“Effect and safety of Mycophenolate Mofetil in Idiopathic Pulmonary Fibrosis. A retrospective study”.

Evangelos Bouros

Department of Pneumonology, Medical School, Democritus University of Thrace and University Hospital of Alexandroupolis, Greece

Laboratory of Pharmacology, Democritus University of Thrace and University Hospital of Alexandroupolis, Greece
Mycophenolate Mofetil (MMF) (I)

- IMDPH inhibition (MMF metabolite-mycophenolic acid) (Jayne D. Curr Opin Nephrol Hypertens 1999.)
- Purine biosynthesis
- Inhibition T-cell proliferation
- Downstream effect on adhesion to endothelial cells
- Immunosuppression
- Immunomodulation

IMP dehydrogenase is an enzyme that converts inosine monophosphate to xanthosine monophosphate:

\[
\text{inosine 5'-phosphate} + \text{NAD}^+ + \text{H}_2\text{O} \rightarrow \text{xanthosine 5'-phosphate} + \text{NADH} + \text{H}^+
\]
Mycophenolate Mofetil (MMF) (II)

- Rejection prevention after solid-organ transplantation. 
  *Ciancio et al. Transplantation 2005, Kobashigawa et al. Transplantation 2005*

- Beneficial in lupus nephritis.  
  *Appel et al. Transplantation 2005*

- Anti-proliferative properties.  
  *Waller et al. Transplant Proc 2005*

- Anti-fibrotic properties (attenuation of TGF-b expression).  
  *Guo et al. Lupus 2005*
Mycophenolate mofetil as first-line treatment improves clinically evident early scleroderma lung disease

S. N. C. Liossis, A. Bounas and A. P. Andonopoulos

Effect of Mycophenolate Mofetil on Pulmonary Function in Scleroderma-Associated Interstitial Lung Disease*

Anthony J. Gerbino, MD; Christopher H. Goss, MD, FCCP; and Jerry A. Molitor, MD
Aim – Nature of the study

• Determine safety and efficacy profile of MMF in IPF patients (no available data in current literature)

• Retrospective study
Study methodology

1. Identification of IPF patients (based on ATS/ERS 2000 criteria)
2. Per-os administration of 1.44 gr/d of MMF >6 mo
4. Mean time from diagnosis to drug initiation = 9+2 mo
5. Assessment of routine laboratory tests (WBCs, Hct, liver enzymes)
6. Assessment of PFTs (FVC, DLco, TLC) at baseline - 6 - 12 mo post-treatment
7. Assessment of 6MWD, PA-aO_2 at baseline – 12 mo post-treatment
8. Assessment of HRCT at baseline – 12 mo post-treatment based on simple staging system (Goh N, Wells AU et al. Am J Respir Crit Care Med 2008; 177(11):1248-1254.)
Results
### Table 1. Baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>10</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>63 (44-73)</td>
</tr>
<tr>
<td>Smokers</td>
<td>10</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>10</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>0</td>
</tr>
<tr>
<td>Prior treatment (steroids) received</td>
<td>3</td>
</tr>
<tr>
<td>Other treatment received</td>
<td>3</td>
</tr>
<tr>
<td>VATS</td>
<td>6</td>
</tr>
<tr>
<td>sPAP (by echocardiography) mmHg</td>
<td>37.2 ± 19.6</td>
</tr>
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</table>
Safety profile

No cases of liver toxicity, leucopenia, infection
Efficacy profile
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 mo</th>
<th>12 mo</th>
<th>p-value ¹</th>
<th>p-value ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (%)(pred)</td>
<td>59.2 ± 17.1</td>
<td>58.2 ± 17.2</td>
<td>55 ± 14.9</td>
<td>0.228</td>
<td>0.081</td>
</tr>
<tr>
<td>TLC (%)(pred)</td>
<td>53.9 ±10.2</td>
<td>53.6 ± 12.3</td>
<td>52 ±12.8</td>
<td>0.702</td>
<td>0.081</td>
</tr>
<tr>
<td>DL\textsubscript{CO} (%)(pred)</td>
<td>39.4 ± 9.3</td>
<td>38.5 ± 9</td>
<td>35.2 ± 8.8</td>
<td>0.47</td>
<td>0.053</td>
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<tr>
<td>6MWD</td>
<td>441 ±124</td>
<td>NA</td>
<td>421 ±123</td>
<td>NA</td>
<td>0.09</td>
</tr>
<tr>
<td>P\textsubscript{A-a}O\textsubscript{2}</td>
<td>27.4 ± 11.5</td>
<td>NA</td>
<td>27.7 ±11.2</td>
<td>NA</td>
<td>0.67</td>
</tr>
</tbody>
</table>
**Table 3. HRCT scores before and after MMF treatment**

