***Etude rétrospective sur les maladies associées aux IgG4 traitées par DUPILUMAB***

***Questionnaire ou CRH anonymisé***

**A renvoyer à Flora Finet :** [**flora.finet@aphp.fr**](mailto:flora.finet@aphp.fr) **ou Robin Dhôte :** [**robin.dhote@aphp.fr**](mailto:robin.dhote@aphp.fr) **ou Sébastien Abad :** [**sebastien.abad@aphp.fr**](mailto:sebastien.abad@aphp.fr) **ou Benjamin Terrier :** [**benjamin.terrier@aphp.fr**](mailto:benjamin.terrier@aphp.fr)

**Nom et email du médecin :** ………………………………………………………………………….

**Ville :** …………………………………………………………………………………………………….

# DÉMOGRAPHIE

**Nom (3 lettres) :** ⎣\_⎦⎣\_⎦⎣\_⎦ **Prénom (2 lettres) :** ⎣\_⎦⎣\_⎦

**Date de naissance (MM/AAAA):** ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦ **Sexe (H/F) :** ⎣\_⎦

**Si vous souhaitez ne pas remplir la fiche de recueil, vous pouvez envoyer les comptes rendus des patients anonymisés.**

# TERRAIN AU MOMENT DU DIAGNOSTIC DE MALADIE ASSOCIEE AUX IgG4

**Principales comorbidités** : Asthme ☐ Dermatite atopique ☐

Rhinite chronique avec polypose nasale ☐

Maladie auto-immune ☐ Si oui, type : ……………………

Cancer solide ☐ Hémopathie ☐ Si oui, type : ……………………

Autres ☐ : ……..………………………

**Traitements** : ………………………………………………………………………………………….

# DIAGNOSTIC INITIAL DE MALADIE ASSOCIEE AUX IgG4

Date du début des symptômes (MM/AAAA) : ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦

Date du diagnostic (MM/AAAA) : ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦

Validation des critères ACR (2019, cf annexe) :Oui ☐ Non ☐ Ne sait pas ☐

Organe(s) atteint(s)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Organe** | **Imagerie (préciser)** | **Biopsie** | **Organe** | **Imagerie (préciser)** | **Biopsie** |
| Pancréas |  |  | Rétropéritoine |  |  |
| Voies biliaires |  |  | Poumon |  |  |
| Glandes salivaires |  |  | Aorte |  |  |
| Région orbitaire |  |  | Thyroïde |  |  |
| Rein |  |  | Pachyméninge |  |  |
| autre |  |  |  |  |  |

**Au diagnostic :**

Taux d’IgG4 (G/l): ……………….

Taux d’IgG3 (G/l) : ……………….

Taux d’IgG2 (G/l): ……………….

Taux d’IgG1 (G/l) : ……………….

Taux d’éosinophiles (G/l) : ……………..

# TRAITEMENT

Immunothérapie avant le diagnostic de maladie à IgG4 ☐ Si oui, type : ……………………

Traitement(s) pour la maladie à IgG4 mis en place avant le DUPILUMAB  ☐

Si oui, type : ……………………

Date d’introduction du DUPILUMAB (MM/AAAA) : ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦

Schéma d’administration du DUPILUMAB : …………………………

Indication du DUPILUMAB : …………….

Type et posologie de glucocorticoïde à l’initiation du DUPILUMAB :…………………………….

Autre(s) traitement(s) pour la maladie à IgG4 lors de l’introduction du DUPILUMAB ☐

Si oui, type : ……………………

Organe(s) atteint(s) lors de l’introduction du DUPILUMAB : ……………………………………...

IgG4-RD responder index (cf annexe) lors de l’initiation du DUPILUMAB (si possible) : ……..

Evolution : rémission complète ☐ rémission partielle ☐ pas de rémission ☐

Organe(s) n’ayant pas répondu au DUPILUMAB : ………………………..

IgG4-RD responder index (si possible) à la dernière visite : ……………………

Type et posologie de glucocorticoïde lors des dernières nouvelles ou à l’arrêt du DUPILUMAB : ………………………..

Arrêt du DUPILUMAB ☐Si oui, date (MM/AAAA) : ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦,

