Reader's Guide to the Fireside Chat: IgG4-RD and Treatment

Hosted by Dr. John Stone, with Dr. Arezou Khosroshahi & Dr. Guy Katz

In this Fireside Chat, leading experts share how they approach the treatment of IgG4-related disease (IgG4-RD)—what's working today, what's coming next and how patients can be informed partners in their care. This guide walks you through the major themes so you can follow along—or skip to what maters most for you.

Introduction:

- Welcome from Dr. Stone
- Announcements:
    - The upcoming **PeachJAM** patient event in Atlanta
    - New **mental health resources** on the website
    - Launch of the **IgG4 Me** app—a free tool to help track flares, infusions, labs, vaccines, and more

Segment 1: When Should IgG4-RD Be Treated?

- Most patients **do** need treatment—especially to prevent long-term damage
- **Head and neck involvement** (like submandibular glands) *may sometimes* be monitored instead of treated—but **only with** regular check-ins
- **Serum IgG4 levels** help assess disease activity, but don't tell the whole story
- Doctors often use **CT scans and labs** to rule out "silent" involvement in organs like the pancreas, kidneys, or lungs
- Deciding whether to treat is a shared decision between doctor and patient

"We don't always know who will flare. But if inflammation is left unchecked, it can damage organs, so early treatment often makes sense."

Segment 2: Steroids—Helpful but Imperfect

- **Steroids (like prednisone)** work quickly and help confirm diagnosis
- Side effects: bone loss, diabetes, weight gain, mood changes
- Doctors aim to use **short tapers (often 8 weeks)** and transition to longer-term medications
- In some mild cases, a short steroid course may be all that's needed—but most patients will relapse without further treatment

"We're thankful for steroids—but we're even more thankful when we can stop them."

Segment 3: B-Cell Depletion—A Game-Changer

- **B cells** are part of the immune system and help make antibodies. In IgG4-RD, they misbehave
- Two key therapies:
    - **Rituximab** (older, partly mouse-derived, not approved for IgG4-RD)
    - **Inebilizumab** (newer, fully humanized, recently FDA approved for IgG4-RD)
- Both are effective—but inebilizumab may have fewer side effects, faster infusion times, and greater efficacy
- Benefits:
    - Fewer relapses
    - Potential for long-term freedom from steroids
    - Long-term disease control
- Risks:
    - Infections (especially early post-infusion)

- Low immunoglobulin levels (hypogammaglobulinemia)
- Poor vaccine response (vaccine timing is critical)

"With inebilizumab, we're now aiming to control the disease without relying on steroids at —all."

Segment 4: What's Next in Treatment?

Emerging therapies offer new hope:

- **Obexelimab** – A B-cell *down-regulator* (non-depleting)
- **BTK inhibitors** – Oral therapy (pills) in clinical trials now
- **Cell-based therapy (ACE-1831)** – Using engineered immune cells to deliver targeted therapy
- **Potential for a cure?** – Not yet, but long-term remission may be within reach

"We've moved from control to the possibility of remission. In time, we may even be talking about cure."

Key Takeaways

- **Most patients need treatment** to prevent irreversible organ damage
- Steroids work fast but come with side effects—so doctors aim to **minimize their use**
- **B-cell depletion** (like rituximab or inebilizumab) is now first-line in many cases
- New treatments are in the pipeline—including **oral pills** and **less immunosuppressive options**
- Monitoring and shared decision-making are crucial
- **You are not alone—**resources, tools, and community are growing every day

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