists prescribed short courses of general corticosteroid therapy for adult atopic dermatitis. Its use should be limited to patients with a severe form, at a dose of less than 0.5 mg/kg/day and with a maximum duration of 8 days.<sup>8</sup> The need for repeated use illustrates the severity of atopic dermatitis and the need for specific systemic treatment.<sup>9</sup>

It should be noted that the proportion of dermatologists prescribing dupilumab is higher than those prescribing cyclosporine or methotrexate. This reflects an interest in new therapies for atopic dermatitis as well as a tolerance profile and manageability considered superior to that of systemic treatments.

The majority of dermatologists do not use an assessment score before initiating systemic treatment for adult

**Table 1** Results by Mode of Exercise (Hospital and Mixed Practice/Private Practice)

|  | Hospital/Mixed Practice (n= 175) | Liberal Practice (n=131)   | Chi Square |
|--|----------------------------------|----------------------------|------------|
| Prescription of methotrexate                             | 68.9% (n=115/167)<br>MD: 8       | 34.6% (n=46/127)<br>MD: 4  | ≤ 0.001    |
| Reason for not prescribing methotrexate                  | n=52                             | n= 83                      |            |
| - Absence of eligible patients                           | -57.7% (n=30/52)                 | -39.8% (n=33/83)           |            |
| - No marketing authorisation for AD                      | -46.1% (n=24/52)                 | -48.2% (n=40/83)           |            |
| - No experience with methotrexate                        | -9.6% (n=5/52)                   | -34.9% (n=29/83)           |            |
| - Lack of training/information                           | -21.1% (n=11/52)                 | -50.6% (n=42/83)           |            |
| Prescription of cyclosporine                             | 75.1% (n=124/165)<br>MD: 10      | 10.3% (n=13/126)<br>MD: 5  | ≤ 0.001    |
| Reason for not prescribing cyclosporine                  | n= 41                            | n=113                      |            |
| • Absence of eligible patients                           | -26.8% (n=11/41)                 | -23.9% (n=27/113)          |            |
| • Lack of knowledge of the recommendations               | -0                               | -13.3% (n=15/113)          |            |
| • No experience with cyclosporine                        | -78% (n=32/41)                   | -79.6% (n=90/113)          |            |
| • Lack of training/information                           | -41.5% (n=17/41)                 | -56.6% (n=64/113)          |            |
| • Requires initial hospital prescription                 | -4.9% (n=2/41)                   | -40.7% (n=46/113)          |            |
| Prescription of oral corticoids                          | 7.9% (n=13/164)<br>MD: 9         | 12.1% (n=15/124)<br>MD: 7  | NS         |
| Prescription of dupilumab                                | 80.5% (n=132/167)<br>MD: 8       | 25% (n=31/124)<br>MD: 7    | ≤ 0.001    |
| Absence of use of score before methotrexate prescription | 39.5% (n=66/167)<br>MD: 8        | 64.6% (n=82/127)<br>MD: 4  | ≤ 0.001    |
| Absence of use of score before cyclosporine prescription | 35.1% (n=58/165)<br>MD: 10       | 84.9% (n=107/126)<br>MD: 5 | ≤ 0.001    |

Abbreviations: MD, missing data; AD, atopic dermatitis; NS, not significant.

atopic dermatitis. This makes it more difficult to assess the severity of atopic dermatitis and the effectiveness of treatments. Lack of familiarity with atopic dermatitis assessment scores (SCORAD, EASI, Patient Oriented Eczema Measure, etc.) and the absence of a consensus definition of the severity of atopic dermatitis, unlike other chronic inflammatory dermatoses such as psoriasis, may explain this low use.

## Conclusion

Our study showed that half of French dermatologists use systemic treatments in topical dermatitis in adults. Methotrexate is used more than cyclosporine, probably due to greater familiarity with this medication and the absence of an initial hospital prescription. Dupilumab, although more recently available, is already quite widely used. Our study also highlights an underutilisation of assessment scores for atopic dermatitis prior to the introduction of systemic treatments.

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## Disclosure

Dr Laure Mery-Bossard reports personal fees from sanofi, during the conduct of the study; personal fees and/or non-financial support from Abbvie, Janssen, Novartis, Leo pharma, outside the submitted work. Dr Ziad Reguini is consultant, advisory board member, speaker and/or investigator for SANOFI, Lilly, Abbvie, MEDAC, PFIZER, PIERRE FABRE DERMATOLOGIE, LA ROCHE POSAY, CERAVE, Leo Pharma, and ALMIRALL, during the conduct of the study. The authors report no other conflicts of interest in this work.

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# Use of Methotrexate in the Treatment of Moderate to Severe Plaque Psoriasis in France: A Practice Survey

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**Purpose:** To evaluate the modalities of methotrexate prescription for moderate to severe psoriasis by dermatologists in France.

**Patients and Methods:** We performed a national online practice survey between October and December 2020.

**Results:** A total of 254 dermatologists responded, 237 reported prescribing methotrexate for moderate to severe psoriasis in adults, of which 57% as a first line systemic treatment. Nineteen percent reported performing a test dose at the initiation of treatment. Methotrexate was prescribed orally in 54.7% of cases, subcutaneously in 44.8% of cases and intramuscularly in 0.4% of cases. The initial weekly dose of methotrexate was <15 mg for 30% of the dermatologists and ≥15 mg for 70% of them. Two hundred and three dermatologists had already change the route of administration for methotrexate from the oral to injectable form due to poor tolerance (48.3%), lack of efficacy (35%) or lack of compliance (16.7%). Two hundred thirty-four dermatologists (98.7%) reported prescribing folic acid with methotrexate, and 79.3% reported prescribing tests evaluating the risk of hepatic fibrosis. Forty-three percent of dermatologists have not initiated or have reduced their prescriptions since the beginning of the pandemic of COVID-19. Prescribing patterns were different according to the type of practice (private practice versus hospital/mixed practice).

**Conclusion:** Methotrexate is used by the majority of dermatologists interviewed for moderate to severe psoriasis in adults, with heterogeneity of practices.

**Keywords:** psoriasis, methotrexate, practice survey, dermatologists

Adult psoriasis is a frequently occurring chronic inflammatory dermatosis, the prevalence of which is estimated to be 4.4% in France.<sup>1</sup> Moderate to severe forms, defined by a Psoriasis Activity and Severity Index (PASI) score >10, an affected skin surface >10, a Dermatology Life Quality Index (DLQI) score >10, or the involvement of particular locations (palms and soles, scalp, face, genital area, nails, etc.) justify prescription of a systemic treatment.<sup>2</sup> Methotrexate is the first-line systemic treatment recommended in France.<sup>3</sup> Surveys of international practice have highlighted heterogeneity in the prescription of methotrexate for this indication.<sup>4,5</sup> Herein, we evaluate the modalities of methotrexate prescription for moderate to severe psoriasis by dermatologists in France.

## Patients and Methods

We conducted a practice survey of Reso member dermatologists. Reso gathers more than 700 French dermatologists [ie nearly one French dermatologist out of 4].

These dermatologists work exclusively in hospitals, exclusively in private practice or in a mixed practice. They were asked by email to answer a digital questionnaire between October and December 2020. In the invitation email to participate in the project, each doctor had to confirm his or her agreement to participate in order to access the online questionnaire. They were under no obligation to respond and were not paid for it.

## Questionnaire

The questionnaire was developed by dermatologists and a physician specialist in public health. It collected the age of the dermatologist, the length of the practice, the mode of practice (hospital, private or mixed), whether consultation dedicated to psoriasis is offered, and the prescription of methotrexate for adult psoriasis. It collected information on the methods of prescribing methotrexate, including the method of administration, dose, concomitant prescription of folic acid, monitoring methods, as well as the impact of the COVID-19 pandemic on prescriptions. The reasons for not prescribing methotrexate were collected for dermatologists who stated that they did not prescribe methotrexate for this indication.

For this type of study, French regulations do not require submission to an ethics committee as this study does not enter the field of the deliberation n°2018-154 of the 3rd of May 2018 (JORF n°0160 of the 13th of July 2018).

## Statistics

Quantitative data are expressed as the average  $\pm$  standard deviation (SD), and qualitative data are expressed as percentages (%). Means were compared using Student's *t*-test, and frequencies were compared using Chi-square test. A value of  $p < 0.05$  was considered statistically significant. Statistical analyses were performed using R software version 3.5.1.

## Results

### Characteristics of Dermatologists

Two hundred fifty-four dermatologists answered the questionnaire, representing 7.6% of French dermatologists [source JO Sénat du 11/12/2014 - page 2726]. The average length of practice was 18.9 years; 74 (29.1%) worked in hospitals, 93 (36.6%) in private practice and 87 (34.2%) in a mixed practice; and 71 (27.9%) offered consultation dedicated to psoriasis.

### Prescription of Methotrexate

Two hundred thirty-seven dermatologists (93.3%) reported prescribing methotrexate for moderate to severe psoriasis in adults. This proportion was 100% for dermatologists with hospital activity and 90% for those in private or mixed practices.

Seventeen dermatologists declared themselves to be non-prescribers. Among these physicians, 9 were in private practice, and 8 were in a mixed practice. Reasons given for non-prescription included fear of side effects ( $n=8$ ), lack of experience ( $n=7$ ), and dearth of eligible patients ( $n=2$ ).

### Prescription Modalities

Among prescribers, 57% stated that they prescribed methotrexate as a first line systemic treatment for adult psoriasis, 29% as a second line treatment and 14% as a third line treatment or less frequently. Dermatologists estimated the percentage of their moderate to severe psoriatic patients treated with methotrexate to be 36.2%.

Forty-six dermatologists (19%) reported that they perform a test dose at the initiation of treatment. Methotrexate was prescribed orally in 54.7% of cases, subcutaneously in 44.8% (pen, 36.1%; syringe, 8.7%), and intramuscularly in 0.4% of cases. The proportion of patients judged to be autonomous in carrying out the injections was 65.4%. The initial weekly dose of methotrexate was less than 15 mg for 30% of the dermatologists (7.5 mg: 7.6%; 10 mg: 16%; and 12.5 mg: 6.7%) and  $\geq 15$  mg for 70% (15 mg: 51.9%; 17.5 mg: 7.1%; 20 mg: 9.7%; 22.5 mg: 0.4%; and 25 mg: 0.4%). The time elapsing between dermatologists prescribing and evaluating the efficacy of methotrexate was less than 6 weeks for 9% (2 weeks: 0.4%; 4 weeks: 8.4%), from 6 to 8 weeks for 13% (6 weeks: 4.6%; 8 weeks: 8%) and greater than or equal to 10 weeks for 78% (10 weeks: 1.3%; 12 weeks: 30.4%; and 16 weeks: 46.8%). Two hundred and three dermatologists (86%) stated that they had already changed the route of administration for methotrexate (from the oral to injectable form) due to poor tolerance (48.3%), lack of efficacy (35%) or lack of compliance (16.7%).

