

**Preparation for a historically controlled trial of StemEx: Comparing logistic regression with propensity score for estimating the treatment effect**

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Introduction: Patients with hematologic malignant disease who require stem cell transplantation but have no matched bone marrow donor may be treated with a transplant of umbilical cord blood. While this approach is widely used in the pediatric setting, cord blood transplantation in adults and adolescents is limited by the relatively low number of stem cells per patient's body weight in a cord blood unit, which leads to high morbidity and mortality. StemEx<sup>®</sup> provides an alternative treatment and is a stem/progenitor cell-based product of ex vivo expanded allogeneic umbilical cord blood, which is administered in combination with the unmanipulated portion of the same cord blood unit (CBU).

The preparation for the historically Controlled group involved conducting a meta-analysis of 514 control patients drawn from three cord blood transplant registries (CIBMTR, NCBP and Eurocord) and building a prognostic model for mortality within 100 days that is based on cell dose, CMV infection, age, disease/stage, and size of treatment center. After the trial, it is planned to use the same prognostic model together with a treatment indicator to compare the StemEx group (100 patients) with these historical controls by logistic regression. The drug regulatory authority also requested a second comparison of 100-day mortality using a propensity score.

Searching the literature, we found a few published comparisons of these two competing methods for adjusting treatment comparisons for imbalance in prognostic factors based on Monte-carlo simulations (e.g. Cepeda et al (2003\*)). However, in a paper that compares the two methods on real data, Kurth et al (2005\*\*) wrote: "It is unclear which adjustment method is preferable in which situation". We wished to understand better the relative properties of the two methods in our context before embarking on their use in our trial.

In this presentation we will examine and compare these two methods of adjustment, logistic regression and propensity score, using Monte-Carlo simulations. We will generate the data of the StemEx group under different assumptions regarding (a) the outcome model and (b) the trial selection model, and compare the results given by the two methods under these different assumptions. Our main concern will be to compare the relative biases, precisions, and mean squared errors of the two methods in estimating the treatment effect.

\* Cepeda M.S., Boston R., Farrar J. T., Strom B. L. Comparison of Logistic Regression versus Propensity Score When the Number of Events Is Low and There Are Multiple Confounders . *Am J Epidemiol.* 2003; 158:280-287.

\*\* Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of non-uniform effect. *Am J Epidemiol.* 2006; 163:262–270.