



Capstone Research Paper Proposal

Students are required to submit and present their Capstone proposal to the MSCR Director and Assistant Director **prior to embarking on the Capstone project** in order to show the intended direction and scope of the project. Capstone proposals are very important because they give us a chance to review and approve the work **before** you thoroughly invest yourself in your topic.

Capstone proposals may take any of various formats, such as bullet points, outline or paragraph form. The proposal should be well conceptualized and contain sufficient detail to enable us to understand the focus of your project and how you intend to accomplish it. Your proposal should contain the following information:

1. **Background:** A brief background (no more than a paragraph) to establish the rationale for your project.

Ex. *A high dose chemotherapy regimen (HDT) followed by autologous stem cell transplantation (ASCT) has demonstrated therapeutic value for patients with relapsed/refractory (R/R) aggressive non-Hodgkin lymphoma (especially diffuse large B cell lymphoma (DLBCL¹)) and Hodgkin lymphoma (HL)^{2,3}. This modality is currently the standard of care for patients who are refractory or who relapse after first-line therapy, at least if their lymphoma demonstrates sensitivity to salvage chemotherapy. Several studies have previously determined prognostic factors for ASCT outcome for both DLBCL and HL. However, most of these studies were conducted in an era where computed tomography (CT) scans and not functional imaging (FI) (gallium scanning or positron emission tomography (PET) imaging) was performed to assess remission pre transplant. More recently, a number of groups have reported that the results of FI after salvage chemotherapy and before ASCT is a very strong predictor of transplant outcome^{4,5}. It remains unclear whether other prognostic factors remain significant when accounting for the results of FI. While pre-transplant FI is clearly of high predictive value, relapse still occurs in patients with negative FI. More importantly, a substantial fraction (20-40%) of patients with residual disease by FI prior to ASCT still appear to be cured by the transplant⁶. Thus, FI alone is not sufficient to select patients for transplantation. It would be valuable to determine what additional factors, if any, impact the prognosis of patients undergoing ASCT. This may allow the creation of a prognostic score that would provide better prognostic information than FI alone; more importantly, it may also help to identify a group of patients whose outcomes after ASCT are poor enough to justify using alternative treatment modalities (such as allogeneic transplantation or tandem transplantation approaches).*

2. **Research Question:** A clear, concise question of the position you will defend in your paper. The question should argue a position, not summarize information.

Ex. *Can clinical factors be used to construct a prognostic score using pre-transplant FI data for patients undergoing ASCT?*

3. **Study Design & Methods:** A description of the study design and a description of the variables & methods that will be used to address your research question.

Ex. *Based on the accumulated experience at Boston Medical Center using pre-transplant PET scans and HDT/ASCT treatment for relapsed HL, a retrospective study of outcomes of patients treated within the institution will be conducted.*

4. **Endpoints/Outcomes of Interest:** A description of the Outcome Measures (Primary and secondary endpoints) you will use in your study.

Ex. *The primary endpoint of this study will be progression free survival after ASCT. Secondary outcomes will include overall survival and cumulative incidence of relapse and non-relapse mortality.*

5. **Planned Statistical Analysis:** A brief description of the statistical analyses that will be used to assess your outcome measures, i.e. primary endpoint, secondary endpoints.

Ex. *Patient baseline characteristics will be analyzed descriptively. Overall survival and progression-free survival will be calculated using the Kaplan-Meier method. Overall survival will be defined as the time from stem cell infusion to death from any cause. Patients who were alive or lost to follow-up will be censored at the time last seen alive. Progression-free survival will be defined as the time from stem cell infusion to the first indication of disease progression, relapse, or death from any cause, whichever occurred first. Patients who were alive without progression will be censored at the time last seen alive and progression-free. The log-rank test will be used for comparisons of Kaplan-Meier curves for OS and PFS. Cox proportional hazards models will be used to determine significant predictors of OS and PFS. Cumulative incidence curves for non-relapse mortality and relapse with or without death will be constructed reflecting time to relapse and time to non-relapse death as competing risks. The difference between cumulative incidence curves in the presence of a competing risk will be tested using the Gray method. Time to relapse and time to non-relapse death will be measured from the date of stem cell infusion. Competing risks regression model (for relapse and non-relapse mortality) will be used to study prognostic factors for relapse and NRM.*

6. **Proposed Timeline:**

Ex. *Using the transplant database, information on clinical factors will be collected from the medical records of participants through May 2012. During the first two weeks of June 2012, R will be utilized to perform analyses on the factors extracted from the database. The Capstone Research Paper will then be written and given to the readers in early July.*

7. **References (in AMA format):**

Ex.

1. Philip T, Guglielmi C, Hagenbeek A, et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. *N Engl J Med.* 1995; 333:1540-1545.
2. Linch DC, Winfield D, Goldstone AH, et al. Dose intensification with autologous bone-marrow transplantation in relapsed and resistant Hodgkin's disease: results of a BNLI randomised trial. *Lancet.* 1993; 341:1051-1054.
3. Schmitz N, Pfistner B, Sextro M, et al. Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin's disease: a randomised trial. *Lancet.* 2002;359:2065-2071.
4. Schot BW, Zijlstra JM, Sluiter, WJ, et al. Early FDG-PET assessment in combination with clinical risk scores determines prognosis in recurring lymphoma. *Blood.* 2007;109: 486-491.
5. Moskowitz CH, Yahalom J, Zelenetz AD, et al. High-dose chemo-radiotherapy for relapsed or refractory Hodgkin lymphoma and the significance of pre-transplant functional imaging. *British Journal of Haematology.* 2010;148:890-897.