In the event of a therapeutic response being deemed insufficient, 40 dermatologists (16.9%) declared changing to subcutaneous administration, 20 (8.4%) changing treatment and 177 dermatologists (74.7%) to increasing the dose of methotrexate. Of these changes, the adjustment steps were 2.5 mg/week in 54.9% of cases, 5 mg/week in



41.8% of cases, and other in 3.4% of cases. In the case of digestive side effects, 172 dermatologists (72.6%) reported switching to subcutaneous administration, 29 (12.2%) to decreasing the dosage of methotrexate, and 36 (15.2%) to changing treatment. In cases of asthenia, 122 dermatologists (51.5%) reported reducing the dose of methotrexate, 87 (36.7%) changing treatment, and 28 (11.8%) switching to subcutaneous administration.

Two hundred thirty-four dermatologists (98.7%) reported prescribing folic acid with methotrexate. The dose was 5 mg/week for 59 dermatologists (24.9%), 10 mg/week for 134 (56.5%) and more than 10 mg/week for 44 (18.6%). The recommended day of use was the day after taking methotrexate for 24 dermatologists (10.1%), 48 hours after taking methotrexate for 204 dermatologists (86.1%), and every day except for the day of methotrexate use for 9 dermatologists (3.8%).

One hundred eighty-eight dermatologists (79.3%) stated that they prescribed tests evaluating the risk of hepatic fibrosis, including Fibrotest® for 25 (13.3%), pro-collagen III assay for 110 (58.5%) and Fibroscan for 132 (70.2%).

Since the start of the COVID-19 pandemic, 128 dermatologists (54%) reported that their methotrexate prescriptions for psoriasis had remained stable, 71 (30%) that they had decreased, and 3 (1.3%) that they had increased. Twenty-eight (11.8%) reported that they had not initiated methotrexate since the beginning of the pandemic.

Prescribing patterns by type of practice are shown in Table 1.

## Discussion

The results of this survey underline the heterogeneity of practices in the prescription of methotrexate in moderate to severe psoriasis in adult patients in France. In fact, even though almost all dermatologists questioned used methotrexate for moderate to severe psoriasis in adults, the methods of prescription vary, apart from the association with folic acid supplementation, which is almost systematic.

Only slightly more than one-half of dermatologists questioned indicated that they prescribe methotrexate as a first-line systemic treatment for moderate to severe psoriasis, whereas it is the first-line systemic treatment recommended in France.<sup>3</sup> A fifth of dermatologists questioned stated that they perform a test dose, which is currently no longer compulsory<sup>3</sup> but may be useful in fragile patients.<sup>6,7</sup> Almost two-thirds of dermatologists questioned start at

a dose between 7.5 and 15 mg/week, in accordance with French recommendations.<sup>3</sup> However, a high cumulative dose during the first month of treatment (between 60 and 75 mg) was associated with improved efficacy in one study,<sup>8</sup> while an initial dose of 15 mg/week was proposed in some recommendations.<sup>7,9</sup> The oral route of administration is preferred, although recent data have shown better efficacy and tolerance with a subcutaneous route of administration in a cohort of German patients.<sup>9</sup> Even though the different recommendations agree on the need for folic acid supplementation,<sup>3,7,10</sup> prescription modalities differ: while there are currently no British recommendations,<sup>10</sup> a daily supplementation, except if methotrexate is administered concomitantly is suggested by American recommendations<sup>7</sup> and a 5mg supplementation, 24h after the intake of methotrexate, is suggested by French recommendation.<sup>3</sup> The time taken to evaluate the efficacy of treatment is more than 10 weeks for 78% of dermatologists, consistent with the kinetics of the molecule.<sup>3,7</sup> The vast majority of dermatologists interviewed stated that they monitor the risk of hepatic fibrosis upon methotrexate use by dedicated testing. This risk remains debated since meta-analyses have yielded contradictory results; the cumulative dose of methotrexate has not been systematically identified as a risk factor, in contrast to diabetes, alcoholism and obesity.<sup>11,12</sup> The COVID-19 pandemic has impacted the prescription of methotrexate among the dermatologists questioned, since 43% of them have not initiated or have reduced their prescriptions since the beginning of the pandemic. However, data have highlighted the absence of a seriously increased risk of COVID-19 in those undergoing systemic treatment for psoriasis, whether in the initiation or maintenance phase of treatment.<sup>13</sup> It might be useful to vaccinate against COVID-19 before initiating methotrexate treatment, particularly in patients at risk of severe COVID-19, as there is a lower vaccine response in patients on this treatment.<sup>14</sup>

For the analysis, we grouped dermatologists in mixed and hospital-based practices together, as practising in a hospital environment in France allows access to the primary prescription of certain psoriasis treatments (cyclosporine and biotherapy). This study highlights differences in practice according to prescribing patterns. Dermatologists in hospital and mixed practice more frequently prescribe methotrexate as a first line systemic treatment at a higher initial dosage, more often in the form of subcutaneous pens, and evaluate their patients later. This may reflect a greater habit of methotrexate use. Their patients are more autonomous in performing subcutaneous injections, likely because

**Table 1** Results by Mode of Practice (Hospital and Mixed Practice/Private Practice)

| <b>Study Population</b>  | <b>Hospital/Mixed Practice (n=161)</b> | <b>Private Practice (n=93)</b> | <b>Chi Square</b> |
|--|--|--------------------------------|-------------------|
| Prescription of methotrexate   | 93.3% (n=153/161)                      | 90.32% (n=84/161)              | NS                |
| Average length of service (years)                                    | 18.2                                   | 19.9                           | p=0.02            |
| <b>Analyse population</b>  | <b>Hospital/mixed practice (n=153)</b> | <b>Private practice (n=84)</b> | <b>Chi square</b> |
| Average length of service (years)                                    | 18.2                                   | 19.9                           | p=0.02            |
| Systemic treatment line in which methotrexate is prescribed          |  |                                | p=0.001           |
| • 1st line   | 69.93% (n=107)                         | 33.3% (n=28)                   |                   |
| • 2nd line   | 23.5% (n=36)                           | 39.3% (n=33)                   |                   |
| • 3rd line   | 6.5%(n=10)                             | 25% (n=21)                     |                   |
| • 4th line   | 0%(n=0)                                | 2.4% (n=2)                     |                   |
| Carrying out a test dose at initiation                               | 19.6% (n=30)                           | 19% (n=16)                     | NS                |
| How methotrexate is administered                                     |  |                                | NS                |
| • Per os   | 52.2%                                  | 59.4%                          |                   |
| • Subcutaneous pen   | 40%                                    | 29%                            | p=0.007           |
| • Subcutaneous syringe   | 7.4%                                   | 11%                            | NS                |
| • Intramuscular  | 0.3%                                   | 0.6%                           | NS                |
| Percentage of patients who are autonomous in carrying out injections | 69.4%                                  | 58.2%                          | p= 0.04           |
| Initiation dosage of methotrexate                                    |  |                                | p<0.001           |
| • < 15 mg/week   | 21%(n=32)                              | 52.4%(n=40)                    |                   |
| • ≥ 15 mg/week   | 79%(n=121)                             | 47.6%(n=44)                    |                   |
| Time frame for evaluating the effectiveness of methotrexate          |  |                                | p< 0.003          |
| • < 6 weeks  | 4.6%(n=7)                              | 16.7%(n=14)                    |                   |
| • 6 to 8 weeks   | 11.1%(n=17)                            | 15.4% (n=13)                   |                   |
| • ≥10 weeks  | 84.3%(n=129)                           | 67.9%(n=57)                    |                   |
| Dose adjustment level used   |  |                                | p< 0.001          |
| • 2.5 mg/week  | 47.1%(n=72)                            | 69% (n=58)                     |                   |
| • 5 mg/week  | 50.3%(n=77)                            | 26.2%(n=22)                    |                   |
| • Others   | 2.6% (n=4)                             | 4.8%(n=4)                      |                   |
| Reasons for switching from an oral to an injectable form             | 91%                                    | 76%                            | p< 0.001          |
| • Poor tolerance   | 43.9%(n=61)                            | 57.8%(n=37)                    |                   |
| • Lack of efficacy   | 35.2%(n=49)                            | 34.4%(n=22)                    | p=0.004           |
| • Lack of compliance   | 20.9%(n=29)                            | 7.8%(n=5)                      |                   |
| Concomitant prescription of folic acid                               | 98.9%                                  | 98.3%                          | NS                |
| Prescription test for the evaluation of hepatic fibrosis             | 77.8%(n=119)                           | 82.1%(n=69)                    | p< 0.001          |

Abbreviation: NS, not significant.

they benefit from therapeutic education by paramedical staff. Dermatologists in private practice, on the other hand, carry out more tests to monitor risk to the liver. We have assessed whether the date of graduation has an impact, it does not for

the prescription of methotrexate, test dose or fibrosis test, only the initiation dose is different.

The limitations of this study are the declarative nature of the data and the method of recruitment of the



dermatologists questioned as they all participate in a network dedicated to chronic inflammatory dermatoses.

## Conclusion

The results of our study show that methotrexate is used by the majority of dermatologists interviewed for moderate to severe psoriasis in adults. We highlighted heterogeneity in prescription modalities depending on the mode of practice (hospital based or private) but not the years of experience.

## Disclosure

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The authors report no other conflicts of interest in this work.

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# Biological Therapies or Apremilast in the Treatment of Psoriasis in Patients with a History of Hematologic Malignancy: Results from a Retrospective Study in 21 Patients

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**Background:** Few studies addressing the safety and efficacy of biological therapy (BT) or apremilast (APR) in patients with psoriasis with a history of hematologic malignancy (HM) exist.

**Aim:** To describe the tolerance and efficacy of BT and APR in moderate-to-severe psoriasis in patients with a history of in-remission or evolving HM.

**Methodology:** A retrospective, multicenter chart review of the tolerance and efficacy of BT or APR in patients with moderate-to-severe psoriasis and a clinical history of in-remission or evolving HM.

