touch™ IMMUNOLOGY

IgG4-related disease:
How to identify, diagnose and treat

Practice aid for IgG4-related disease

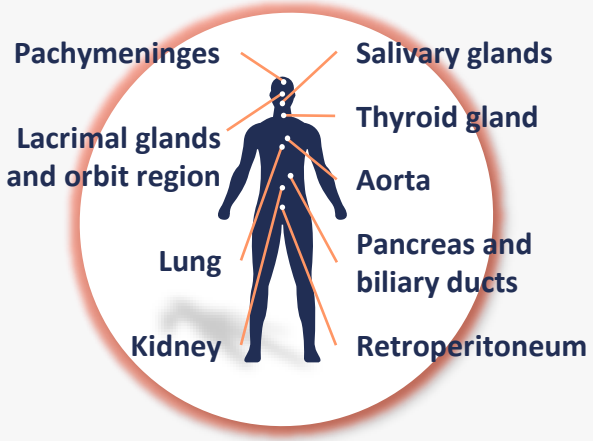
For more information, visit www.touchimmunology.com

Diagnosis of IgG4-RD requires a comprehensive assessment that combines clinical, radiological, serological and pathological findings[1,2]

The 2019 ACR and EULAR classification criteria for IgG4-RD[2]

Entry criteria

Clinical or radiological involvement of a typical organ OR **pathological evidence of an inflammatory process accompanied by a lymphoplasmacytic infiltrate of uncertain aetiology in one of the same organs**



Exclusion criteria

Presence of any exclusion criteria rules out an IgG4-RD diagnosis:

Clinical
e.g. fever, no objective response to GCs

Radiological
e.g. suspicious for malignancy, rapid radiological progression

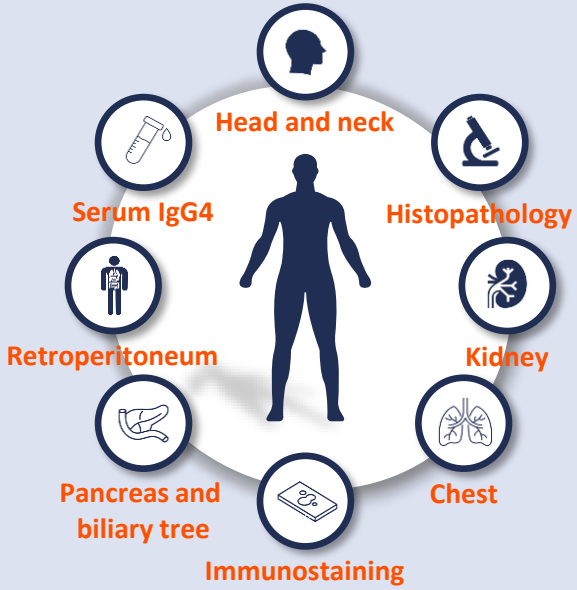
Serological
e.g. cryoglobulinaemia, peripheral eosinophilia

Pathological
e.g. prominent neutrophil inflammation, necrotizing vasculitis

Comorbid conditions
e.g. MCD, Hashimoto thyroiditis (only if thyroid affected)

Inclusion criteria

Application of weighted items across eight inclusion criteria domains:



Diagnosis of IgG4-RD: If the entry criteria are met, no exclusion criteria are present, and the total score is ≥20 points across the inclusion criteria domains

touch™ IMMUNOLOGY

Diagnosis of IgG4-RD requires a comprehensive assessment that combines clinical, radiological, serological and pathological findings[1,2]

The 2020 Japanese RCD criteria for IgG4-RD[3]

		Possible	Probable	Definitive
1	**Clinical and radiological**: **One or more organs with characteristics of IgG4-RD:** • **Diffuse/localized swelling** or • **A mass** or **nodule** (In single organ involvement, lymph node swelling is omitted)	✓	✓	✓
2	**Serological**: **Serum IgG4 levels >135 mg/dL**	✓		✓
3	**Pathological**: **Positive for two criteria:** 1. **Dense lymphocyte and plasma cell infiltration with fibrosis** 2. **IgG4+ plasma cells/IgG+ cells >40%** and **IgG4+ plasma cells >10/hpf** 3. **Typical tissue fibrosis,** particularly storiform fibrosis, or obliterative phlebitis		✓	✓

