VACCINATION AND SCREENING FOR INFECTIONS DURING ANTI-TNFα TREATMENT OF PATIENTS WITH IBD

Katrine Risager Christensen, Herlev Hospital, 2014
Introduction

• TNF-inhibitors are generally well-tolerated, but may increase the risk of infections due to the general immunosuppression induced by these agents

• International and national organizations such as ECCO and AGA recommend screening and vaccination prior to treatment

• Clinical studies and experience suggest that few patients are aware of the need for vaccinations
Guidelines for screening of infections and vaccinations in patients with IBD

American Gastroenterological Association (AGA):

- Type, anatomic location and activity documented
- Preventive care: corticosteroid sparing therapy
- Preventive care: corticosteroid related iatrogenic injury — bone loss assessment
- Preventive care: influenza immunization
- Preventive care: pneumococcal immunization
- Testing for latent TB before initiating anti-TNF therapy
- Assessment of hepatitis B status prior to initiating anti-TNF therapy
- Testing for Clostridium difficile in IBD patients who develop diarrhea

Retningslinjer for screening, profylakse og information før behandling med anti-TNF-alfa

Forfattere og korrespondanse

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When are patients with IBD in risk of infections?

• Malnourished patients

• Patients of old age

• Treatment with immunomodulators: Corticosteroids (>20 mg in > 2 weeks), thiopurines, methotrexate, calcineurin inhibitors, and anti-TNF-α therapy

• Combination of two or more of above mentioned immunomodulators increases the risk further

Rahier, J. et al; Jour. of Crohn's & colitis 2013
## Screening recommendations

<table>
<thead>
<tr>
<th>Virus</th>
<th>Screening</th>
<th>Who?</th>
<th>Relevant tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>✓</td>
<td>All (should be considered)</td>
<td>HIV p24-antigen and antibodies</td>
</tr>
<tr>
<td>HCV</td>
<td>✓</td>
<td>All (should be considered)</td>
<td>HCV-antibodies and HCV-RNA</td>
</tr>
<tr>
<td>HBV</td>
<td>✓</td>
<td>All</td>
<td>HBsAg, anti-HBs and anti-HBc</td>
</tr>
<tr>
<td>VZV</td>
<td>✓</td>
<td>All without previously history of chicken pox</td>
<td>VZV-antibodies</td>
</tr>
<tr>
<td>HSV</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CMV</td>
<td>✓</td>
<td>If no response to treatment during a flare</td>
<td>Biopsy from affected area and PCR</td>
</tr>
<tr>
<td>EBV</td>
<td>✓</td>
<td>All (should be considered)</td>
<td>Antibodies and PCR. Consider monospot test</td>
</tr>
<tr>
<td>HPV</td>
<td>✓</td>
<td>All women &gt; 23 years</td>
<td>Cervical smear according to national screening program</td>
</tr>
</tbody>
</table>
## Screening recommendations

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Screening</th>
<th>Who?</th>
<th>Relevant tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TB</strong></td>
<td>✓</td>
<td>All</td>
<td>X-ray of thorax, Interferon gamma test</td>
</tr>
<tr>
<td><strong>Streptococcus pneumonia</strong></td>
<td>(✓)</td>
<td>If symptoms of pneumonia and meningitis</td>
<td>Cerebrospinal fluid, Other relevant test</td>
</tr>
<tr>
<td><strong>Legionella pneumophila</strong></td>
<td>(✓)</td>
<td>If symptoms of pneumonia</td>
<td>Sputum test</td>
</tr>
<tr>
<td><strong>Listeria monocytogenes</strong></td>
<td>(✓)</td>
<td>If systemic and central neurological diseases</td>
<td>Blood culture, Cerebrospinal fluid</td>
</tr>
<tr>
<td><strong>Samonella spp. og Cl. difficile</strong></td>
<td>(✓)</td>
<td>IBD flare</td>
<td>Fecal test</td>
</tr>
</tbody>
</table>

Rahier, J. et al; Jour. of Crohn's & colitis 2013
## Vaccination recommendations

<table>
<thead>
<tr>
<th>Infection</th>
<th>Vaccination</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>✓</td>
<td>For seronegative patients</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>✓</td>
<td>If travelling to or living in endemic areas</td>
</tr>
<tr>
<td>Influenza</td>
<td>✓</td>
<td>Annual</td>
</tr>
</tbody>
</table>
| Pneumococcus                                  | ✓           | 1. dose: PCV13  
2. dose: PPV23 (8 weeks after PCV13)  
Revaccination every 3-5 years with PPV23  
during immunosuppressive treatment         |
| Human papilloma virus, HPV                    | ✓           | According to national guidelines                                    |
| Varicella zoster virus, VZV                   | ✓           | Seronegative patients  
Attention: Live vaccine, 3 weeks before  
initiation of treatment                     |

**Vaccination against:** Measles, mumps, rubelavirus, poliomyolitis, pertussis, diphtheria,  
tetanus, haemophilus influenza in seronegative patients

Rahier, J. et al; Jour. of Crohn's & colitis 2013
Attention!