**Results:** Twenty-one patients with severe psoriasis and a history of HM were included in France by the GEM Resopso study group. Of the 16 patients treated with one or more BT lines, none showed recurrence of their HM which was considered as stable or in remission, and only 2 patients showed an evolution of their HM which had been considered as stable at the beginning of treatment. In the 10 patients treated with APR, the HM of one patient who also received BT worsened. The 3 evolutions did not impact the treatment with BT or APR. Tolerance was very satisfactory, with a low occurrence of infections. Regarding efficacy, only one patient treated with APR did not achieve any notable clinical improvement.

**Conclusion:** Despite supportive data regarding tolerance, the heterogeneity of the analyzed population and limited available data, BT and APR should be used with caution in this patient population and investigations on larger cohorts should be conducted to further assess their tolerance in this patient population.

**Keywords:** biological therapies, apremilast, psoriasis, hematological malignancies

## Introduction

Biological therapies (BT) are humanized proteins synthesized by genetic engineering. BT in psoriasis comprise anti-TNF $\alpha$  (adalimumab, etanercept, infliximab, certolizumab pegol) and anti-interleukins including ustekinumab (anti-IL-12/23), secukinumab and ixekizumab (anti-IL-17), brodalumab (anti-receptor of IL-17), guselkumab and risankizumab (anti-IL-23).<sup>1,2</sup>

BT are well tolerated in patients with psoriasis. The most commonly reported adverse effects (AEs) associated with BT were upper respiratory tract infections.<sup>3</sup> Generally the incidence of severe AEs in psoriatic patients receiving anti-IL-12/23



antibody or IL-17 inhibitors was reported to be lower than that of TNF- $\alpha$  inhibitors, although that of TNF- $\alpha$  inhibitors is still very low.<sup>4</sup>

Apremilast (APR, phosphodiesterase inhibitor 4) is an immunomodulator marketed since 2015 in Europe.<sup>5,6</sup> In vitro and in vivo studies showed that APR is efficient on PDE4 activity, inflammatory signal expression, and dermal psoriasiform signs. In patients with moderate-to-severe psoriasis, APR significantly reduced plasma levels of interleukin (IL)-17F, IL-17A, IL-22, and tumor necrosis factor- $\alpha$  as well as of cytokines.<sup>7,8</sup> Overall, treatment with APR is safe. However, a few common ( $\geq 5\%$  of patients) mild to moderate AEs have been reported, including diarrhea, nausea, headache, and nasopharyngitis.<sup>9</sup>

Patients with psoriasis have been reported to present with an increased risk of cancer, which may be due to impaired immune surveillance, immune modulatory treatments, chronic inflammation and/or co-risk factors such as obesity. BT are independently associated with a slight increase risk of cancer, but this is less than cyclosporine, with the risk confounded by disease severity and other co-risk factors. The data on small molecule therapies such as APR are currently considered to be immature for comment, although no signal has yet been identified.<sup>10</sup>

In France, BT and apremilast APR are recommended as a treatment option in adults with moderate-to-severe psoriasis that has not responded to at least 2 standard systemic therapies, such as cyclosporine, methotrexate, or phototherapy; or in patients who are intolerant of, or have a contraindication to these treatments.<sup>11</sup>

The use of BT and APR is currently not contraindicated in patients with psoriasis and a history of hematological malignancies (HM).<sup>12</sup> However, several recommendations encourage caution and propose to limit their use to severe psoriasis after consultation with a hematologist as part of an individual benefit/risk consideration.<sup>13,14</sup>

The influence of BTs on the evolution of HM remains largely unknown. The evidence from basic research does not support the existence of a potentially deleterious effect of TNF $\alpha$  or interleukin inhibition on the evolution of blood disorders.<sup>15–20</sup> Conversely, in some situations, treatments with anti-TNF alpha or anti-IL17 have been proposed for the treatment of different malignant hematologic diseases.<sup>21–24</sup> The most substantiated clinical information from registries relates to the risk of relapse of TNF lymphoma during rheumatoid arthritis with reassuring conclusions. However, these findings are based on a small

number of patients and a limited follow-up.<sup>25,26</sup> Except for these data, there is no information available in the literature about the risk of recurrence or evolution of any malignant HM, and especially in indications other than RA, particularly in psoriasis. No treatment-related carcinogenic risk with APR has been identified in animal carcinogenicity studies.<sup>27</sup> However, no current practice data are available to discuss its potential impact on patients with HM.

The purpose of this study was to describe the tolerance and efficacy of BT and APR in moderate-to-severe psoriasis in patients with a history of in-remission or evolving HM.

## Methodology

This study was a national-wide, retrospective, multicenter observational chart review conducted in France in private practice or at hospital sites by the GEM Resopso study group. Resopso (<http://resopso.fr>) is an association of dermatologists throughout France involved in the care and research of patients with psoriasis. The research protocol was approved by the local research and innovation department (Direction de la Recherche Clinique et de l'Innovation CHU Amiens – ref: PI2020-843-0025). According to the French law JARDE (Décret no 2016–1537), patients had to provide a written non-opposal for using their data for this project. The study was conducted according to the principles of the declaration of Helsinki and conformed to local legal data protection requirements (CNIL, MR003).

Any adult patients receiving BT or APR for their moderate-to-severe psoriasis (ongoing or discontinued) and who had a clinical history of remission or of an evolving HM were suitable for the study. Data from patients with a history of monoclonal gammopathies of undetermined significance were not to be included.

The following data were collected: demographic, psoriasis severity before BT/APR, type of HM prior to BT/APR, type of BT, efficacy of BT or APR on psoriasis, reported adverse events with BT or APR and evolution of HM during treatment with BT or APR.

Data about the HM stage according to its classification as well as its prognostic score, if indicated, were collected in order to assess its severity. For each type of HM, its status (in remission, stable or evolving before initiating BT or APR) was indicated.

Evolution was defined as a) in remission, if clinical and biological normalization; b) stable, if no worsening of the



HM or no introduction of a new-treatment for HM and c) evolving, in case of worsening of the HM stage or exacerbation of HM (eg evolution into acute myeloid leukemia for myelodysplastic syndrome (MDS), or evolution into lymphoma for chronic lymphoid leukemia (CLL)) and/or in the event of a newly initiated treatment for HM and/or recurrence of HM.

Tolerance was assessed according to the evolution of HM after treatment with BT or APR had started. Adverse events (infections or other events) that occurred during treatment with BT or APR were collected.

The efficacy of BT or APR was evaluated, based on the psoriasis severity score assessed during the last dermatology consultation using the psoriasis global assessment (PGA), body surface area (BSA), and psoriasis area severity index (PASI).

Descriptive statistics were performed for all parameters. For categorical variables, numbers and frequencies were calculated. For continuous numerical variables, averages, median, minimum, maximum and standard deviations were calculated.

## Results

### Patient and Disease Data

We analyzed data from 21 patients, 4 women and 17 men; the mean age was 63, ranging from 50 to 82 years. Twenty (20) patients had plaque psoriasis, the remaining patient had palmoplantar pustular psoriasis.

Eighteen (18) patients had past first-line psoriasis treatments including phototherapy, acitretin, methotrexate and cyclosporine prior to BT or APR. In total, 24 treatment courses with BT (7 etanercept, 2 adalimumab, 2 infliximab, 7 ustekinumab, 4 secukinumab, 1 ixekizumab, 1 guselkumab) were identified in 16 patients; 10 patients received APR. Of those 10, 3 received APR prior to and 2 after treatment with BT, and 5 received only APR.

The median treatment duration with BT and APR was 16 months [3–120] and 6 months [2–30] respectively. Seven (7/21) patients had been on BT/APR treatment for less than one year and the majority of patients (14/21) had been on BT/APR treatment for more than 2 years at the last evaluation.

The delay between diagnosis of HM and initiation of BT or APR was on average 54 months, ranging from 0 to 240 months.

Detailed patient and disease information is provided in Table 1.

## Tolerance

Detailed tolerance results for each of the 21 patients are provided in Table 2.

Of the 9 patients considered in remission before BT/APR, none had recurrence reported. Four (4) patients received BT, 4 received APR, and one received both. Only one patient was still receiving maintenance treatment (brentuximab for anaplastic large-cell stage IV T-lymphoma).

Eleven (11) patients had a stable HM at the time BT or BT/APR was started. HM had been stabilized in 8 patients. The other 3 patients observed an evolution of their HM during treatment with BT (2 patients) and APR (one patient). One of these patients had a multi-treated Vaquez polycythemia, stabilized under ruxolitinib. After 31 months of successive treatments with etanercept, APR and secukinumab, his Vaquez disease evolved into a severe secondary myelofibrosis grade 3, requiring the introduction of erythropoietin and multiple transfusions of globular caps. Because of the patient's transition to palliative care, and to maintain his comfort, secukinumab was maintained. The second patient, followed by essential thrombocythemia JAK2 +, under simple supervision before the introduction of treatment with BT, presented with an ischemic stroke at 9 months from the start of the treatment with etanercept, associated with thrombocytosis, which motivated the introduction of treatment with hydroxycarbamide. Treatment with etanercept was continued with no evolution of HM. Finally, the last patient had a stable CLL grade A for 4 years after successive treatments with etanercept then adalimumab. Ten (10) months after switching to APR, an evolution of CLL was observed leading to the introduction of a treatment with obinutuzumab and chlorambucil. APR was continued and then stopped, due to a lack of efficacy.

The patient with an HM evolving prior to the introduction of BT/APR was followed for a recurrent stage IV follicular B lymphoma along with a severe psoriasis outbreak. Two (2) months after the initiation of APR, the patient had received vinblastine and was waiting for treatment with CAR-T cells (gene therapy, manufactured from the patient's T lymphocytes).