Sensitivity of criteria:[4]			**88%;**	**100%**
Specificity of criteria:[4]			**88%;**	**50%**

touch™ IMMUNOLOGY

IgG4-RD is a highly treatment-responsive disease[5]

Induction

GCs are the cornerstone of treatment[6]

- **30–40 mg/day prednisone, for 4 weeks[5]**
- GC dose is then **gradually tapered over 8–12 weeks[6]**

Relapses are common following steroid tapering[6]

- Relapse treated as per induction regimen[6]

Maintenance

Long courses of low-dose GCs[1,6]

- **2.5–10 mg/day prednisone[7]**

Long-term GC treatment is associated with adverse effects.[5]

Alternative treatments:

- GCs and immunosuppressants, but evidence for efficacy is slim[5]
- Targeted therapy, including B cell depletion (off-label)[5]

Monitoring

Clinical monitoring for early detection of flares[7]

- Sequential assessment of **clinical, biochemical** and **radiological parameters[8]**
- **Biomarkers of IgG4-RD activity,** e.g. serum IgG4 levels[7]

Life-long follow-up is advisable[9]

Treatment decisions should be individualized[10]

Disease-related factors

- Disease subtype[5]
- Disease phenotype[11,12]
- Urgency of presentation[11,13]
- Predictors of relapse[14–16]

