Icatibant treats hereditary angioedema with normal C1-INH but not angioedema caused by ACE-inhibitors

**Time to Onset of Symptom Relief After Icatibant (Hours vs Survival-Proportion)**

**Title: Icatibant in the Winnipeg Regional Health Authority**

**PRESENTER:** George Cai

**BACKGROUND:** Icatibant is indicated to treat Hereditary Angioedema types I and II. It is also used off-label to treat:
1. Hereditary Angioedema with normal C1-INH (HAE-nC1INH), and
2. ACE-Inhibitor-Induced Angioedema (ACEI-AE)

The Winnipeg Regional Health Authority became the first Canadian jurisdiction to add icatibant to its formulary in 2015. We describe the timeline to icatibant treatment, its effectiveness and the presence of confounding factors.

**METHODS**
1. Retrospective chart review identified 23 emergency department angioedema attacks treated with icatibant.
2. Survival analysis was performed on the time from emergency department presentation to:
   a. Non-icatibant treatment
   b. Allergist consult
   c. Icatibant dispensation
   d. Icatibant administration
   e. Onset of Symptom Relief (TOSR)
   f. Discharge or attack Resolution (TR)
3. Data was compared with reference data from a reference clinical randomized controlled trial or between subgroups of the study population, stratified by potential risk-factors.

**RESULTS**
100% of our HAE subgroup had HAE-nC1INH (n=10): the median TOSR and TR were similar to reference HAE type I/II clinical trial data [1.13 vs 0.8 hours, p = 0.34; 3.50 vs 8.0 hours, p=0.11].
Icatibant-treated ACEI-AE (n=12) had a greater median TOSR than reference HAE type I/II data [4.86 vs 0.8 hours, p=0.01] and had a greater TR compared to our HAE-nC1INH subgroup [19.5 vs 3.5 hours, p=0.02].
In support of this, the median ACEI-AE TR was not different from natural history [19.53 vs 4.0 hours, p=0.18].
Conventional trials of non-icatibant treatment significantly delays time to treatment (7.78 vs 2.06 hours, p=0.03).

**CONCLUSION**
Icatibant may be an effective treatment for HAE-nC1INH but not for ACEI-AE. Trialing conventional treatment delays icatibant treatment.

**Table:**

<table>
<thead>
<tr>
<th>Category</th>
<th>Strata</th>
<th>Time to onset of symptom relief (median, hours)</th>
<th>p-value (vs control)</th>
<th>Time to overall clinical outcome (median, hours)</th>
<th>p-value (vs control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
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<td>0.02*</td>
<td>4.86 0.01 19.53 0.01</td>
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<td>4.08 0.01 19.53 0.01</td>
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<td>Treatment</td>
<td>FFP</td>
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<tr>
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<td>1.13 0.40 7.75 0.01 7.75 0.02*</td>
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**Supplemental:**

**Time to event milestone (hours)**

<table>
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<th>No Conventional Treatment</th>
<th>Conventional Treatment</th>
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<td>Presentation to Icatibant Administration</td>
<td>Presentation to Pharmacy Dispensation</td>
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<tr>
<td>Presentation to Allergy Consult</td>
<td>Presentation to Conventional Treatment</td>
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**Reference**