OUTLINE

- Review vaccine technologies and mechanisms
  - COVID Vaccines
- Present data on infections and systemic therapeutics
- Discuss evidence on vaccinations with systemic therapeutics

VACCINE BASICS

TYPES OF VACCINES

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Vaccine technology</th>
<th>Route administered</th>
<th>Disease targeted</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA plasmid</td>
<td>DNA encoding viral</td>
<td>Mouse, chicken</td>
<td>Hepatitis A, type B</td>
</tr>
</tbody>
</table>
COVID VACCINES IN THE US

- Moderna → mRNA
- Pfizer → mRNA
- Johnson & Johnson → Adenovirus expressing spike protein

COVID-19 vaccines: modes of immune activation and future challenges

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COVID-19 AND BIOLOGICS

BACKGROUND
- COVID-19 has raised concerns about management of patients with immunosuppressive biologicals treated with immunosuppressive biologics. Reports from large cohorts of patients treated with these medications suggest their safety. However, population-level analyses of this vulnerable patient population remain limited.

OBJECTIVES
- To determine the incidence of COVID-19 and subsequent mortality in a retrospective analysis of a large cohort of patients treated with immunosuppressive biologics and matched controls living in Massachusetts during the first wave of the pandemic.

METHODS
- Retrospective cohort study of all patients with at least one prescription for a biologic between July 1, 2019, and February 29, 2020, and age, sex, race, and ethnicity-matched, and time-matched controls. The study was performed in Massachusetts.
- COVID-19 status for all patients was confirmed using the Massachusetts Department of Public Health (MDPH) internal databases as of June 15, 2020.

N = >7,000 Biologic-Treated Patients

In this large retrospective cohort study, patients treated with immunosuppressive biologic therapy were not at increased risk of COVID-19 and subsequent mortality, after adjusting for demographic variables, medical comorbidities, and local infection rates.

COVID-19 AND BIOLOGICS

N = >7,000 Biologic-Treated Patients

In this large retrospective cohort study, patients treated with immunosuppressive biologic therapy were not at increased risk of COVID-19 and subsequent mortality, after adjusting for demographic variables, medical comorbidities, and local infection rates.
METHOTREXATE: RISK FOR INFECTIONS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MTX</td>
<td>PSO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusi et al.</td>
<td>13</td>
<td>18</td>
<td>0.0%</td>
<td>2.40 [0.25, 24.21]</td>
<td></td>
</tr>
<tr>
<td>Shread et al.</td>
<td>165</td>
<td>104</td>
<td>24.22%</td>
<td>1.24 [0.59, 2.59]</td>
<td></td>
</tr>
<tr>
<td>Wernars et al.</td>
<td>36</td>
<td>35</td>
<td>0.0%</td>
<td>2.03 [0.19, 21.61]</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>285</td>
<td>187</td>
<td>100.0%</td>
<td>2.93 [0.59, 15.92]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PSO</td>
<td>MTX</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Ta = 6.00, CV = 0.00, df = 2 P = 0.00, Ψ = 0.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.11 (P = 0.04)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Frequencies and proportions of outcomes in the ordinal COVID-19 severity scale according to baseline use of biologic or targeted synthetic disease-modifying antirheumatic drug for patients with rheumatoid arthritis at the time of COVID-19 onset (N=2680)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall</th>
<th>N=2680</th>
<th>N=2228</th>
<th>N=452</th>
<th>N=178</th>
<th>N=190</th>
<th>N=222</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>157 (5.9)</td>
<td>10 (0.0)</td>
<td>144 (0.0)</td>
<td>21 (4.6)</td>
<td>0 (0.0)</td>
<td>24 (10.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hospitalised with oxygen or ventilators</td>
<td>510 (19.1)</td>
<td>117 (4.1)</td>
<td>393 (8.6)</td>
<td>63 (13.9)</td>
<td>18 (10.1)</td>
<td>45 (23.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hospitalised without oxygen</td>
<td>137 (5.1)</td>
<td>12 (0.4)</td>
<td>125 (2.7)</td>
<td>21 (4.6)</td>
<td>0 (0.0)</td>
<td>20 (10.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Not hospitalised</td>
<td>2246 (84.8)</td>
<td>200 (7.2)</td>
<td>2046 (43.7)</td>
<td>210 (46.6)</td>
<td>109 (61.3)</td>
<td>250 (130.8)</td>
<td>210 (9.4)</td>
</tr>
</tbody>
</table>

WHAT ABOUT JAK INHIBITORS BEING USED FOR COVID-19 INFECTION?

Baricitinib Therapy in Covid-19 Pneumonia — An Unmet Need Fulfilled

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- Immunogenicity was characterized by testing IgG antibodies against the COVID-19 spike protein after
- Average methotrexate dose: 15 mg weekly

**TEMPORARY DISCONTINUATION OF MTX FOR FLU VACCINE**

- Study done in South Korea with quadrivalent seasonal flu vaccine

**TNF INHIBITORS MAY AFFECT COVID VACCINATION**

- 7226 patients recruited with 865 receiving infliximab and 428 receiving vedolizumab for IBD and received either mRNA vaccine (Pfizer) or ChAdOx1 nCoV-19 (Astra Zeneca)
Kennedy NA, et al., Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD. Gut. 2021 Apr 26:gutjnl-2021-324789.

**TNF INHIBITORS MAY AFFECT COVID VACCINATION**

Both mycophenolate and rituximab attenuated response to the first dose of the mRNA vaccine. Tacrolimus and TNF inhibitors were noted to have a trend on p value.

**MYCOPHENOLATE ATTENUATES ANTIBODY RESPONSE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Antibody response to the first dose of mRNA vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>100%</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>80%</td>
</tr>
<tr>
<td>Rituximab</td>
<td>60%</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>40%</td>
</tr>
<tr>
<td>TNF inhibitors</td>
<td>20%</td>
</tr>
</tbody>
</table>

*Data p values were lower than expected, the trend is low. It is possible that the result is due to chance.*

MMF AND VACCINES

A previous study showed reduced antibody responses to a polyvalent pneumococcal vaccine (PPSV23).


DUPILUMAB EFFECTS ON NON-COVID VACCINES

IXEKIZUMAB AND VACCINES

*Mean inferiority Margin

Treatment Difference (Ixekizumab – Control)

SECUKINUMAB AND VACCINES
USTEKINUMAB AND VACCINES

- ACR Guidelines – hold JAK inhibitors for 1 week after each vaccine dose
- JAK inhibitors affect T cell function
- B cell function takes weeks to return to normal after vaccine
- Evidence suggests reasonable vaccine response while on JAKi therapy

VACCINES AND TOFACITINIB

- Tofacitinib users showed diminished responses to PPSV-23 but not influenza virus
- Worse with concomitant MTX use
- A study in a psoriasis cohort showed adequate antibody titers for both PCV-13 and tetanus vaccines

JAK INHIBITORS AND VACCINES

- ACR Guidelines – hold JAK inhibitors for 1 week after each vaccine dose
- JAK inhibitors affect T cell function
- B cell function takes weeks to return to normal after vaccine
- Evidence suggests reasonable vaccine response while on JAKi therapy

SUMMARY

- Most psoriasis and atopic dermatitis biologics appear to be safe to use in the era of COVID-19
- Patients on rituximab should utilize extra caution
- Mixed data on JAK inhibitors and COVID-19 infection – may improve outcomes in cytokine storm but patients on JAK inhibitors at baseline may have poorer outcomes
- No concern for vaccine response with 2-dose vaccines and biologics
- Vaccine response with MTX may be a concern, as well as JAK inhibitors