Five (5) patients presented a total of 7 significant adverse events. Three (3) patients had infectious complications: 2 patients with one episode of herpes skin infection after 3 months of secukinumab treatment and 6 months of ustekinumab treatment, respectively (the latter

**Table 1** Patient Demographic and Disease Data

|  |            |
|--|------------|
| <b>Gender, N (%)</b>   |            |
| Women  | 4 (19)     |
| Men  | 17 (81)    |
| <b>Age (years)</b>   |            |
| Median [min-max]   | 63 [50–82] |
| <b>Main psoriasis type, N (%)</b>  |            |
| Plaque type  | 20 (95)    |
| Palmoplantar Pustular  | 1 (5)      |
| <b>Severity score prior to treatment, Mean±SD</b>  |            |
| PASI   | 16.6 (8)   |
| PGA  | 3.6 (0,85) |
| BSA  | 29 (15)    |
| <b>Prior systemic treatment, N (%)</b>   | 18 (86)    |
| Phototherapy   | 11 (52)    |
| Methotrexate   | 13 (61)    |
| Cyclosporine   | 2 (10)     |
| Acitretine   | 12 (57)    |
| Etretinate   | 1 (5)      |
| <b>BT type administered, N (%)</b>   |            |
| Etanercept   | 7 (33)     |
| Infliximab   | 2 (10)     |
| Adalimumab   | 2 (10)     |
| Ustekinumab  | 7 (33)     |
| Secukinumab  | 4 (19)     |
| Ixekizumab   | 1 (5)      |
| Guselkumab   | 1 (5)      |
| <b>APR, No (%)</b>   | 10 (48)    |
| <b>Type of malign HM, N (%)</b>  |            |
| Non-Hodgkin's lymphoma   | 5 (24)     |
| Hodgkin's lymphoma   | 4 (19)     |
| Chronic lymphoid leukemia  | 5 (24)     |
| Multiple myeloma   | 1 (5)      |
| Waldenström disease  | 1 (5)      |
| Vaquez disease   | 3 (14)     |
| Essential thrombocythemia  | 2 (10)     |
| <b>Delay between diagnosis and start of PT/<br/>APR treatment, Median [min-max]<br/>(months)</b> | 53 [0–204] |

Abbreviations: APR, apremilast; BT, biological treatment; HM, hematologic malignancy; PASI, psoriasis area severity index; PGA, psoriasis global assessment; BSA, body surface area.

patient had been treated for more than 2 years with several successive BTs). The third patient presented with an acute prostatitis and secondary bilateral broncho-pneumopathy, which occurred more than 10 years after the start of his etanercept treatment and which led to its temporary suspension. One patient had multiple squamous cell

carcinomas treated with surgery, 4 years after the onset of BT. This patient had previously received treatment with multiple sessions of phototherapy, prior to the onset of BT.

Two (2) patients had a stroke after taking etanercept for 9 months and more than 10 years after treatment had started; treatment was maintained (Table 2).

## Efficacy

Mean psoriasis severity scores were evaluated during the last treatment received (BT or APR) for psoriasis. The PASI, PGA and BSA average scores at introduction of BT or APR were 16.6, 3.6 and 29% respectively. Improvement was significant in almost all patients (20/21) with average scores at the end of follow-up of 2.2, 0.9 and 2.6%. Eighteen (18) of the 21 patients had a PGA 0/1 of which 6 had their psoriasis cured. Only one patient had not shown a marked improvement during treatment of more than 2 years of APR, with a PGA score of 4 to 3 at the end of the follow-up.

## Discussion

This study analyzed data from 21 patients with severe psoriasis, who had a history of HM and were treated with BT or APR. Of the 16 patients treated with one or more BT lines, none showed recurrence and only 2 patients had an evolving HM. The HM of one patient who received APR and BT worsened. However, none of these 3 relapses impacted treatment with BT or APR. Tolerance was very satisfactory, as shown through the low occurrence of infectious episodes. Regarding efficacy, only one patient treated with APR did not achieve any notable clinical improvement.

To our knowledge, this is the most important series of cases of patients with a history of HM treated with BT for psoriasis. Furthermore, to date, no studies have evaluated the tolerance of APR regardless of the indication, in cases of a history of hematologic malignancy. Only Kahn et al, in 2019, reported results for patients treated with BT or APR for psoriasis with a history of cancer.<sup>28</sup> In total, of the 16 patients with a history of cancer out of 690 patients in the cohort, only one patient had a history of hematologic malignancy and with no recurrence after a treatment lasting 23 months.

In the majority of our patients, HM did not recur or remained stable during treatment with BT or APR. Nevertheless, 3 patients observed an evolution of their HM. Two (2) cases of evolution observed with BT were reported



Table 2 Tolerance of BT/APR Treatment in 21 Patients with Psoriasis and a History of HM in Remission or in an Evolving Stage

| Gender/<br>Age | HM                                     | Prognostic<br>Score of HM                                | HM Treatment<br>Prior to BT/<br>APR  | HM<br>Treatment<br>During BT/<br>APR | HM Evolution<br>Status Prior to<br>BT/APR | Delay<br>Between HM<br>Diagnosis<br>and<br>Initiation of<br>BT/APR | Duration of BT/<br>APR After HM<br>Diagnosis  | Evolution of HM<br>During BT/APR   | Complications<br>During BT/<br>APR |
|----------------|--|--|--|--------------------------------------|---|--|---|--|------------------------------------|
| M 54           | Essential<br>thrombocytopenia<br>JAK2+ | Score=1<br>intermediate risk<br>according to IPSET       | Hydroxy-<br>carbamide  | Hydroxy-<br>carbamide                | Stable                                    | 4 years and 1<br>month   | ETN: 4 years and 8<br>months  | Stable   | None                               |
| M 70           | CLL stage A                            | Score=2<br>intermediary risk<br>according to CLL-<br>IPI | None   | None                                 | Stable                                    | 4 years  | ETN: 13 months<br>ADA: 3 months<br>IFX: 1 year and 3<br>months<br>USK: 10 months<br>SKN:3 months<br>GSK: 1 year | Stable   | Cutaneous<br>herpes infection      |
| F 82           | Vaquez disease                         | NA   | Pipobroman and<br>hydroxy-<br>carbamide,<br>interferon,<br>Thiospa-VPI6<br>ruxolitinib | Ruxolitinib                          | Stable                                    | 10 years   | ETN: 3 months<br>APR: 13 months<br>SKN: 1 year and 3<br>months  | Progression into severe<br>myofibrosis stage 3<br>with blood transfusion | None                               |
| F 59           | Multiple indolent<br>myeloma           | Stage I according<br>to ISS                              | Conditioning<br>chemotherapy and<br>autologous<br>transplants                          | None                                 | Remission < 5<br>ans                      | 10 years and 7<br>months   | SKN: 1 year<br>IXX: 1 months  | No recidivism  | Cutaneous<br>herpes infection      |
| M 59           | Essential<br>thrombocytopenia<br>JAK2+ | Score=0 low risk<br>according to IPSET                   | None   | None                                 | Stable                                    | 1 year   | ETN: 5 years and 2<br>months  | Progression due to<br>initiation of hydroxy-<br>carbamide                | One episode of<br>stroke           |
| M 67           | Vaquez disease                         | NA   | Bleeding   | Bleeding                             | Stable                                    | 5 years  | ETN: 2 years  | Stable   | None                               |

(Continued)

Table 2 (Continued).

| Gender/<br>Age | HM  | Prognostic<br>Score of HM                           | HM Treatment<br>Prior to BT/<br>APR  | HM<br>Treatment<br>During BT/<br>APR | HM Evolution<br>Status Prior to<br>BT/APR | Delay<br>Between HM<br>Diagnosis<br>and<br>Initiation of<br>BT/APR | Duration of BT/<br>APR After HM<br>Diagnosis | Evolution of HM<br>During BT/APR | Complications<br>During BT/<br>APR                                      |
|----------------|---|---|--|--------------------------------------|---|--|--|----------------------------------|---|
| M 68           | Hodgkin's<br>lymphoma stage III                     | NR  | Chemotherapy   | None                                 | Remission > 5<br>years                    | 2 years  | ETN: 10 years and<br>3 months                | No recidivism                    | Prostatitis and<br>broncho-<br>pneumopathia<br>one episode of<br>stroke |
| M 72           | Anaplastic<br>T-Lymphoma with<br>big cells stage IV | Score=2 low<br>intermedial risk<br>according to IPI | Brentuximab ICE<br>followed by<br>brentuximab alone<br>as maintenance<br>treatment       | Brentuximab                          | Remission < 5<br>years                    | APR: 2 years/<br>USK: 3 years                                      | APR: 1 year and 6<br>months USK: 7<br>months | No recidivism                    | None  |
| M 56           | CLL stage A   | Score=0 low risk<br>according to CLL-<br>IPI        | None   | None                                 | Stable                                    | 1 year   | USK: 3 months                                | Stable                           | None  |
| M 66           | Waldenström<br>disease                              | Score=1 low risk<br>according to ISS                | 6 cures with RCD   | None                                 | Remission > 5<br>years                    | > 5 year   | APR: 3 months                                | No recidivism                    | None  |
| F 71           | Follicular<br>lymphoma B stage<br>IV                | Score=3 high risk<br>according to FLIPI             | RCHOP following<br>RDHAX<br>(recidivism)<br>following<br>vinblastine (2nd<br>recidivism) | Vinblastine                          | In evolution                              | 7 years  | APR: 2 months                                | Stable                           | None  |
| M 52           | Diffuse big cell<br>lymphoma B stage<br>IV          | Score=2 low<br>intermedial risk<br>according to IPI | 8 cures of RCHOP   | None                                 | Remission < 5<br>years                    | 4 years et 9<br>months   | APR: 8 months                                | No recidivism                    | None  |

| M 74 | CLL grade A                                   | Score=2<br>intermedial risk<br>according to CLL-<br>IPI | None                                     | None     | None                   | Stable CLL<br>diagnosed during<br>etanercept<br>treatment<br>received since 2<br>years | 0                       | ETN: 2 years                     |               | Progression into Stage<br>C ongoing treatment<br>with APR, initiation of<br>obinituzumab,<br>chlorambucil | Multiples<br>epidermoid<br>carcinomas<br>treated by<br>excision |
|------|---|---|--|----------|------------------------|--|-------------------------|----------------------------------|---------------|---|---|
|      |   |   |  |          |                        |  |                         | ADA: 2 years                     | APR: 1 year   |   |   |
| M 81 | B-Lymphoma of<br>the marginal zone<br>stage I | Score=1 low risk<br>according to IPI                    | None                                     | None     | None                   | Stable   | 5 months                | USK: 13 months                   | Stable        | None  |   |
| M 55 | Hodgkin's<br>lymphoma stage<br>IIIB           | NR  | 2 cures of<br>BEACOPP                    | None     | None                   | Remission < 5<br>years   | 6 months                | USK: 1 year                      | No recidivism | None  |   |
| M 52 | Hodgkin's<br>lymphoma stage<br>IIIB           | NR  | Radio-<br>chemotherapy                   | None     | None                   | Remission > 5<br>years   | 17 years                | IFX: 14 months                   | No recidivism | None  |   |
| M 50 | Vaquez disease                                | NA  | Bleeding                                 | Bleeding | Stable                 | Stable   | 4 years                 | APR: 4 months,<br>USK: 13 months | Stable        | None  |   |
| F 72 | B-Lymphoma of<br>marginal zone<br>stage IV    | Score = 4 high risk<br>according to IPI                 | Splenectomy                              | None     | Remission < 5<br>years | Stable   | 11 months               | APR: 2 months                    | No recidivism | None  |   |
| M 52 | CLL grade A                                   | NR  | None                                     | None     | Stable                 | Stable   | 2 years et 7<br>months  | USK: 7 months                    | Stable        | None  |   |
| M 53 | CLL grade A                                   | Score=2<br>intermedial risk<br>according to CLL-<br>IPI | None                                     | None     | Stable                 | Stable   | 6 years                 | APR: 2 months<br>SKN: 22 months  | Stable        | None  |   |
| M 54 | Hodgkin's<br>lymphoma stage<br>IA             | NR  | Chemotherapy<br>ABVD and<br>radiotherapy | None     | Remission < 5<br>years | Stable   | 4 years et 10<br>months | APR: 2 years and 6<br>months     | No recidivism | None  |   |

