Designer management is here – individualizing treatment choices for people with IBD

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This is what we all want!
We are not there yet, but we are learning and making progress!

Objectives

- To review tools that we already have
- Identifying the right patients for the right treatment strategy
- Looking towards the future of personalized medicine
Already in our toolbox

- TPMT genetic testing and dose optimization for thiopurines (6-mercaptopurine/azathioprine)
- Therapeutic drug monitoring for biologics
Enzyme levels (TPMT) to help with 6MP and azathioprine dosing


Intermediate – 11%
Normal – 89%

Poor – 0.3%

More likely to respond

Severe neutropenia

Number of patients (%)

TPMT enzyme activity (IU/ml)
Therapeutic drug monitoring (TDM)

- **REactive drug monitoring**: our norm. Wait until something bad happens (e.g., loss of response, infusion reaction) then try to fix it.
- **PROactive drug monitoring**: optimize dosing to maximize chance of and prevent loss of response.
Proactive therapeutic drug monitoring to optimize infliximab maintenance therapy in IBD

- Patients with IBD in clinical remission on infliximab
  - Infliximab dose optimization to trough concentrations 5–10 µg/mL (n=48) versus
  - No infliximab dose optimization (n=78)

Dose optimization increases probability of remaining on infliximab up to 5 years
Choosing the right treatment for the right person
Can one determine a prognosis to help identify the best treatment strategy for the individual patient?

Mild, slow moving

Aggressive, fast moving
Predictors of more severe Crohn’s disease

<table>
<thead>
<tr>
<th>Risk Factor</th>
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<tbody>
<tr>
<td>Age of onset &lt; 40 years</td>
</tr>
<tr>
<td>Small bowel and colonic disease</td>
</tr>
<tr>
<td>Smokers</td>
</tr>
<tr>
<td>Perianal lesion at diagnosis</td>
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<tr>
<td>Required steroids for first flare</td>
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Blood test antibody markers can help us

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Antigen</th>
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<tbody>
<tr>
<td>ASCA</td>
<td>Mannose of <em>Saccharomyces cerevisiae</em></td>
</tr>
<tr>
<td>pANCA</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>OmpC</td>
<td>Outer membrane porin</td>
</tr>
<tr>
<td>I2</td>
<td><em>Pseudomonas fluorescens</em></td>
</tr>
<tr>
<td>CBir1</td>
<td>Flagellin</td>
</tr>
<tr>
<td>ACCA</td>
<td>Glycan (chitobioside)</td>
</tr>
<tr>
<td>ALCA</td>
<td>Glycan (laminaribioside)</td>
</tr>
<tr>
<td>AMCA</td>
<td>Glycan (mannobioside)</td>
</tr>
</tbody>
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Blood tests (antibody tests) can predict disease severity

![Graph showing the frequency of disease behavior per number of antibody responses.](image)

*P trend < 0.0001

Dubinsky et al, Clin Gastroenterol Hepatol 2008
Genetics can help us predict who will develop a stricture in their bowel more quickly.

- **Patients with normal CARD15**
- **Patients with 1 CARD15 variant**
- **Patients with 2 CARD15 variants**

log rank p<0.0001
Can we predict the future?
A patient communication tool to display individualized Crohn’s disease predicted outcomes based on clinical, serologic and genetic variables

We learned from patients and designers
Example Patient #1's predicted risk of a complication from Crohn's disease

Based on the specific characteristics of your Crohn's disease, the graph below shows your risk of developing complications such as fistulas and blockages, which often lead to surgery.
The future is soon

- There is progress on understanding who will respond to specific biologic therapies
  - Clinical markers
  - Genetic markers
  - Cytokine markers
Predicting response to etrolizumab

- Etrolizumab is an anti-β7 antibody
- Recognized that patients with colon tissue expressing high levels of integrin αE gene (ITGAE) had better responses
- Differences of ITGAE and GZMA (granzyme A) mRNA levels can identify patients with UC who are most likely to respond to etrolizumab

Designer Management for IBD is here!

Tools that we already have

Predicting the Future

Finding the right drug for YOU