Therapeutic applications of prostaglandins and thromboxane A2 inhibitors in AAA

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Disclosure of Interest

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- I do not have any potential conflict of interest
Multimodality imaging assessment of the deleterious role of the intraluminal thrombus on the growth of abdominal aortic aneurysm in a rat model

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Role of the ILT in the progression of AAA

- Source of Inflammatory cells, proteases, cytokines and oxydative stress.
- Involves in the growth of aneurysm
- Accumulation of platelets and generation of active thrombin allows the formation of a fibrin network.
- The fibrin clot represents a dynamic entity with a constant balance between fibrinogenesis and fibrinolysis.

Table 2  AAA findings on FDG PET/CT examinations with regard to the presence or absence of ILT

|                        | ILT (n = 11) | No ILT (n = 7) | p-value*
|------------------------|--------------|----------------|---------
| AAA diameter (mm)      | 6.51 ± 1.17  | 2.66 ± 0.95    | <0.001  |
| Visual FDG uptake      | 11           | 0              | NA      |
| Maximal SUV            | 2.65±1.07    | 0.98 ± 0.29    | < 0.001 |

*p-values are corrected for repeated measurements
Abbreviations as in the text
Prostanoids

Only 9 human studies targeting prostanoids pathways

NSAID

Aspirin

Contradictory results in AAA

Platelet aggregation and activation

Vasoconstriction, angiogenesis and inflammatory response of endothelial cells
Specific inhibitors of TXA2 synthases or receptor TP antagonists

Unconclusive results in atherosclerosis

Platelet aggregation and activation

Vasoconstriction, angiogenesis and inflammatory response of endothelial cells
Drug with dual effects on TXA2: TXA2 synthase inhibitors and TP receptors antagonists

BM-573

Platelet aggregation and activation

Vasoconstriction, angiogenesis and inflammatory response of endothelial cells
Preliminary results:

J0, J2, J5 (US), J7 (US), J9 (US), J10 (US), J12 (US), J14 (US)

Surgery -> BM-573

B

AAA diameter (mm)

CTL | BM-573

AA induction (days)
Modification in genes expression after 14 days

<table>
<thead>
<tr>
<th></th>
<th>CTL (n=9)</th>
<th>BM-573 (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COL1A1</td>
<td>1.47 (0.94-1.69)</td>
<td>1.21 (1.03-1.62)</td>
<td>0.390</td>
</tr>
<tr>
<td>SMA</td>
<td>0.50 (0.17-0.77)</td>
<td>0.34 (0.26-0.46)</td>
<td>0.302</td>
</tr>
<tr>
<td>MMP9</td>
<td>0.89 (0.59-1.54)</td>
<td>0.99 (0.69-1.61)</td>
<td>0.286</td>
</tr>
<tr>
<td>MMP12</td>
<td>1.02 (0.68-1.28)</td>
<td>1.10 (0.81-1.30)</td>
<td>0.414</td>
</tr>
<tr>
<td>TIMP1</td>
<td>2.15 (1.06-3.71)</td>
<td>1.07 (0.83-1.23)</td>
<td>0.027*</td>
</tr>
<tr>
<td>TIMP2</td>
<td>1.44 (0.78-1.92)</td>
<td>0.85 (0.66-1.43)</td>
<td>0.137</td>
</tr>
<tr>
<td>uPA</td>
<td>1.58 (1.12-1.71)</td>
<td>0.91 (0.80-1.22)</td>
<td>0.007**</td>
</tr>
<tr>
<td>tPA</td>
<td>0.87 (0.69-1.45)</td>
<td>0.66 (0.50-0.77)</td>
<td>0.008**</td>
</tr>
<tr>
<td>PAI-1</td>
<td>0.85 (0.71-2.36)</td>
<td>1.07 (0.65-1.40)</td>
<td>0.369</td>
</tr>
<tr>
<td>COX2</td>
<td>1.00 (0.66-2.50)</td>
<td>0.58 (0.44-1.33)</td>
<td>0.039*</td>
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<tr>
<td>IL6</td>
<td>3.90 (0.84-11.17)</td>
<td>1.14 (0.53-2.11)</td>
<td>0.067</td>
</tr>
<tr>
<td>RANTES</td>
<td>1.00 (0.61-1.09)</td>
<td>0.61 (0.32-0.75)</td>
<td>0.014*</td>
</tr>
</tbody>
</table>

- COX2, RANTES and IL6 are pro-inflammatory factors.
- uPA and tPA are activators of MMPs
- TIMP1 is an inhibitor of MMPs

BM-573 inhibits inflammation and extracellular matrix remodeling
Therapeutic Applications of Prostaglandins and Thromboxane A₂ Inhibitors in Abdominal Aortic Aneurysms

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- Audrey Purnelle
- Giorgos Makrygiannis
- Vincent Demesmaker
- Maïté Paolucci
- Renzo Granato
- Alain Nchimi

- Bernard Pirotte
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