Abbreviations: ABVD, adriamycin-bleomycin-vinblastine-dacarbazine; ADA, adalimumab; APR, apremilast; BEACOPP, bleomycin-etoposide-adriamycin-cyclophosphamide-oncovin-prednisone-procarbazine; BT, biological therapy; ETN, etanercept; FLIPI, Follicular Lymphoma International Prognostic Index; ICE, ifosfamide, carboplatin and etoposide; IFX, infliximab; IPI, international prognostic score in essential thrombocythemia; ISS, International Staging System; GSK, guselkumab; IXK, ixekizumab; CLL, chronic lymphoid leukemia; HM, hematological malignancy; NA, not applicable; NR, non reported; RCD, rituximab-cyclophosphamide-dexamethasone; RCHOP, rituximab-cyclophosphamide-hydroxy doxorubicin-vincristine-prednisone; R-DHAX, rituximab-dexamethasone-cytarabine; R-DHAX, rituximab-dexamethasone-cytarabine; SK-N, secukinumab; USK, ustekinumab.



for one patient with a Vaquez polycythemia, and for one patient with a JAK2+ essential thrombocythemia. The patient with Vaquez's polycythemia was followed for more than 10 years during the transformation into myelofibrosis. However, as Vaquez polycythemia or an essential thrombocythemia may progress into secondary myelofibrosis in about 10% of cases after 10 years of follow-up depending on the studies, BT might not be considered to be responsible for the evolution.<sup>29</sup> The second patient had an essential thrombocythemia that worsened following a stroke 9 months after the introduction of etanercept. The stroke was considered a progressive sign of hematology caused by the introduction of hydroxycarbamide. However, this interpretation can be weighted by the fact that thrombocythemia was not treated at the time of the introduction of BT and that platelet counts remained stable during the first months of BT treatment prior to introduction of hydroxycarbamide.

Evolution when taking APR was observed in one patient with a grade A CLL. The evolution of the disease to high-stage CLL led to the introduction of obinutuzumab and chlorambucil. As the risk of evolution from stage A to stage B or C, regardless of treatment with BT or APR is 50%, treatment with APR was considered not to be responsible for the evolution by the hematologists.<sup>30</sup> APR was continued and then stopped, due to lack of efficacy.

Despite an increased risk of infection in patients with HM, and particularly when considered active, BT treatment tolerance was acceptable in 16-patient series after a median treatment duration of 16 months. Two patients had herpes skin infection, a well-known adverse effect in patients treated with BT outside of any history of cancer or hematology. Another patient presented successively with acute prostatitis and pneumopathy under etanercept, which evolved favorably after a transient cessation of BT. No opportunistic or mycobacterial infections, and no serious sepsis were reported. Furthermore, no infectious complications were observed in patients who received APR. This favorable result of APR is consistent with tolerance results of the Phase III studies, which note the absence of a significant difference with placebo regarding the occurrence of infections, since these events are also considered exceptional and of low severity.<sup>18</sup>

The efficacy of BT and APR was very satisfactory in patients with severe psoriasis that was not controlled by one or more conventional systemic treatment lines. This point is important to underline because these cases are difficult to manage due to their malignant hematology, excluding certain immunosuppressants usually used in severe psoriasis.

Despite the encouraging results, our data analysis has certain limitations. The main limit of our study is the lack of data that would have possibly allowed a comparison reflecting a rare prescription circumstance, whether in the field of Dermatology, Rheumatology or Gastroenterology. Our workforce remains relatively small despite the involvement of the multi-center RESOPSO group. It is also likely that the low numbers are related to the reluctance of prescribers who suffer from a lack of clear recommendations when BT is indicated in patients with a history of HM. The majority of patients had a confirmed history of HM with a status considered to be in remission or stable, and therefore results cannot be generalized to HM with a less favorable prognosis. Furthermore, one third of the patients received BT or APR for less than one year at the time of inclusion. We agree that a longer follow-up of these patients would have been preferable in order to confirm the good tolerance and efficacy of the treatments.

In conclusion, despite the present supportive tolerance data, the heterogeneity of our population and the limited available data, BT and APR should be used with caution in this patient population and investigations on larger cohorts should be conducted in order to further assess its tolerance in this type of patient with HM.

## Abbreviations

APR, Apremilast; BSA, Body surface area; BSRBR, British Society of Rheumatology Biologics Register; BT, Biological therapy; CLL, Chronic lymphoid leukemia; HM, Hematological malignancies; MDS, Myelodysplastic syndrome; PASI, Psoriasis area severity index; PGA, Psoriasis global assessment; TNF, Tumor necrosis factor.

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# PRESENTATIONS A DES CONGRES 2021

## GERDA

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Antoine Badaoui, Emmanuelle Amsler, Anne- Sophie Darrigade, Anne- Claire Fougerousse, Ziad Reguiat, Florence Castelain, Angèle Soria et Groupe Urticaire de la SFD et du GEM Reso

## CFA

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Anne- Cécile EZANNO 1, Anne- Claire Fougerousse, Pierre- André Becherel , Philippe Guillemand GEM RésoVerneuil

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Anne- Claire Fougerousse, Ziad Reguiat et Pour le GEM ResoVerneuil

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Caroline Jacobzone Leveque, Ziad Reguiat, Anne Claire Fougerousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Charlotte Fite, Laure Mery, Claire Abasq, Emmanuel Mahe et GEM RESO

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Caroline Jacobzone Leveque, Ziad Reguiat, Anne Claire Fougerousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Catherine Goujon Henry, Dominique Lons Danic, Emmanuel Mahe et GEM RESO

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Anne- Cecile Ezanno, Anne- Claire Fougerousse , Manuela Perez, Pierre- André Becherel, Juliette Delaunay, Christelle Perat, Philippe Guillem et GEM ResoVerneuil

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Anne- Cecile Ezanno, Anne- Claire Fougerousse , Manuela Perez, Pierre- André Becherel, Juliette Delaunay, Christelle Perat, Philippe Guillem et GEM ResoVerneuil

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Caroline Jacobzone Leveque , Ziad Reguiat, Anne Claire Fougerousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Catherine Goujon Henry, Dominique Lons Danic, Magali Bourrel, Laure Mery, Claire Abasq, Claire Alice de Salins,, Charlotte Lepelley, Emmanuel Mahe et GEM RESO

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Anne- Claire Fougerousse\*, Laure Mery- Bossard, Josiane Parier, Charles Taieb, Antoine Bertolotti, François Maccari et Pour le GEM Resopso

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Caroline Jacobzone Leveque, Ziad Reguiat, Anne Claire Fougerousse, Francois Maccari, Antoine Badaoui, Eric Esteve, Jean Luc Perrot, Domitille Thomas Beaulieu, Edouard Begon, Juliette Delaunay, Michelle Pillette Delarue, Nicole Jouan, Marie Jachiet, Valérie Pallure, Nathalie Beneton, Josiane Parier, Laurent Misery, Charlotte Fite, Emmanuel Mahe et GEM RESO



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Anne-Claire Fougerousse, Valérie Failla, Emmanuel Mahé, Guillaume Chaby, François Maccari, Jean-Luc Perrot, Claire Boulard, Emilie Brenaut, Pierre-Dominique Ghislain, Céline Girard, Pierre-André Becherel, Charlotte Lepelley-Dupont, Josiane Parier, Nathalie Quiles, Edouard Begon, Anne-Sophie Dillies, Valérie Florin, Caroline Jacobzone, Sophie Osdoit, Mahtab Samimi, Hervé Maillard, Laure Mery-Bossard et Pour le GEM Resopso

### Tolérance et efficacité du traitement du psoriasis par biothérapies ou apremilast en cas d'antécédent d'hémopathie maligne : étude multicentrique rétrospective.

Raphaella Cohen-Sors, Guillaume Chaby, Anne-Claire Fougerousse, François Maccari, Aude Roussel, Ziad Reguici, Emmanuel Mahe, Maud Amy de la Breteque, Juliette Delaunay, Anne-Caroline Cottencin, Antoine Bertolotti, Helene Kemp et Groupe RESOPSO

**RESO** DERMATITE ATOPIQUE DU SUJET AGE. Cohorte Daphné P259 **JDP** Société dermatologique de Paris 30 NOVEMBRE 04 DÉCEMBRE

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**INTRODUCTION**  
La dermatite atopique (DA) est une dermatose inflammatoire chronique fréquente évoluant par poussées dont les caractéristiques cliniques et épidémiologiques sont bien documentées chez l'enfant. En France, selon l'observatoire Objectifs Peau [SFD 2017] ce sont 2,5 millions (4,6%) de français de 15 ans et plus qui sont atteints de DA. Alors que la DA de l'adulte commence à être mieux connue, nous avons voulu regarder les caractéristiques de cette pathologie chez les patients plus âgés (âge > 65 ans).

**MATERIEL ET METHODE**  
Il s'agit de l'analyse des résultats issus de l'étude DAPHNE, étude multicentrique transversale en vie courante, sans modification de prise en charge. L'objectif était de décrire les caractéristiques de la DA de l'adulte en recueillant les données cliniques et épidémiologiques. Les patients adultes atteints de DA étaient inclus consécutivement à l'issue d'une consultation spontanée. Dans cette partie de l'étude nous avons comparé les DA chez les patients de plus de 65 ans aux DA des adultes de moins de 65 ans.

