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\(^1\)\(^-\)\(^3\)
- May help avoid lack of response due to under-treatment\(^1\)
- Assist in preventing and managing loss of response due to immunogenicity\(^4\)\(^-\)\(^5\)
- Minimize cost to patient by avoiding unhelpful dose escalation, especially in the setting of immunogenicity\(^1\)\(^,\)\(^6\)

<table>
<thead>
<tr>
<th>Biologic Drug Name</th>
<th>Primary Target</th>
<th>Clinical Indications</th>
<th>LabCorp(^a) Test</th>
<th>LabCorp(^a) Test #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab Remicade(^a)<em>; Inflectra(^a)</em></td>
<td>TNF</td>
<td>CD, UC **</td>
<td>Infliximab Concentration and Anti-Infliximab antibody (Serial Monitor)</td>
<td>503870</td>
</tr>
<tr>
<td>Adalimumab Humira(^a)*</td>
<td>TNF</td>
<td>CD, UC, RA</td>
<td>Adalimumab Concentration and Anti-Adalimumab Antibody (Serial Monitor)</td>
<td>503890</td>
</tr>
</tbody>
</table>

\(^a\)Also approved for pediatric forms of CD & UC

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

**Therapeutic Drug Monitoring (TDM)**

- Biologics have variable pharmacokinetics.\(^3\)\(^,\)\(^7\)
- Dosing by weight and empiric dose adjustment are inefficient and suboptimal.\(^3\)\(^,\)\(^7\)
- TDM for Biologics is a valuable tool to evaluate doses and to tailor dose adjustments to your individual patient.\(^3\)\(^,\)\(^7\)
- 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.\(^1\)
- TDM has been shown to be cost-effective and may direct more appropriate care.\(^1\)\(^,\)\(^6\)

**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.\(^5\)\(^,\)\(^9\)
- Anti-drug antibodies may appear as early as after the first infusion and persist for years.\(^8\)
- Anti-drug antibodies can adversely affect the amount of drug in the body.\(^8\)
- Sufficient drug levels (e.g. infliximab >3ug/mL), concomitant use of immunomodulating agents, and regular dosing may protect against the risk of developing anti-drug antibodies.\(^17\)\(^,\)\(^19\)
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/mL1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 - 10 µg/mL2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.0 µg/mL for mucosal healing12</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Approx 2 weeks</td>
<td>≥ 4.9 µg/mL12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 5.85 µg/mL14</td>
</tr>
</tbody>
</table>

§Note: These targets ranges were those used in landmark studies and do not necessarily translate into general recommendations for individual patients.

Interpreting Anti-Drug Antibody Levels

- Anti-drug antibodies can impact pharmacokinetics, efficacy, and the cost effectiveness of biologics.2
- 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 titers.9
- In contrast, high titers 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 concomitant free drug level.

<table>
<thead>
<tr>
<th>Anti-Drug Antibodies</th>
<th>Quantitative Range</th>
<th>Result Interpretation</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>
</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>
</tr>
</tbody>
</table>

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 1,700 **patient service centers** located nationwide.

Visit www.LabCorp.com or call 800-444-9111 for more information.

References