INFLAMMATORY BOWEL DISEASE
OPTIMIZING TREATMENT WITH BIOLOGICS

New Biologics Monitoring Assays help physicians maximize treatment response using a personalized, patient-specific approach

- Help aid in titrating doses or adjusting frequency to optimize effectiveness
- May help avoid lack of response due to under-treatment
- Assist in preventing and managing loss of response due to immunogenicity
- Minimize cost to patient by avoiding unhelpful dose escalation, especially in the setting of immunogenicity

LabCorp Biologic Tests provide both drug concentration (TDM) & anti-drug antibody (immunogenicity)

**Therapeutic Drug Monitoring (TDM)**
- Biologics have variable pharmacokinetics.
- Dosing by weight and empiric dose adjustment are inefficient and suboptimal.
- TDM for Biologics is a valuable tool to evaluate doses and to tailor dose adjustments to your individual patient.
- TDM can help differentiate under-treatment from other causes of lack of response.
- Proactive dose optimization using TDM may improve clinical scores and prolong duration of anti-TNF therapy.
- TDM has been shown to be cost-effective and may direct more appropriate care.

**Immunogenicity Testing (Anti-drug Antibody level)**
- All biologics have the potential to induce an antibody-mediated immune response.
- Close to half of IBD patients on biologic therapy may develop anti-drug antibodies.
- Anti-drug antibodies may appear as early as after the first infusion and persist for years.
- Anti-drug antibodies can adversely affect the amount of drug in the body.
- Sufficient drug levels (e.g. infliximab >3μg/mL), concomitant use of immunomodulating agents, and regular dosing may protect against the risk of developing anti-drug antibodies.
Interpreting Drug Concentrations

- Detectable drug levels are associated with better clinical outcome as measured by mucosal healing, lower C-reactive protein, higher remission rate, and less relapse.1,2,10,11
- Target ranges and maximally effective concentrations have not been established.3
- Optimal drug concentration depends on the desired therapeutic endpoint and may differ case by case.12

<table>
<thead>
<tr>
<th>Drug</th>
<th>Normal half-life</th>
<th>Proposed Target Trough Concentrations$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>7.7 to 9.5 days</td>
<td>≥ 3.7 µg/mL; 5 - 10 µg/mL; &gt; 4.0 µg/mL for mucosal healing3; ≥ 10.0 µg/mL may be required for fistula healing26</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Approx 2 weeks</td>
<td>≥ 4.9 µg/mL13; ≥ 5.85 µg/mL14</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>Approx 25 days</td>
<td>&gt; 30 µg/mL has been associated with greater mucosal healing21</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Approx 2 weeks</td>
<td>≥ 4.27 µg/mL correlated with greater response and remission22</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Approx 3 weeks</td>
<td>&gt; 4.5 µg/mL has been associated with greater rate of endoscopic response23</td>
</tr>
</tbody>
</table>

$Note: These trough levels were those used in landmark studies and do not necessarily translate into general recommendations for individual patients.

* Target ranges for vedolizumab & golimumab have yet to be established.

Interpreting Anti-Drug Antibody Levels

- Anti-drug antibodies can impact pharmacokinetics, efficacy, and the cost effectiveness of biologics.
- Low titer antibodies may have little to no effect on drug levels or clinical outcome but evidence suggests they may lead to later development of higher titer.9
- In contrast, high titer of antibodies are likely to be more consequential, leading to loss of drug efficacy by preventing drug binding to TNF and/or increasing drug clearance.9,15
- Anti-drug antibody positivity should be interpreted in the context of the comoncomitant free drug level.

<table>
<thead>
<tr>
<th>Anti-Drug Antibodies</th>
<th>Quantitative Range</th>
<th>Result Interpretation</th>
<th>Interpreting Anti-Drug Antibody Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Infliximab Abs</td>
<td>22-10,000+ ng/mL</td>
<td>Antibodies are reported as Low, Intermediate or High Titer</td>
<td></td>
</tr>
<tr>
<td>Anti-Adalimumab Abs</td>
<td>25-10,000+ ng/mL</td>
<td>Antibodies are reported as Low, Intermediate or High Titer</td>
<td></td>
</tr>
<tr>
<td>Anti-Vedolizumab Abs</td>
<td>25-10,000+ ng/mL</td>
<td>Stratification into low to high titer has yet to be determined.</td>
<td></td>
</tr>
<tr>
<td>Anti-Golimumab Abs</td>
<td>20-10,000+ ng/mL</td>
<td>Stratification into low to high titer has yet to be determined.</td>
<td></td>
</tr>
<tr>
<td>Anti-Ustekinumab Abs</td>
<td>40-10,000+ ng/mL</td>
<td>Stratification into low to high titer has yet to be determined.</td>
<td></td>
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</tbody>
</table>

• Patient-specific clinical context must be taken into account when evaluating drug and anti-drug antibody
• Serial measurements over time may be helpful

When & where to collect blood on my patients?

- The timing of sample collection is important because the drug concentration will change during the dosing interval.

- The Trough Concentration (TC) is measured at the least variable time in the dosing interval, just before the next dose (same day to within < 7 days depending on the drug’s normal half-life).

- During induction and maintenance phases, trough collections are usually recommended because target ranges are defined using TC.

- Blood can be drawn at any of LabCorp’s 1700 patient service centers located nationwide.

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