**RESULTATS**  
816 patients ont été inclus et 66 (8,1%) d'entre eux avaient plus de 65 ans. Le sex-ratio était significativement en faveur des hommes [61,5 vs 43,1%, p=0,004] chez les plus âgés. On notait moins de comorbidités atopiques (asthme 29,7 vs 44,4%, p=0,01 ; rhinite saisonnière 32 vs 49,4%, p=0,008 ; allergie alimentaire 6,6 vs 20,9% p=0,004 ; conjonctivite allergique 24,2vs 34,0%, p=0,07) et moins de début précoce avant l'âge de 2 ans (6,9 vs 47,6%, p<0,001) dans cette population. Il n'y avait pas de différence en termes de sévérité de la maladie à l'inclusion. Les patients de plus de 65 ans avaient préalablement traités plus souvent par méthotrexate (19,6vs 16,7%, p=0,02) et photothérapie (31,6vs 20,9%, p=0,03), mais moins souvent par ciclosporine (3,8 vs 15,80, p=0,02). Les patients de plus de 65 ans souffraient plus de troubles anxieux (26,2 vs 15,5%, p= 0,07 et syndromes dépressifs (23,1 vs 9%, p<0,001). Les présentation phénotypiques étaient aussi différentes avec significativement plus de DA à type de prurigo (9,1 vs 3,8%, p=0,04) et moins d'atteinte des mains (4,5 vs 14,0%, p=0,03) chez les patients plus âgés.

**DISCUSSION**  
Un biais de mémoire peut être responsable de différences observées entre les 2 populations en ce qui concerne l'âge de début de la maladie et les comorbidités atopiques personnelles ou familiales. Néanmoins, des différences sont à noter chez les personnes plus âgées : un début qui semble plus tardif, moindres antécédents atopiques, une présentation à type de prurigo plus fréquente, et une plus forte fréquence des antécédents anxio-dépressifs. La prise en charge semble aussi différente, ce qui est peut être lié à l'âge (moins de ciclosporine) ou aux formes cliniques (méthotrexate pour le prurigo). Une meilleure connaissance des particularités de cette population fragile est importante à connaître et peut influencer la prise en charge.

**EN RESUME :**

- Début plus tardif
- Moins d'ATCD atopique
- Plus d'ATCD anxio-dépressif
- Plus de prurigo

Les Journées Dermatologiques de Paris 2021 - 30 novembre au 4 décembre 2021 Assur-confé d'intérêt à déclarer

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### INTRODUCTION

Chez l'adulte, les présentations cliniques de la dermatite atopique (DA) peuvent être trompeuses et variables au fil du temps chez un même individu. Nous avons voulu étudier les caractéristiques cliniques et épidémiologiques des patients adultes atteints de DA à type de prurigo, en s'appuyant sur le registre Daphné (816 adultes souffrant de DA).

### MATERIEL ET METHODES

Étude multicentrique transversale en vie courante ayant inclus 816 patients. Les patients adultes atteints de DA étaient inclus consécutivement à l'issue d'une consultation spontanée. Dans cette partie de l'étude nous avons comparé les patients présentant un phénotype prurigo à ceux présentant la forme dite « classique » (zones bastions atteintes, sans localisations prédominantes).

### RESULTATS

34 (4,2%) patients avaient un prurigo et 360 (44,1%) une forme classique. On ne notait pas de différence entre les hommes et les femmes mais un âge moyen plus élevé (45,1 vs 36,1 ans,  $p=0,006$ ) au moment de l'inclusion chez les patients atteints de prurigo. Dans cette population, il y avait moins de DA à début précoce avant l'âge de 2 ans (23,5 vs 48,8%,  $p=0,001$ ). On notait moins de comorbidités atopiques (rhinite saisonnière 30,3 vs 53,3%,  $p=0,01$  ; conjonctivite allergique 31,3 vs 38,5%,  $p=0,35$ ) chez les patients ayant un prurigo mais plus de comorbidités anxio-dépressives (troubles anxieux 32,4 vs 14,7%,  $p=0,006$  ; syndromes dépressifs (23,5 vs 8,5%,  $p=0,004$ ). Il y avait plus d'obèses (IMC > 30 kg/m<sup>2</sup>) dans le groupe prurigo (88,8 vs 72,7%,  $p=0,008$ ). Il n'y avait pas de différence en termes de sévérité de la maladie à l'inclusion. Les patients atteints de prurigo étaient traités (30,3 vs 11,2%,  $p=0,001$ ) ou avaient préalablement été traités plus souvent par du méthotrexate (37,5 vs 10,8%,  $p=0,01$ ), et avaient eu moins recours aux médecines alternatives (17,6 vs 33,7%,  $p=0,05$ ) que les patients atteints de forme classique.

### DISCUSSION

La DA de l'adulte représente un groupe hétérogène de phénotypes. Le prurigo est souvent plus difficile à traiter avec un fort retentissement sur la qualité de vie. On note chez les patients présentant un prurigo par rapport au phénotype dit classique des différences : un début qui semble plus tardif, moins d'antécédents atopiques, et une plus forte fréquence des antécédents anxio-dépressifs. La prise en charge thérapeutique aussi différente, avec plus de prescription de méthotrexate. Une meilleure connaissance des phénotypes de la DA de l'adulte et en particulier du type prurigo est importante car peut influencer la prise en charge de ces patients.

- Début plus tardif
- Moins d'ATCD atopique
- Plus d'ATCD anxiodépressifs
- Prise en charge thérapeutique différente

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### INTRODUCTION

La dermatite atopique (DA) est une dermatose inflammatoire chronique fréquente bien connue chez l'enfant ; sa prévalence est de l'ordre de 18 à 25 %. En France, selon Objectifs Peau (SFD 2017) ce sont 2,5 millions de français de 15 ans et plus qui seraient atteints de DA (4,6%). Chez l'adulte, les présentations cliniques peuvent être trompeuses et variables au fil du temps chez un même individu.

### MATERIEL ET METHODES

Étude multicentrique transversale en vie réelle, sans modification de prise en charge dont l'objectif était de décrire les caractéristiques cliniques et épidémiologiques de la DA de l'adulte. Les patients adultes atteints de DA étaient inclus consécutivement à l'issue d'une consultation spontanée. Les données étaient rapportées par le dermatologue en charge du sujet.

### RESULTATS

Nous présentons les résultats issus des données obtenues entre décembre 2018 et mars 2020. 30 dermatologues hospitaliers et libéraux français avaient inclus 816 patients. Le sexratio est en faveur des femmes (55,4%). L'âge moyen au moment de l'inclusion était de 36,9 ans. 25,1% des patients avaient débuté leur DA à l'âge adulte. On notait un début précoce avant l'âge de 2 ans chez 45,1%. Une évolution biphasique (début dans l'enfance, rémission complète et réapparition à l'âge adulte) était rapportée chez 32,8% des patients. Les comorbidités atopiques associées étaient la rhinite saisonnière (48,1%), l'asthme (43,2%), la conjonctivite allergique (33,2%) et les allergies alimentaires (20,1%). On notait des troubles anxieux et syndrome dépressifs chez respectivement 16,4% et 10,1% des patients. 30,3% des patients avaient eu recours aux médecines alternatives et 48,9% avaient consulté un allergologue à l'âge adulte. La sévérité de la maladie à l'inclusion était élevée (IGA moyen à 2,7).

La répartition des formes phénotypique était la suivante : forme clinique dite « classique » (zones bastions atteintes, sans localisations prédominantes) chez 44,8% des individus suivie de la forme « tête et cou » (28,1%), viennent ensuite par ordre de fréquence l'eczéma chronique des mains (13,3%), l'eczéma nummulaire (8,2%), l'érythrodermie (4,5%), le prurigo (4,2%), la dyshidrose (4,1%) et l'eczéma craquelé (1,1%).

| Forme clinique | N   | %     |
|----------------|-----|-------|
| Classique      | 360 | 44,1% |
| Tête et cou    | 230 | 28,1% |
| Prurigo        | 34  | 4,2%  |
| ECM            | 67  | 8,2%  |
| Dyshidrose     | 33  | 4,1%  |
| Erythrodermie  | 37  | 4,5%  |
| ECM des mains  | 108 | 13,3% |
| ECM craquelé   | 9   | 1,1%  |
| Nummulaire     | 67  | 8,2%  |



### DISCUSSION

Les résultats de l'étude DAPHNE montrent l'hétérogénéité de la dermatite atopique de l'adulte avec des phénotypes et évolution variables. Contrairement aux données précédentes de la littérature retrouvant environ 12% d'évolution biphasique de la DA, nous notons plus de formes récidivantes. Les formes d'apparition tardive sont moins fréquentes (25% versus 20/40%). Les formes classiques, « tête et cou » et eczéma chronique des mains sont les plus représentées. La relative sévérité de la DA au moment de l'inclusion peut être liée à un biais de recrutement plus hospitalier que libéral.

Il s'agit de la première étude en vie réelle de description de la dermatite atopique de l'adulte en France fait par des dermatologues.



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**INTRODUCTION**

La dermatite atopique (DA) est une dermatose à fort retentissement sur la qualité de vie et une longue durée d'évolution.

Les traitements conventionnels sont non curateurs, souvent contraignants et sujets à inquiétude de la part des patients qui peuvent être tentés des se tourner vers des médecines dites alternatives (MA). Dans cette partie de l'étude nous nous sommes intéressés à la fréquence du recours aux MA et le profil des patients en consommant.

**RÉSULTATS**

248 patients (30,4%) souffrant de DA avaient eu recours aux MA. On ne notait pas de différence entre hommes et femmes, ni en fonction de l'âge des patients ; Par contre un début avant 2 ans de la DA était associée à plus d'utilisations de MA (57,4 vs 39,6%, p<0,001).

Les patients avaient par ordre de fréquence plus recours à l'homéopathie (17,6%), aux guérisseurs (15,9%), acupuncteurs (4,8%), ou magnétiseurs (3,2%). Les autres MA avaient été essayées par moins de 1% des patients.

Ce groupe de patients avaient suivi plus de régimes alimentaires en lien avec leur DA (13,9 vs 5,1%, p<0,001) et avait eu plus recours à un allergologue (67,5 vs 49,8%, p=0,01) et réalisé des patch tests 49,8 vs 25,4%, n p=0,01) à l'âge adulte.

