# Pharmacy

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### BEAM AUTOGRAFT IN A DIALYSIS PATIENT: A CASE REPORT

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In September 2004 YC was diagnosed with relapsed Hodgkin Disease as an incidental finding during work up for a renal transplant for reflux nephropathy. Despite her dependence on haemodialysis three times a week, she was only 24 years old and otherwise well so she was planned for salvage chemotherapy. Treatment consisted of stemcell mobilisation with dose modified cyclophosphamide and G-CSF followed by two cycles of modified ADEC (cytarabine, dexamethasone, etoposide and cyclophosphamide) followed by BEAM autograft. Very little information was available to guide dosing for conditioning in this patient. A 50% dose reduction was selected for melphalan and serum melphalan levels were collected 5minutes and 12hours post dose. Both levels were lower than the range observed in patients with normal renal function. Dose reduction of melphalan for renal dysfunction may not be appropriate even in patients on dialysis. YC is alive and in remission 2 years after her transplant.

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### A DOUBLE BLINDED PILOT STUDY OF APREPITANT VS PLACEBO COMBINED WITH STANDARD ANTIEMETICS FOR THE CONTROL OF NAUSEA AND VOMITING DURING HEMATOPOIETIC CELL TRANSPLANTATION

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Despite advances in antiemetic therapy, HSCT conditioning regimens of high dose chemotherapy +/- TBI, continue to cause significant rates of nausea and vomiting (N/V). The role of the neurokinin antagonist, aprepitant (A), when added to standard antiemetic therapy was investigated to determine if it improved control of N/V. During cyclophosphamide-based conditioning therapy patients were randomized to receive ondansetron (O) +/- dexamethasone plus A or a placebo (P) on days of chemo/radiotherapy. The primary aim of this study was to reduce N/V both during and after HSCT conditioning. Nausea, emesis, and nutritional intake, were evaluated from the start of conditioning through day +7. Since A is a substrate & moderate inhibitor of $CYP_{450}3A4$, busulfan dosing was targeted to disease appropriate AUCs & pharmacokinetic (PK) analysis was performed on cyclophosphamide (Cy), metabolites (HCY & CEPM), and A. Patients were similar demographically for age & gender with 10 patients randomized per arm. Nine patients received TBI (1200 cGy) CY (120 mg/kg) and 11 received Bu (16 mg/kg) CY (120 mg/kg). A/P was begun on Day –7 (125 mg) with the first O dose and continued daily (80 mg) through day +4 (alone on days –1 through +4). Responses were defined as complete (CR), no emesis, mild-moderate nausea, and major (MR), 1-2 emesis on only 1 day with any level nausea or no emesis with severe nausea. Overall responses (CR + MR) were seen in 9/10 A patients and 4/10 P patients. ($p=0.03$) Reviewing emesis solely, no emesis was seen in 7/10 A patients and 4/10 P patients ($p=0.18$). Preliminary PK show the observed AUCs of CY, HCY and CEPM for both preparative regimens were within the lower range of previously reported data and the PK differences between regimens were also consistent with previous data. All patients in both arms required busulfan dose adjustments (primarily reductions) to stay within target AUCs. Anti-seizure prophylaxis with phenytoin may significantly decrease A levels, but this didn't appear to be clinically relevant in this study and further PK evaluation is needed. Adverse effects were similar between arms with one case of sinusoidal obstruction syndrome in the P arm.

In this interim analysis, aprepitant added to standard antiemetics provides improvement in emesis prevention over standard antiemetics alone during cyclophosphamide-containing conditioning therapy prior to HSCT, without significant changes in cyclophosphamide pharmacokinetics or increased toxicity.

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### USE OF LOW DOSE RASBURICASE IN THE MANAGEMENT OF HYPERURICEMIA IN TUMOR LYSIS SYNDROME

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**Background:** Hyperuricemia is a complication of tumor lysis syndrome (TLS) in patients with high grade lymphomas, leukemias, and bulky tumors. Rasburicase is a recombinant form of urate oxidase which converts uric acid to a more soluble form, allantoin. It is indicated for the management of hyperuricemia in tumor lysis syndrome. City of Hope is a National Cancer Institute (NCI) designated comprehensive cancer center specializing in oncology, hematology, and hematopoietic stem cell transplantation (HSCT). The primary goal of this study is to determine the efficacy of low-dose rasburicase in treatment of hyperuricemia secondary to TLS. Based on the previous experience with low-dose rasburicase at City of Hope and small studies supporting the use of low-dose rasburicase, a TLS management guideline was developed in November 2005, using low-dose rasburicase. The guidelines also address the proper handling of the blood samples, since laboratory techniques in collecting and processing blood specimen are critical in obtaining accurate uric acid levels.

**Methods:** This study compared the efficacy of low-dose rasburicase versus the manufacturer recommended dose of 0.15-0.2mg/kg for five days both pre-guideline and post-guideline from January 2002 to April 2006. For the purpose of this study, doses less than 0.13 mg/kg would be considered low-dose and doses greater than or equal to 0.13mg/kg would be considered standard dose.

**Results:** Data was collected from the pharmacy information system, hospital record system, patient charts, and the laboratory information system. Uric acid levels collected at baseline and post-treatment, and serum creatinine levels were reviewed. The percent successful treatment in both low-dose and standard-dose rasburicase was 100%. The percent serum uric acid level decline within 24 hours of rasburicase administration was 73% pre-guideline and 79% post-guideline for a low-dose treatment group and 92% pre-guideline and 97% post guideline for a standard-dose treatment group.

**Conclusion:** This retrospective study shows that although the magnitude of serum uric acid level decline differs between the pre- and post-treatment groups, low-dose rasburicase is as effective as the standard-dose rasburicase in normalizing serum uric acid levels.

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### TRIAZOLE-RESISTANT *CANDIDA GLABRATA* ORAL CANDIDIASIS AND ASSOCIATED GASTROINTESTINAL SYNDROME IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT: SUCCESSFUL TREATMENT WITH ORAL AMPHOTERICIN B

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Oral candidiasis (OC) is common in patients undergoing hematopoietic cell transplant (HCT). *Candida glabrata*, the second most frequently isolated species in OC, has proven more difficult to treat and usually presents asymptomatically. The clinical significance of symptoms is contentious and the literature lacks effective therapeutic guidelines for treatment. We herein describe a series of 6 HCT patients with OC due to triazole-resistant *C. glabrata*. The data were prospectively collected. Mouth swabs for fungal stain, culture and sensitivity were sent