- The vaccinations should be administrated before treatment with TNF-inhibitors or other immunomodulating agents for most optimal response to vaccination
  - Examples: Vaccination against Hepatitis B and against pneumococcal infections

- Live vaccinations are contraindicated in immunosuppressed patients:
  - Examples: vaccination against varicella zoster virus, nasal vaccination against influenza virus, vaccination against yellow fever
# Hand out: pocket card

## SCREENING before anti-TNFα therapy

<table>
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<th>Infections</th>
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<td>X-ray of thorax</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interferon gamma test</td>
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<td>HBV</td>
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<td>Cervical smear according to national screening program</td>
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## VACCINATION before and during anti-TNFα therapy

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<thead>
<tr>
<th>Infections</th>
<th>Who?</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>Seronegative patients</td>
<td>Before starting treatment</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Travellers</td>
<td>If travelling to or living in endemic areas</td>
</tr>
<tr>
<td>Influenza</td>
<td>All</td>
<td>Annual</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>All</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose: PCV13 before starting treatment, 2&lt;sup&gt;nd&lt;/sup&gt; dose: PPV23 (8 weeks after PCV13) Revaccination every 3-5 years with PPV23 during immunosuppressive treatment</td>
</tr>
<tr>
<td>Human papilloma virus, HPV</td>
<td>Women</td>
<td>According to national guidelines</td>
</tr>
<tr>
<td>Varicella zoster virus, VZV</td>
<td>Seronegative patients</td>
<td>Attention: Live vaccine, 3 weeks before initiation of treatment</td>
</tr>
</tbody>
</table>

Vaccination against: Measles, mumps, rubelavirus, poliomyelitis, pertussis, diphtheria, tetanus, haemophilus influenza in seronegative patients
Thank you for your attention

• Links to guidelines:

ECCO:
www.ecco-ibd.eu → guidelines → “Second European evidence-based Consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease”

AGA:

Questionnaire regarding vaccinations (Study Part I-II)

1. What kind of biological treatment do you receive? (please check one box only)
   - Infliximab
   - Adalimumab
   - Certolizumab pegol
   - Golimumab

2. Have you been recommended vaccinations during treatment with biologics? (please check one box only)
   - Yes (continue to question 2b)
   - No (skip to question 6)
   - I do not remember whether I have been recommended vaccinations (skip to question number 6)

   b) If yes, what kind of information have you received? (please check one box only)
      - Oral
      - Written
      - Both
      - I do not remember

   c) Who recommended vaccinations to you? (please check all that apply)
      - The physician at the IBD Clinic
      - The nurse at the IBD Clinic
      - General practitioner
      - I do not remember
      - Others (please detail):________________________________________

3. Have you been explained why you need vaccinations? (please check one box only)
   - Yes
   - No
   - I do not remember

4. Why do you think you need vaccinations during your treatment with biologics? (please check all that apply)
   - The treatment is more effective, when I am vaccinated
   - The treatment suppresses my immune system and hence increases the risk of infectious diseases
   - To avoid side effects caused by the treatment
   - Inflammatory bowel disease increases my risk of infectious diseases
   - The healthcare professionals routinely recommend vaccinations in outpatients clinic
   - In order to not infect other people
   - I do not know
   - Other (please detail):________________________________________

5. Have you received any of the recommended vaccinations? (please check one box only)
   - Yes (skip to question 6)
   - No (continue to question 5b)
   - Some of them (continue to question 5b)
b) If you answered ‘No’ or ‘Some’ in 5a): For what reason(s) did you not receive any or only some of the recommended vaccinations? *(please check all that apply)*

- I cannot afford the vaccinations
- I can only afford some of the vaccinations
- If I could have the vaccinations for free, I would get them all
- I find it too expensive to be vaccinated and do not want to prioritize it
- I am concerned about the side effects of the vaccinations
- I am worried I would be sick because of the vaccinations
- I do not think the vaccinations can help me
- I am principally against all types of vaccinations
- I do not understand why I need vaccinations
- I do not wish to receive any more medication than I already do
- I have forgotten to get the vaccinations
- I do not remember, which vaccinations I have received already
- My general practitioner says it is not necessary for me to receive vaccinations
- I need more knowledge about vaccinations
- I need more knowledge of which specific vaccinations I need
- I am never sick so I do not need vaccinations
- Other reasons (please detail): ______________________________________

6.

a) Which of the following vaccinations did you have because of other reasons or before you received the vaccination recommendations during biologics? *(please check all that apply)*

- Hepatitis A vaccination
- Hepatitis B vaccination
- Pneumococcal vaccination
- Annual influenza vaccination
- Varicella zoster vaccination (chicken pox vaccination)
- Human papilloma virus vaccination (HPV vaccination)
- I do not remember
- None of the above
- Others (please detail): ______________________________________

b) Why did you receive vaccination for other reasons or before the biological treatment? *(please check all that apply)*

- Travelling
- Work related
- My own initiatives because of TV-campaigns and commercials.
- National vaccination program
- I do not know
- Have not been vaccinated for other reasons/before biologics
- Other (please detail): ______________________________________

7. *Skip this question if you answered “no” in 2a).*

If you received vaccinations because of the recommendations during treatment with biologics, which vaccinations did you receive then? *(please check all that apply)*