, motif : ……………………………

Date dernières nouvelles (MM/AAAA) : ⎣\_⎦⎣\_⎦ / ⎣\_⎦⎣\_⎦⎣\_⎦⎣\_⎦

*Critères ACR/EULAR 2019*

Wallace, Z.S., Naden, R.P., Chari, S., Choi, H., Della-Torre, E., Dicaire, J.-F., Hart, P.A., Inoue, D., Kawano, M., Khosroshahi, A., Kubota, K., Lanzillotta, M., Okazaki, K., Perugino, C.A., Sharma, A., Saeki, T., Sekiguchi, H., Schleinitz, N., Stone, J.R., Takahashi, N., Umehara, H., Webster, G., Zen, Y., Stone, J.H. and (2020), The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. Arthritis Rheumatol, 72: 7-19. <https://doi.org/10.1002/art.41120>

|  |  |
| --- | --- |
| **Step 1. Entry criteria**  Characteristic clinical or radiologic involvement of a typical organ (e.g. pancreas, salivary glands, bile ducts, orbits, kidney, lung, aorta, retroperitoneum, parenchymeninges or thyroid gland [Riedel’s thyroiditis]) OR pathologic evidence of an inflammatory process accompanied by a lymphoplasmacytic infiltrate of uncertain etiology in one of these same organs. | Yes ☐ No ☐ |
| **Step 2. Exclusion criteria : domains and items**  *Clinical:* Fever, no objective response to glucocorticoids  *Serologic:* Leukopenia and thrombocytopenia, peripheral eosinophilia, positive antineutrophil cytoplasmic antibody (specifically against proteinase 3 or myeloperoxidase), positive SSA/Ro or SSB/La antibody, positive double-stranded DNA, RNP or Sm antibody, other disease-specific autoantibody  *Radiologic:* known radiologic findings suspicious for malignancy or infection that have not been sufficiently investigated, rapid radiologic progression, long bone abnormalities consistent with Erdheim-Chester disease, splenomegaly  *Pathologic:* cellular infiltrates suggesting malignancy that have not been sufficiently evaluated, markers consistent with inflammatory myofibroblastic tumor, prominent neutrophilic neutrophilic inflammation, necrotizing vasculitis, prominent necrosis, primarily granulomatous inflammation, pathologic features of macrophage/histiocytic disorder  *Known diagnosis of the following:* multricentric Castelman’s disease, Crohn’s disease or ulcerative colitis (if only pancreatobiliary disease is present), Hashimoto thyroiditis (if only the thyroid is affected) | Yes ☐ No ☐ |
| **Step 3. Inclusion criteria : domains and items**  Histopathology   * Uninformative biopsy * Dense lymphocytic infiltrate * Dense lymphocytic infiltrate and obliterative phlebitis * Dense lymphocytic infiltrate and storiform fibrosis with or without obliterative phlebitis | 0  +4  +6  +13 |
| Immunostaning   * The IgG4+:IgG+ ratio is 0–40% or indeterminate and the number of IgG4+ cells/hpf is 0–9 * 1) the IgG4+:IgG+ ratio is ≥41% and the number of IgG4+ cells/hpf is 0–9 or indeterminate; or 2) the IgG4+:IgG+ ratio is 0–40% or indeterminate and the number of IgG4+ cells/hpf is ≥10 or indeterminate * 1) the IgG4+:IgG+ ratio is 41–70% and the number of IgG4+ cells/hpf is ≥10; or 2) the IgG4+:IgG+ ratio is ≥71% and the number of IgG4+ cells/hpf is 10–50 * The IgG4+:IgG+ ratio is ≥71% and the number of IgG4+ cells/hpf is ≥51 | 0  +7  +14  +16 |
| Serum IgG4 concentration   * Normal or not checked * > Normal but <2× upper limit of normal * 2–5× upper limit of normal * >5× upper limit of normal | 0  +4  +6  +11 |
| Bilateral lacrimal, parotid, sublingual, and submandibular glands   * No set of glands involved * One set of glands involved * Two or more sets of glands involved | 0  +6  +14 |
| Chest   * Not checked or neither of the items listed is present * Peribronchovascular and septal thickening * Paravertebral band-like soft tissue in the thorax | 0  +4  +10 |
| Pancreas and biliary tree   * Not checked or none of the items listed is present * Diffuse pancreas enlargement (loss of lobulations) * Diffuse pancreas enlargement and capsule-like rim with decreased enhancement * Pancreas (either of above) and biliary tree involvement | 0  +8  +11  +19 |
| Kidney   * Not checked or none of the items listed is present * Hypocomplementemia * Renal pelvis thickening/soft tissue * Bilateral renal cortex low-density areas | 0  +6  +8  +10 |
| Retroperitoneum   * Not checked or neither of the items listed is present * Diffuse thickening of the abdominal aortic wall * Circumferential or anterolateral soft tissue around the infrarenal aorta or iliac arteries | 0  +4  +8 |
| **Step 4. Total inclusion points**  A case meets the classification criteria for IgG4-RD if the entry criteria are met, no exclusion criteria are present, and the total points is ≥20. | |

