**AUTOLOGOUS TRANSPLANTS**

**109 APERPANT (AP) FOR PREVENTION OF NAUSEA AND VOMITING SECONDARY TO HIGH-DOSE CYCLOPHOSPHAMIDE (CY) ADMINISTERED TO PATIENTS UNDERGOING AUTOLOGOUS (A) PERIPHERAL BLOOD PROGENITOR CELL (PBPC) MOBILIZATION: FINAL RESULTS OF A PHASE II TRIAL**

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AP is a neurokinin-1 receptor antagonist with unique anti-emetic activity. We conducted a phase II trial evaluating efficacy & safety of AP in combination with 5-HT3 antagonists & adjusted dose of dexamethasone (D) in pts receiving high-dose CY for stem cell mobilization. High-dose CY is associated with significant nausea & vomiting. CY and filgrastim provides a better PBPC yield as compared to filgrastim (failure rate5-20%). Primary endpoint was the control of vomiting without the use of rescue anti-emetics at 24 hours after high dose CY. Secondary objectives were to evaluate side effects, control of nausea & delayed vomiting. Tertiary objective was to estimate the rate of successful CD34+ mobilization (minimum 2 million CD 34+ cells/kg body weight).

**Methods:** From May 2005 to June 2009, 40 pts were enrolled, five of whom were not evaluable for response. All received CY 4gm/m2 and filgrastim (10-16mcg/kg/d). Granisetron 1 mg, (D) 10 mg and AP 125 mg were given orally 1 hour before CY followed by AP 80 mg once daily x 2 days. We used Simons optimal two-stage design constrained to fewer than 40 pts with 10% type I error and 85% statistical power. AP is judged to be of sufficient efficacy for further evaluation if it prevents acute vomiting in >45% of pts. Under these assumptions, 18 evaluable pts were enrolled in 1st stage. Acute emesis was controlled in 10 pts therefore meeting the goal & enrollment proceeded to stage 2. An additional 17 pts were enrolled in Stage 2. If acute vomiting is controlled in 20 or more of the 35 pts, AP is judged worthy of further study.

**Results:** Twenty out of 35 response-evaluable patients (57%) did not develop vomiting or require rescue anti-emetics, thus achieving the critical value for success. A total of 22 (63%) of 35 response-evaluable pts met the criterion for the secondary endpoint of control of delayed vomiting defined as no vomiting episodes during days 2 – 5 and no rescue medications; exceeding the critical value for success. Thirty four out of 35 pts had a successful stem cell mobilization, thus far exceeding the critical value of 23 of 35 pts. Two pts had grade 3 toxicity; I had pain (probably AP related) & another reported diarrhea (possibly AP related). Thus the rate of serious toxicity was 6% meeting the criterion for acceptable toxicity.

**Conclusion:** This final analysis demonstrate that AP has potential to effectively control acute & delayed emesis in pts receiving high-dose Cy and should be evaluated further.

**Table 1. Patients Characteristics**

<table>
<thead>
<tr>
<th>Race</th>
<th>Caucasians</th>
<th>African Americans</th>
<th>Native American</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Male/ Female</td>
<td>20/15</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Median Age(years)</td>
<td>48 (range: 23-64)</td>
<td>45</td>
<td>1</td>
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**A RISK ADAPTED APPROACH UTILIZING PLERIXAFOR IN AUTOLOGOUS PERIPHERAL BLOOD STEM CELL MOBILIZATION**

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**Introduction:** Many patients (pts) who are eligible for ASCT are unable to collect a minimum number of CD34 + stem cells to support high dose chemotherapy and ASCT. Plerixafor, a CXCR4 antagonist, in combination with G-CSF mobilizes more CD34+ stem cells when compared to G-CSF alone. Due to its cost, we commenced a risk adapted approach to the utilization of plerixafor for stem cell mobilization in pts undergoing ASCT. Our goal was to add plerixafor in pts who had ineffective mobilization thereby preventing mobilization failures. Re-mobilization results in added costs, delays with possible disease progression and time lost for the pts.

**Methods:** The study was restricted to pts mobilized with 10 mcg/kg/day GCSF alone. There were two patient populations: those who had plerixafor added in the evening of day 5 if PB CD34 < 10/L with apheresis commencing the following morning; and those who during apheresis had a daily collection yield of < 0.5 x 10^6 CD34/kg. Morning administration of G-CSF and evening dosing of plerixafor continued daily until apheresis was complete.

**Results:** From February to July 2009, 147 mobilization attempts occurred with G-CSF alone (Myeloma 61, NHL 54, Amyloid 17, Hodgkin 10, POEMS 4 and 1 solid tumor). Median CD34 yield: 5.5 x 10^6 CD34/kg; median apheresis 3. 67 pts (46%) received plerixafor; 37 during mobilization and 30 during collections. Overall, 7 of 147 (5%) failed to achieve a minimum of 2 x 10^6 CD34/kg compared to a prior 22% failure rate. Day 4 PB CD34 count and day 1 apheresis yield were analyzed to predict who would require plerixafor under these guidelines (Table 1). 72% of pts whose PB CD34 < 10 on day 4 received plerixafor vs 10% if ≥ 10. 110 pts did not start plerixafor prior to day 1 collection; if day 1 apheresis yield was <1.5, 76% subsequently received plerixafor.

**Conclusions:** Implementing this risk adapted approach allows poor mobilizers to be identified promptly and for initiation of plerixafor during mobilization and collection, thereby reducing the number of failures. In pts whose PB CD34 < 10 on day 4 of G-CSF or whose day 1 yield is <1.5 x10^6 CD34/kg, earlier addition of plerixafor may result in fewer apheresis days. Based on this data, we are implementing the earlier addition of plerixafor. This risk adapted approach with early implementation of plerixafor may be more cost effective than waiting for failure