- Hepatitis A vaccination
- Hepatitis B vaccination
☐ Pneumococcal vaccination
☐ Annual influenza vaccination
☐ Varicella zoster vaccination (chicken pox vaccination)
☐ Human papilloma virus vaccination (HPV vaccination)
☐ I do not remember
☐ None of the above
☐ Others (please detail):________________________________________________

8. How important is it for you to be vaccinated during your treatment with biologics? (please check all that apply)
☐ 1 Not important
☐ 2
☐ 3
☐ 4
☐ 5 Important
☐ 6
☐ 7
☐ 8
☐ 9
☐ 10 Very important

Note: The questionnaire is validated in Danish, and translated to English afterwards.
QUESTIONNAIRE REGARDING VACCINATION ROUTINES DURING ANTI-TNF THERAPY (STUDY PART III)

1. What type of physician are you?

☐ Gastroenterologist resident
☐ Gastroenterologist specialist
☐ Other (please specify): ________________

2.
   a) Do you know of specific guidelines for screening and vaccinations for patients with inflammatory bowel disease (IBD) before and during anti-TNF therapy? (please check one box only)

☐ Yes
☐ No
☐ Partially

b) If yes or partially: How did you hear about the screening and vaccination guidelines for patients with IBD? (please check all that apply)

☐ Educational sessions
☐ Guidelines online
☐ Information from fellow physicians
☐ Other (please specify): __________________________
3. What is recommended in international screening and vaccination guidelines from ECCO (European Crohn and Colitis Organisation)? *(please check all that apply)*

☐ Hepatitis A screening
☐ Hepatitis A vaccination
☐ Hepatitis B screening
☐ Hepatitis B vaccination
☐ Hepatitis C screening
☐ Varicella zoster virus screening
☐ Varicella zoster vaccination
☐ HPV screening (for women)
☐ HPV vaccination (for women)
☐ Herpes simplex virus screening
☐ Epstein-Barr virus screening
☐ Cytomegalovirus screening
☐ HIV screening
☐ Annual influenza vaccination
☐ Tuberculosis screening
☐ Tuberculosis vaccination
☐ Yellow fever vaccination
☐ Typhoid vaccination
☐ Screening for fungus and parasites
☐ Pneumococcal vaccination
☐ None of the above
☐ Do not know
☐ Others: _______________________________
4. Which screening tests do you perform and which vaccinations do you recommend to patients prior to and during treatment with biologics? (please check all that apply)

☐ Hepatitis A screening
☐ Hepatitis A vaccination
☐ Hepatitis B screening
☐ Hepatitis B vaccination
☐ Hepatitis C screening
☐ Varicella zoster virus screening
☐ Varicella zoster vaccination
☐ HPV screening (for women)
☐ HPV vaccination (for women)
☐ Herpes simplex virus screening
☐ Epstein-Barr virus screening
☐ Cytomegalovirus screening
☐ HIV screening
☐ Annual influenza vaccination
☐ Tuberculosis screening
☐ Tuberculosis vaccination
☐ Yellow fever vaccination
☐ Typhoid vaccination
☐ Screening for fungus and parasites
☐ Pneumococcal vaccination
☐ None of the above
☐ Don’t know
☐ Others: ________________________________

5.

a) When do you perform screening tests? (please check one box only)

☐ Never
☐ Before initiating biologics
☐ When I estimate that the patient can tolerate the treatment and I plan to continue the treatment for an extended period of time
☐ Every time I have contact with a patient with IBD who is in treatment with biologics.
☐ Once a year
☐ At random

b) When do you recommend vaccinations?

☐ Never
☐ Before initiating biologics
☐ When I estimate that the patient can tolerate the treatment and I plan to continue the treatment for an extended period of time
Every time I have contact with a patient with IBD and in treatment with biologics
☐ Once a year
☐ At random

6. Do you document that you have performed screening test? (please check one box only)
☐ Yes
☐ No
☐ Sometimes

b) Do you document that you have recommended vaccinations? (please check one box only)
☐ Yes
☐ No
☐ Sometimes

7. If you do not apply, or only partially apply, to the screening and vaccination guidelines then what is the reason(s)?
☐ I do not know of the guidelines
☐ Insufficient time during my consultations
☐ Focus during consultations should be on the treatment with biologics
☐ It is not necessary for patients in biological treatment to receive vaccinations
☐ It is the general practitioner’s responsibility to recommend vaccinations
☐ It is a job of another type of healthcare professional to recommend vaccinations
☐ Forgetfulness
☐ The patients do not want to be vaccinated
☐ The patients think it is too expensive to be vaccinated
☐ Other: ____________________________

8. How important do you find prevention of infections in patients with IBD and in anti-TNF therapy?
☐ 1 Not important
☐ 2
☐ 3
☐ 4
☐ 5 Important
☐ 6
☐ 7
☐ 8
☐ 9
☐ 10 Very important
9. How many IBD patients do you treat every month?
Number: __________

10. How many IBD patients in biologics do you treat every month?
Number: __________

11. How many IBD patients do you start in biologics every month?
Number: ______

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