

## **Troubleshooting: What Should We Do When Infusion Reactions Occur or Patients Stop Responding to Therapy?**

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Several “biological response modifiers” or “biological agents” directed against inflammatory cytokines have been introduced in the market along the last decade for the treatment of a wide panel of immune mediated disorders. Although the overall benefit/risk ratio for such agents is positive, approximately one third of treated patients do not respond or show suboptimal response to the currently available biological agents i.e. anti-TNF $\alpha$  agents (infliximab, etanercept, and adalimumab). Furthermore, patients who respond initially may lose efficacy over time (secondary failure) or develop adverse events. Because significant differences exist among the three TNF $\alpha$  antagonists, switching from one anti-TNF $\alpha$  agent to another could represent an option in patients affected by inflammatory arthritis who fail or are intolerant to the first treatment. The response to second anti-TNF $\alpha$  agent seems to depend by reason for discontinuation of the first treatment: patients who discontinued because of primary failure frequently showed unsatisfactory response. Then for patients stopping anti-TNF $\alpha$  treatment due to primary failure, different biological drugs, such as rituximab and abatacept, might offer a greater chance of therapeutic success.

Of particular concern is the problem of adverse reactions to biologic agents which can occur acutely, within 24 hours from administration, and delayed, developing 2–14 days after initiation of treatment. Pathogenic mechanisms are not yet well understood. Specific IgE has been demonstrated in a very few cases, while more frequent such reaction are considered anaphilactoid. For some iv drugs, infusion reactions may be prevented thanks to the use of premedication. or by slowing the speed of administration. If it is necessary to substitute the drug that has triggered a reaction, it's possible to use an alternative drug (i.e., replace a chimeric antibody with a humanized or human antibody sharing the same target). As an alternative, desensitization protocols have been employed to induce a state of temporary tolerance to the drug in some cases, yielding successful results for infliximab and trastuzumab.