Il n'y avait pas de phénotypes particuliers mais par contre une maladie significativement plus sévère : IGA moyen plus élevée (p<0,001), suivi hospitalier plus fréquent (p=0,048), plus de traitements antérieurs par ciclosporine (p=0,008), UV (p<0,001) et corticoides systémiques (p<0,001) ; et plus de comorbidités atopiques personnelles : asthme (p<0,001), rhinite allergique (p=0,008), allergies alimentaires (p<0,001), et conjonctivite (p<0,001).

**DISCUSSION**

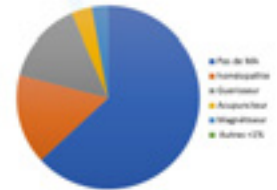
Alors que l'on note une véritable révolution thérapeutique dans la DA de l'adulte, il est intéressant de noter que nombre – près d'un tiers – de patients se tourne vers des MA contre un quart chez les patients psoriasisiques (Misery et al. A/JCD 202). Le début précoce et donc la longue durée d'évolution, à une sévérité plus importante de la maladie, et l'association à d'autres manifestations atopiques peuvent induire une perte de confiance dans la médecine traditionnelle et favoriser le recours à ces MA.

Ce recours aux médecines alternatives doit être connu du dermatologue car inhérent au parcours de soins de bon nombre de ses patients.

**MATÉRIEL ET MÉTHODES**

Etude multicentrique transversale en vie courante ayant inclus 816 patients. Les patients adultes atteints de DA étaient inclus consécutivement à l'issue d'une consultation spontanée. L'homéopathie et le recours à des guérisseurs étaient systématiquement recherchés. Pour les autres types, la question était ouverte.

|                     | Tous       |
|---------------------|------------|
| N                   | 816        |
| Méd. alternatives   | 247 (30,3) |
| Homéopathie         | 144 (21,4) |
| Guérisseur          | 130 (20,4) |
| Acupuncteur         | 33         |
| Magnétiseur         | 26         |
| Hypnose             | 6          |
| Médecine chinoise   | 6          |
| Pendule             | 1          |
| Méd.                | 1          |
| traditionnelle      |            |
| Naturopathe         | 0          |
| Chaman              | 1          |
| Chiropracteur       | 1          |
| Libothérapeute      | 1          |
| Bales d'ortie       | 1          |
| Yoga                | 0          |
| Aïguilles           | 1          |
| Huiles essentielles | 3          |
| Shiatsu             | 2          |
| Reiki               | 1          |



- > 30% des patients
- Début + précoce
- Maladie + sévère

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**Introduction**

- Maladie de Verneuil = antibiothérapie et biothérapies.
- Chirurgie est le seul traitement curatif même si les patients et les praticiens ne le retiennent le plus souvent qu'en dernière intention.

**Matériel et méthodes**

« REcours Localisé après Excision de la maladie de Verneuil »

**RELEVÉ**

- Étude nationale prospective multicentrique
- Recueil de novembre 2020 à septembre 2021
- Patients éligibles à une exérèse élargie de MV
- Recueil données démographiques et médicales
- Prétention de résultats préliminaires



**Résultats**

- 8 centres, 88 patients inclus
- Délai entre les premiers signes de MV et la consultation pour chirurgie d'exérèse de MV 12,3 ± 8,8 ans
- 34% des actes réalisés en ambulatoire avec 93,5% sont anesthésie générale

| Caractéristiques cliniques des patients inclus |                    |            |
|--|--------------------|------------|
| Variable                                       | Moyenne écart type | N (%)      |
| Âge  | 12,21 ± 8,7        |            |
| Âge de début de la maladie (ans (écart type))  | 12,7 ± 9,3         |            |
| Sexe (n/f/m)                                   | 23/64/3            |            |
| Genre  |                    | 9000%      |
| Homme  |                    | 26(27%)    |
| Femme  |                    | 54 (64,4%) |
| Colonne auto                                   |                    |            |
| Âge début opératoire                           | 19,9 ± 6,3         |            |
| Stade de                                       |                    |            |
| Moins  |                    | 8 (20,4%)  |
| Plus   |                    | 38 (89,6%) |
| Site   |                    |            |
| Site   | 12,66 ± 9          |            |
| Prétraitement de l'anté opératoire             |                    | 39 (84%)   |
| Type de traitement                             |                    | 29 (33%)   |
| Antibiothérapie postopératoire                 |                    | 8 (8,4%)   |
| Antibiothérapie au long cours                  |                    | 45 (51,1%) |
| Biothérapie                                    |                    | 13 (14,8%) |
| Chimio   |                    | 1 (1,1%)   |
| Autre  |                    | 1 (1,1%)   |
| Annulation chirurgie de MV                     |                    | 53 (60,3%) |
| Mise à jour                                    |                    | 29 (33,3%) |
| Excision                                       |                    | 5 (5,4%)   |
| Autre (RPO)                                    |                    | 22 (25,0%) |
| Localisation des Malades opérés                |                    | 29 (33,3%) |
| Autres   |                    | 10 (11,4%) |
| Excision bilatérale                            |                    | 10 (11,4%) |
| Excision unilatérale                           |                    | 87 (98,6%) |
| Excision bilatérale                            |                    | 5 (5,4%)   |
| Excision unilatérale                           |                    | 1 (1,1%)   |
| Non opératoire                                 |                    | 8 (20,4%)  |

**Conclusion**

- Délai long entre signes et chirurgie > 10 ans
- Une question: accessibilité de la chirurgie? Collaboration entre dermatologues et chirurgiens.

Je déclare avoir aucun liens d'intérêt à ce jour

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### Introduction

La maladie de Verneuil est une dermatose inflammatoire chronique responsable d'impairments physiques autant esthétiques que relationnels. Pour la majorité des personnes atteintes, vivre avec la maladie de Verneuil est un état handicapant. Nous avons souhaité évaluer la douleur et la qualité de vie péri-opératoire au cours de la maladie de Verneuil.

### Matériel et méthode

« Récidive locale après l'excision de la maladie de Verneuil »

#### RELEVÉ

- Étude nationale prospective multicentrique
- Recueil de novembre 2020 à septembre 2021
- Patients éligibles à une excision large de MV
- Recueil EVA et DLQI en pré-opératoire, à 1 mois et à 6 mois de la chirurgie



Qualité de vie de la phase de 307 patients

### Résultats

18 patients refusés à cause d'un DLQI supérieur à 10

| Caractéristiques cliniques des patients inclus |                      |    |            |
|--|----------------------|----|------------|
| Variable                                       | Moyenne (écart type) | N  | (%)        |
| Age  | 52,23 (8,7)          |    |            |
| IMC (kg/m²)                                    | 25,66 (3,8)          |    |            |
| Sexe   |                      |    | 100(0%)    |
| Homme  |                      |    | 28(27%)    |
| Femme  |                      |    | 54 (54.4%) |
| Stade de Hurley                                |                      |    |            |
| I  |                      | 8  | (20.4%)    |
| II   |                      | 38 | (89.2%)    |
| III  |                      | 11 | (80.3%)    |
| Localisation des lésions opérées               |                      |    |            |
| Auiliaire                                      |                      | 29 | (27.2%)    |
| Auiliaire bilatérale                           |                      | 18 | (8%)       |
| Inguine unilatérale                            |                      | 80 | (88.3%)    |
| Inguine bilatérale                             |                      | 3  | (3.4%)     |
| Sous-mammaire                                  |                      | 1  | (1.2%)     |
| Pied antérieur/postérieur                      |                      | 8  | (80.4%)    |
| EVA  |                      |    |            |
| Pré opératoire (n=88)                          | 5,14 (3,9)           |    |            |
| A 1 mois (n=48)                                | 2,46 (2,3)           |    |            |
| A 6 mois (n=48)                                | 1,86 (2,3)           |    |            |
| DLQI   |                      |    |            |
| Pré opératoire (n=88)                          | 13,46 (5,3)          |    |            |
| A 1 mois (n=48)                                | 10,6 (3,9)           |    |            |
| A 6 mois (n=48)                                | 9,32 (3,9)           |    |            |
| Complication post opératoire                   |                      |    | 3 (7.2%)   |
| Durée de cicatrisation (jours)                 | 16,66 (36,6)         |    |            |
| Récidive locale à 6 mois (sur n=48)            |                      | 13 | (27.0%)    |

### Satisfaction à 6 mois:

- 100% des patients refaisaient cette intervention
- 100% recommanderaient cette intervention à un proche

### CONCLUSION

- Chirurgie et MV = Bénéficiaire patient
- Excision = traitement sûr et efficace avec de faibles taux de complications et de récidive
- Diminution significative du DLQI et de la douleur à 6 mois par rapport au pré opératoire

### Cicatrisation

- la guérison par cicatrisation dirigée est optimale après une excision large dans l'HS

| Type de cicatrisation         | n/N        |
|-------------------------------|------------|
| Fermeture primaire            | 2 (2.7%)   |
| Cicatrisation dirigée/méchage | 59 (79.7%) |
| Cicatrisation dirigée/TFN     | 13 (17.6%) |

Je déclare avoir aucun liens d'intérêt à ce jour.

Anne-Claire Fougereuse 1, Laura Mary-Bossard 2, Josiane Parier 3, Charles Taieb 4, Antoine Berolotti 5, 6, François Maccari 1, 3 pour le GEM Reso/psoriasis  
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Évaluation des modalités de prescription du méthotrexate (MTX), traitement de 1ère intention proposé par les recommandations françaises pour le psoriasis modéré à sévère, par les dermatologues en France

### MATÉRIEL ET MÉTHODES:

Enquête de pratiques auprès des dermatologues membres de Reso entre octobre et décembre 2020

### RÉSULTATS:

- 254 répondants dont 237 prescrivait du MTX
- 17 non prescripteurs, motifs: crainte des effets secondaires n=6, manque d'expérience n=7, absence de patient éligible n=2
- MTX prescrit en 1ère ligne de traitement systémique 57%, 2<sup>e</sup> ligne 29%, 3<sup>e</sup> ligne 14%
- Résultats en fonction du type de pratique dans le tableau
- Impact de l'épidémie de COVID sur les prescriptions de MTX:
  - Prescriptions stables 54%
  - Augmentation des prescriptions 1,3%
  - Diminution des prescriptions 30%
  - Pas d'initiation depuis le début de l'épidémie 11,6%

### DISCUSSION:

- Large utilisation du MTX pour du psoriasis chez les dermatologues interrogés mais hétérogénéité des pratiques
- Association d'acide folique quasi systématique
- 20% de réalisation de dose test, non obligatoire
- Voie orale privilégiée, alors qu'une étude allemande a mis en évidence une efficacité et une tolérance meilleures par voie sous-cutanée
- Impact de l'épidémie de COVID 19 sur les prescriptions, alors qu'il n'y a pas de sur-risque de forme grave documenté en lien avec le MTX.
- Différences de pratique entre dermatologues hospitaliers/mixtes et libéraux, mais pas selon l'ancienneté de l'exercice.

