Post-marketing experience of palonosetron confirms a favorable benefit/risk profile

• ABSTRACT
  Palonosetron hydrochloride (Aloxi®), Onicit® is an antiemetic and anti-nausea agent for the prevention of nausea and vomiting induced by chemotherapy. It is a selective serotonin subtype 3 (5-HT3) receptor antagonist (RA) with a high binding affinity for the 5-HT3 receptor and a long elimination half-life of approximately 40 hours. During clinical development, palonosetron demonstrated a safety profile similar to other 5-HT3 RAs. Experimental studies have shown that palonosetron has a longer duration of action than other 5-HT3 antagonists.5,6,8

• RESULTS
  Palonosetron post-marketing surveillance data
  • PMS data covering the period September 2003 – January 2005 included only 81 spontaneous adverse event reports (cases) out of more than 1.3 million treatment doses administered (0.0016%).
  • Of these 81 spontaneous reports, the great majority (n=69, 85%) were non-serious with only 12 (15%) considered serious.
  • The most frequent adverse events reported referred to headache (n=13), injection site reactions (n=8) and hypersensitivity reactions (n=8) (Table 1).

• BACKGROUND
  • Post-marketing surveillance (PMS) is essential to evaluate drug safety in the general population.
  • PMS is important to monitor rare adverse reactions that are not detected during clinical trials and is critical to the protection of public health.
  • Palonosetron hydrochloride (Aloxi®, Onicit®) is a second-generation 5-HT3 receptor antagonist that provides effective and long-lasting protection from chemotherapy-induced nausea and vomiting (CINV).
  • Palonosetron is a pharmacologically distinct 5-HT3 receptor antagonist with high binding affinity (pKi: 10.45) and an extended half life (approx 40 hours).1,2
  • Palonosetron 0.25 mg iv has been shown to be effective in the prevention of acute and delayed nausea and vomiting following emetogenic cancer chemotherapy.3
  • Palonosetron efficacy in preventing CINV up to 5 days with a single dose may be beneficial for improving antiemetic treatment compliance, which can often be overestimated by healthcare professionals treating cancer.
  • Extensive clinical experience with palonosetron in approximately 1900 patients enrolled in clinical trials allowed the safety profile of this agent to be well characterized.
  • Since its approval and introduction in the United States in September 2003, over 1.3 million doses of palonosetron have been administered.
  • Since 2004, palonosetron has been included in the antimessis guidelines of the National Comprehensive Cancer Network as the preferred 5-HT3 antagonist in patients receiving moderately emetogenic chemotherapy.4

• OBJECTIVES
  • To report the safety experience with palonosetron in clinical practice and collect data on the use of palonosetron in the general population.

• METHODS
  • All adverse events were collected and processed in the Helsinn Global Safety Database (ARGUS by Relsys Inc, USA).
  • In the General SOC, cases of lack of efficacy are included. During this observation period only 21 cases following over 1.3 million doses administered (0.0016%) were recorded, indirectly confirming an excellent efficacy profile.

• Safety profile of palonosetron from clinical trials
  • The safety profile of palonosetron 0.25 mg was evaluated in a phase II double-blind, randomized clinical study and three phase III randomized, double blind, comparative clinical trials versus ondansetron 32 mg or dolasetron 100 mg.3,10
  • The majority of treatment-related adverse reactions were mild in intensity.
  • The distribution and incidence of treatment-related adverse events were comparable among study groups, with headache being the most common adverse reaction in all groups (Table 2).1,10

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Table 1. Most common spontaneous adverse events reported with Aloxi®

<table>
<thead>
<tr>
<th>Reaction Type</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>13 cases</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>8 cases</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
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</tr>
</tbody>
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• CONCLUSIONS
  • Post-marketing surveillance data reported during the period September 2003 - January 2005 show the excellent safety profile of Aloxi® in clinical practice, with headache being the most frequently reported reaction.
  • Following over 1.3 million treatment courses, the very few number of spontaneously reported events supports Aloxi® as a very safe agent for use in the prevention of CINV.
  • No suggestions of previously unrecognized hazards or indications of potential risks were reported during this observation period.
  • In addition, the safety profile defined during controlled clinical studies demonstrated that palonosetron has a pattern, incidence, intensity, and duration of adverse events similar to first-generation 5-HT3 receptor antagonists.
  • Moreover, the mean QTC interval prolongation in patients administered palonosetron shows no clinically meaningful changes from baseline.
  • The post-marketing results combined with the good clinical and efficacy profile of palonosetron as an antiemetic with a positive benefit/risk ratio in the prevention of CINV.

REFERENCES:
8. Data on file, Helsinn Healthcare SA.