Disease deterioration based on total disease extent and ground glass (GGO) extent

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease Extent</th>
<th>Reticular Extent</th>
<th>GGO Extent</th>
<th>Coarseness Reticulation</th>
<th>Proportion</th>
<th>Disease Extent</th>
<th>Reticular Extent</th>
<th>GGO Extent</th>
<th>Coarseness Reticulation</th>
<th>Proportion</th>
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<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>23</td>
<td>5,2</td>
<td>9</td>
<td>22,6</td>
<td>28</td>
<td>18,7</td>
<td>9,3</td>
<td>9</td>
<td>33,21</td>
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<tr>
<td>2</td>
<td>23</td>
<td>10,5</td>
<td>12,5</td>
<td>8</td>
<td>54</td>
<td>52</td>
<td>34,8</td>
<td>17,2</td>
<td>10</td>
<td>32</td>
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<tr>
<td>3</td>
<td>25</td>
<td>22,5</td>
<td>2,5</td>
<td>11</td>
<td>10</td>
<td>28</td>
<td>17,2</td>
<td>10,8</td>
<td>11</td>
<td>38,57</td>
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<tr>
<td>4</td>
<td>59</td>
<td>31,3</td>
<td>27,7</td>
<td>12</td>
<td>47</td>
<td>67</td>
<td>35,1</td>
<td>31,9</td>
<td>12</td>
<td>47,6</td>
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<tr>
<td>5</td>
<td>38</td>
<td>18,2</td>
<td>19,8</td>
<td>10</td>
<td>52,1</td>
<td>64</td>
<td>40,4</td>
<td>23,6</td>
<td>13</td>
<td>36,8</td>
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<tr>
<td>6</td>
<td>32</td>
<td>19,3</td>
<td>15,3</td>
<td>9</td>
<td>36,9</td>
<td>33</td>
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<td>11</td>
<td>36,9</td>
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<tr>
<td>7</td>
<td>33</td>
<td>20,1</td>
<td>14,9</td>
<td>11</td>
<td>37,8</td>
<td>35</td>
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<td>13</td>
<td>35,8</td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>22,1</td>
<td>11,2</td>
<td>10</td>
<td>36,9</td>
<td>46</td>
<td>30,9</td>
<td>26,2</td>
<td>10</td>
<td>39,2</td>
</tr>
<tr>
<td>mean</td>
<td>33</td>
<td>20,7</td>
<td>13,6</td>
<td>10</td>
<td>37,02</td>
<td>44</td>
<td>29,7</td>
<td>20,4</td>
<td>11</td>
<td>37,5</td>
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<tr>
<td>p-value</td>
<td>0.002*</td>
<td>&gt;0.05</td>
<td>0.02*</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 1

Forced Vital Capacity (%predicted)

Months (since starting MMF)

40.00

60.00

80.00

0 6 12
Figure 3

Total Lung Capacity (%predicted) vs. Months (since starting MMF)

[Graph showing trends in Total Lung Capacity (%predicted) over time for different groups, with months since starting MMF on the x-axis and Total Lung Capacity on the y-axis, ranging from 40,00 to 70,00% predicted.]
Figure 4

Distance (m) vs. Months (since starting MMF)

- 0 months: 441 ± 124.5 m
- 12 months: 421 ± 123.7 m

p = 0.090
Figure 5

Baseline

Pt 1

12 mo

Pt 2
Conclusions

- Acceptable safety profile
- Disease stabilization based on PFTs
- Deterioration of total disease and GGO extent based on HRCT
- Study Limitation: Retrospective nature + limited number of subjects
- Larger prospective studies are sorely needed

*Altschuler E. Consideration of mycophenolate mofetil for idiopathic pulmonary fibrosis Med Hypotheses 2001*