*IgG4-RD responder index*

Wallace, Z.S., Khosroshahi, A., Carruthers, M.D., Perugino, C.A., Choi, H., Campochiaro, C., Culver, E.L., Cortazar, F., Della-torre, E., Ebbo, M., Fernandes, A., Frulloni, L., Hart, P.A., Karadag, O., Kawa, S., Kawano, M., Kim, M.-H., Lanzillotta, M., Matsui, S., Okazaki, K., Ryu, J.H., Saeki, T., Schleinitz, N., Tanasa, P., Umehara, H., Webster, G., Zhang, W. and Stone, J.H. (2018), An International Multispecialty Validation Study of the IgG4-Related Disease Responder Index. Arthritis Care Res, 70: 1671-1678. <https://doi.org/10.1002/acr.23543>

**Scoring Rules**

Scoring refers to manifestations of disease activity present in the last 28 days

Scoring: 0 Normal or resolved

1 Improved but still present

2 New / Recurrence while patient is off treatment or unchanged from the previous visit\*

3 Worsened or new disease manifestation despite treatment

\*Unchanged from previous visit will often refer to disease manifestations that require follow-up imaging to assess accurately

**Definitions**

***Organ/Site score:*** The overall level of IgG4-RD activity within a specific organ system

***Symptomatic:*** Is the disease manifestation in a particular organ system symptomatic? (Y = yes; N = no)

***Urgent disease:*** Disease that requires treatment immediately to prevent serious organ dysfunction (Y = yes; N = no)

(*Presence of* ***urgent disease*** *within an organ leads to* ***DOUBLING*** *of that organ system score*)

***Damage:*** Organ dysfunction that has occurred as a result of IgG4-RD and is considered permanent (Y = yes; N = no)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Activity** | | | |  | **Damage** | | |
| Organ/Site | Organ/Site  Score (0-3) | Symptomatic  (Yes/No) | | Urgent  (Yes/No) |  | Yes/No | Symptomatic  (Yes/No) | |
| Meninges |  |  | |  |  |  |  | |
| Pituitary Gland |  |  | |  |  |  |  | |
| Orbital lesion (specify location):  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  |  | |  |  |  |  | |
| Lacrimal Glands |  |  | |  |  |  |  | |
| Parotid Glands |  |  | |  |  |  |  | |
| Submandibular Glands |  |  | |  |  |  |  | |
| Other Salivary Glands (specify):  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  |  | |  |  |  |  | |
| Mastoiditis / Middle ear disease |  |  | |  |  |  |  | |
| Nasal Cavity Lesions |  |  | |  |  |  |  | |
| Sinusitis |  |  | |  |  |  |  | |
| Other ENT Lesions, e.g., tonsillitis, pharyngitis (specify):  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  |  | |  |  |  |  | |
| Thyroid |  |  | |  |  |  |  | |
| Lungs |  |  | |  |  |  |  | |
| Lymph Nodes (please circle site of involvement, below): |  |  | |  |  |  |  | |
| Submental Submandibular Cervical Axillary Mediastinal Hilar  Abdominal/Pelvic Inguinal Other lymph node chains: | | | | |  |  |  | |
|  | **Activity** | | | |  | **Damage** | | |
| Organ/Site | Organ/Site  Score (0-3) | Symptomatic  (Yes/No) | Urgent  (Yes/No) | |  | Yes/No | | Symptomatic  (Yes/No) |
| Aorta / Large Blood Vessels |  |  |  | |  |  | |  |
| Heart/Pericardium |  |  |  | |  |  | |  |
| Retroperitoneal Fibrosis |  |  |  | |  |  | |  |
| Sclerosing Mediastinitis |  |  |  | |  |  | |  |
| Sclerosing Mesenteritis |  |  |  | |  |  | |  |
| Pancreas |  |  |  | |  |  | |  |
| Liver |  |  |  | |  |  | |  |
| Bile ducts |  |  |  | |  |  | |  |
| Kidney |  |  |  | |  |  | |  |
| Skin |  |  |  | |  |  | |  |
| Constitutional symptoms not attributable to involvement of a particular organ (weight loss, fever, fatigue caused by active IgG4-RD) |  |  |  | |  |  | |  |
| Other involvement - specify:  (Consider prostate, breast, gallbladder involvement; and other. Each “Other” item is counted separately.)  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | \_\_\_\_\_\_\_\_  \_\_\_\_\_\_\_\_ | \_\_\_\_\_\_\_\_\_\_  \_\_\_\_\_\_\_\_\_\_ | \_\_\_\_\_\_\_\_  \_\_\_\_\_\_\_ | |  | \_\_\_\_\_\_\_  \_\_\_\_\_\_\_ | | \_\_\_\_\_\_\_\_\_  \_\_\_\_\_\_\_\_\_ |

**Total Activity Score**

Organ/sites (x 2 if urgent): **\_\_\_\_\_\_**

Total **urgent** organs: \_\_\_\_\_\_\_\_\_

Total **symptomatic (active)** organs: \_\_\_\_\_\_\_\_\_

Total **damaged** organs: \_\_\_\_\_\_\_\_\_

Total **symptomatic (damage)** organs: \_\_\_\_\_\_\_\_\_