### CONCLUSION

Les résultats montrent que le méthotrexate est utilisé par la majorité des dermatologues interrogés pour le psoriasis modéré à sévère de l'adulte. L'actualisation des modalités de prescriptions au vu des dernières recommandations et publications, pourrait contribuer à réduire l'hétérogénéité des pratiques.

Avec le soutien institutionnel de Reso (France)

| Population de Pratique  | Hospitaliers/ Mixtes (n=237) | Libéraux (n=24) | DLQI   |
|---|------------------------------|-----------------|--------|
| Prescription de méthotrexate  | 93,3% (201/215)              | 95,8% (23/24)   | NS     |
| Accompagné d'acide folique (oui)  | 92,2                         | 95,8            | <0,001 |
| Prescription de méthotrexate  | 93,3% (201/215)              | 95,8% (23/24)   | NS     |
| Population d'analyse  | Hospitaliers/ Mixtes (n=237) | Libéraux (n=24) | DLQI   |
| Accompagné d'acide folique (oui)  | 92,2                         | 95,8            | <0,001 |
| Type de traitement systémique choisi (après le méthotrexate est prescrit) |                              |                 |        |
| 1 <sup>er</sup> ligne   | 68,8%                        | 58,3%           | <0,001 |
| 2 <sup>e</sup> ligne  | 29,5%                        | 39,2            |        |
| 3 <sup>e</sup> ligne  | 1,6%                         | 2,9%            |        |
| 4 <sup>e</sup> ligne  | 0%                           | 0,4%            |        |
| Réalisation d'une dose test à l'initiation                                | 20% (27/135)                 | 0% (0/23)       | NS     |
| Modes d'administration du méthotrexate                                    |                              |                 |        |
| - Par os  | 12,2%                        | 12,5%           | NS     |
| - Sous-cutané oral  | 40%                          | 29%             | <0,001 |
| - Sous-cutané veineux   | 3,2%                         | 0%              | NS     |
| - Intra musculaire  | 44,6%                        | 58,3%           | NS     |
| Recatégorisation des patients inclus dans la réalisation des réponses     | 88,2%                        | 87,5%           | >0,001 |
| Pourcentage d'initiation du méthotrexate                                  |                              |                 |        |
| n=33 patients   | 0%                           | 40%             | <0,001 |
| n=33 patients   | 33%                          | 50%             |        |
| Modes d'administration de l'acide folique du méthotrexate                 |                              |                 |        |
| 10 patients   | 0%                           | 0%              | <0,001 |
| 3 à 8 semaines  | 0%                           | 0%              |        |
| 100 semaines  | 60%                          | 60%             |        |
| Équipement d'équipement de dose unique - oui /                            |                              |                 |        |
| - à 0 mg/ml   | 61,1%                        | 60%             | >0,001 |
| - à 1 mg/ml   | 38,9%                        | 40%             |        |
| Choix d'une forme orale à l'initiation                                    | 0%                           | 0%              | >0,001 |
| Modèle  |                              |                 |        |
| - Méthotrexate subcutané  | 63,3%                        | 57,1%           | <0,001 |
| - Méthotrexate oral   | 36,7%                        | 42,9%           |        |
| - Méthotrexate intraveineux   | 0,0%                         | 0,0%            |        |
| Prescription concomitante d'acide folique                                 | 93,3%                        | 95,8%           | NS     |
| Prescription de tout d'évaluation de la réponse                           | 77,2%                        | 83,3%           | >0,001 |

NS: non significatif





# Prescription d'omalizumab pendant la grossesse chez des patientes atteintes d'urticaire chronique spontanée : résultats d'une étude retrospective française

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## Introduction

L'urticaire chronique spontanée (UCS) est une pathologie fréquente touchant 1% de la population, le plus souvent des femmes. L'omalizumab est actuellement recommandé dans la prise en charge des UCS résistantes à 4cp/j d'anti-histaminique (1,2). Bien que l'utilisation d'omalizumab ait déjà été rapporté comme sûre chez des patientes enceintes atteintes d'asthme sévère dans une cohorte nord-américaine (3), peu d'études ont étudié les conséquences maternelles et foetales éventuelles de l'omalizumab chez des patientes enceintes atteintes d'UCS (4-7).



## Matériel et Méthode

Etude rétrospective de 12 patientes traitées par omalizumab pour une UCS, qui ont déclaré une grossesse sous ce traitement

## Résultats

Douze patients (29 à 42 ans) ont été incluses dans l'étude. Le traitement par omalizumab avait été introduit à la posologie de 300mg toutes les 4 semaines pour une UCS résistante à 4cp/j d'anti-histaminique. Cinq patientes avaient un terrain atopique. Toutes les patientes avaient une UCS modérée à sévère avec un score UAS > 15 et/ou un score DLQI > 10.

Le traitement par omalizumab avait été introduit avant le début de la grossesse chez toutes les patientes, par conséquent, toutes les patientes ont été exposées à ce traitement pendant le premier trimestre de grossesse. Cinq patientes ont interrompu le traitement pendant le premier trimestre et 2 pendant le deuxième trimestre en raison d'une rémission de l'UCS et de la crainte de complications foetales.

**Sur les 12 patientes, 7 ont eu une grossesse et un accouchement sans complication, 2 ont eu un accouchement par césarienne en raison de trouble du rythme cardiaque foetal, 2 ont eu une fausse couche spontanée au premier trimestre et 1 a eu une fausse couche spontanée au 2ème trimestre.**

Aucune malformation foetale n'est à noter sur les 9 nouveau-nés.



## Discussion

Dans notre étude, aucune complication foetale de l'omalizumab n'a été retrouvée, ce qui est concordant avec les publications antérieures dans l'UCS et dans l'asthme (registre EXPECT). Trois patientes ont eu une fausse couche spontanée (25%) ce qui est comparable au taux de fausse couche spontanée dans la population française (8).

Omalizumab est un traitement sûr et efficace chez les femmes enceintes atteintes d'UCS

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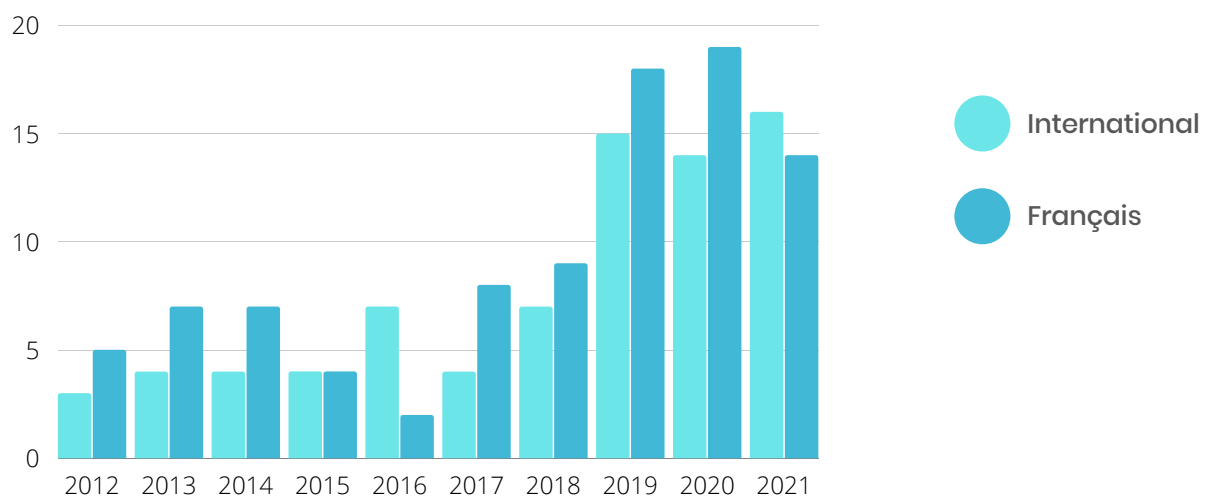




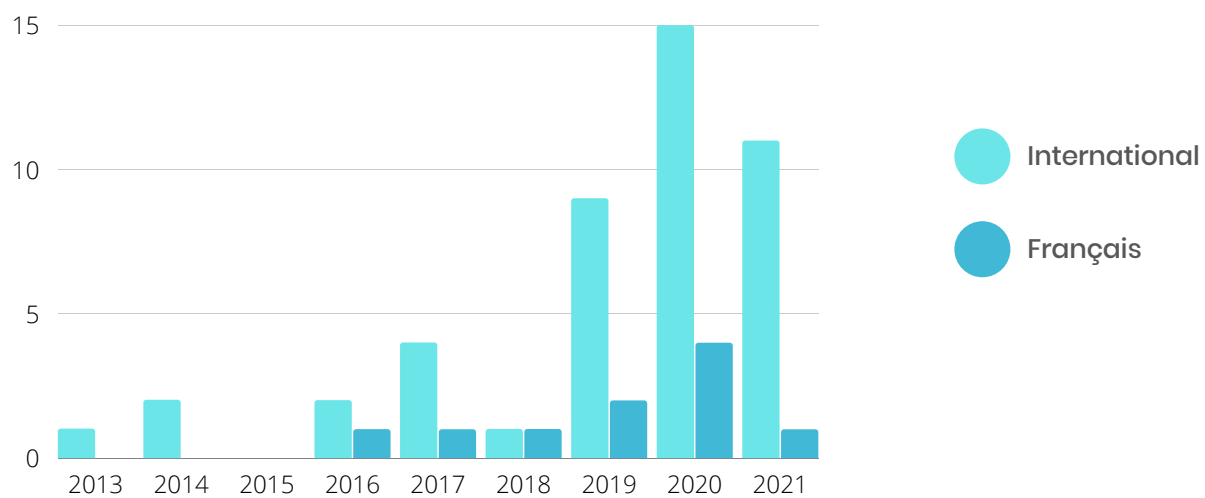


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