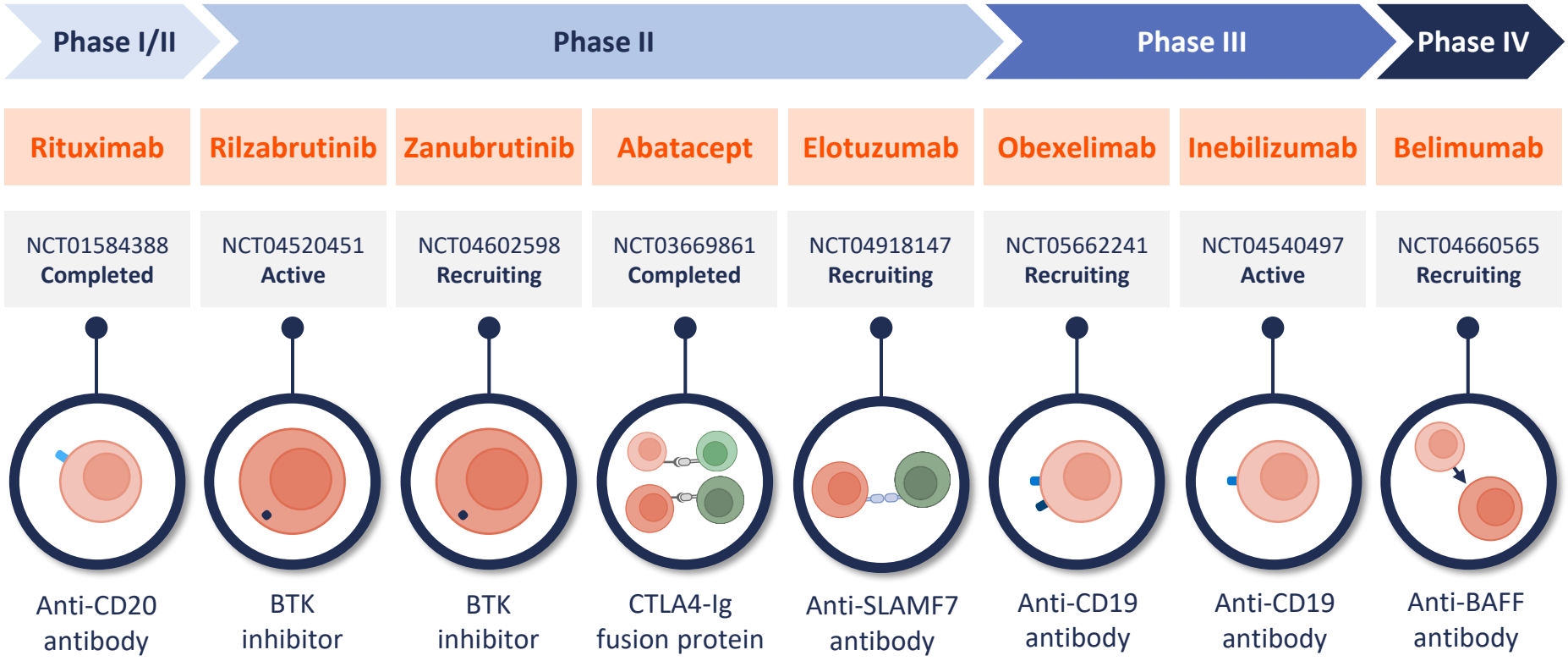
Patient- and social-related factors

- Age[17]
- Comorbidities[18]
- Public health factors[19]
- Insurance coverage[19]

Treatment goals are to reduce inflammation, induce and maintain remission, and preserve organ function, all while minimizing toxicity[5]

touch™ IMMUNOLOGY

Emerging treatments for IgG4-RD[20,21]



Advances in understanding the pathogenesis of IgG4-RD has prompted the development of novel targeted agents that may provide steroid-sparing options in the future[6,22]

touch™ IMMUNOLOGY

Abbreviations and references

Abbreviations

ACR, American College of Rheumatology; BAFF, B-cell activating factor; BTK, Bruton's tyrosine kinase; CD, cluster of differentiation; CTLA4, cytotoxic T-lymphocyte associated protein 4; EULAR, European League Against Rheumatism; GC, glucocorticoids; hpf, high-power field; Ig, immunoglobulin; IgG4-RD, IgG4-related disease; MCD, multicentric Castleman disease; RCD, revised comprehensive diagnostic; SLAMF7, surface antigen CD319.

References

1. Katz G, Stone JH. *Annu Rev Med.* 2022;73;545–62.
2. Wallace ZS, et al. *Arthritis Rheumatol.* 2020;72:7–19.
3. Umehara H, et al. *Mod Rheumatol.* 2021;3:529–33.
4. Kogami M, et al. *Sci Rep*. 2023;13:2509.
5. Tanaka Y, Stone JH. *Mod Rheumatol.* 2023;33:229–36.
6. Abraham M, Khosroshahi A. *Expert Rev Clin Immunol*. 2017;13:867–75.
7. Iaccarino L, et al. *Clin Exp Rheumatol*. 2022;40 Suppl 134:71–80.
8. On W, Huggett MT. *Frontline Gastroenterol.* 2022;13:171–4.
9. Löhr J-M, et al. *United European Gastroenterol J.* 2020;8:637–66.
10. Weiss MA, et al. *Am J Case Rep.* 2018;19:1232–6.
11. Lee C, Hung To C. J Clin Rheumatol. 2023;23:25–34.
12. Chen Y, et al. *Chin Med J (Engl).* 2022;135:381–92.
13. Goodchild G, et al. *Clin Med.* 2020;20:e32–9.
14. Zongfei J, et al. *Arthritis Res Ther.* 2022;24:106.
15. Wallace ZS, et al. *Rheumatology (Oxford).* 2016;55:1000–8.
16. Perugino C, et al. *Rheumatol Ther.* 2023;10:1795–808.
17. Chen C, et al. *Exp Ther Med.* 2018;15:2739–48.
18. Wallace ZS, et al. *Clin Chest Med.* 2019;40: 583–97.
19. Dawkins B, et al. *Trop Med Int Health.* 2021;26:1177–88.
20. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ searchable by NCT number (accessed September 2023).
21. Nakaymada S, Tanaka Y. *Mod Rheumatol.* 2023;33:266–70.
22. Perguino CA, Stone JH. *Z Rheumatol*. 2016;75:681–6.