Seventh International Workshop on Simulation

21-25 May, 2013

Department of Statistical Sciences, Unit of Rimini

University of Bologna, Italy

Book of Abstracts

Edited by Mariagiulia Matteucci

Quaderni di Dipartimento

Serie Ricerche 2013, n. 3

ISSN 1973-9346

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Dipartimento di Scienze Statistiche “Paolo Fortunati”

Models with cross-effect of survival functions in the analysis of patients with multiple myeloma

Alexander Bitukov, Oleg Rukavitsyn
The Hematology Center, Main Military Clinical Hospital name of N.N.Burdenko, Moscow, Russia
82465@bk.ru

Ekaterina Chimitova, Boris Lemeshko, Mariya Vedernikova
Novosibirsk State Technical University, Novosibirsk, Russia
ekaterina.chimitova@gmail.com

Mikhail Nikulin
Universite Victor Segalen, Bordeaux, France
mikhail.nikouline@u-bordeaux2.fr

Accelerated life models are used more and more often in oncology and hematology studies for the problems of relating lifetime distribution to explanatory variables; see Klein and Moeschberger (1997), Piantadosi (1997) and Zeng and Lin (2007). The survival functions for different values of the covariates according to the Cox proportional hazard (PH) model do not intersect. However, in practice this condition often does not hold. Then we need to apply some more complicated models which allow decreasing, increasing or nonmonotonic behavior of the ratio of hazard rate functions. Following Bagdonavicius, Levuliene and Nikulin (2009) and Nikulin and Wu (2006) we give examples to illustrate and compare possible applications of the Hsieh model (see Hsieh (2001)) and the simple cross effect (SCE) model (see Bagdonavicius and Nikulin (2002)), both of them are particularly useful for the analysis of survival data with one crossing point.

The research of various schemes of chemotherapy for the patients with multiple myeloma has been carried out. The purpose of the investigation is to compare the response time to the treatment in two groups of patients who received different treatment. As the Kaplan-Meier estimates of distribution functions in two groups intersect, the Cox PH

model can be inappropriate for these data. For this reason we propose using the models with cross-effect for relating the distribution of response time to the scheme of chemotherapy, type of the response, etc.

A very important practical result of our analysis is the establishment of the influence of Bortezomibe on the speed of the achievement of the response. We have ascertained the fact that responses such as a complete response, partial response, minimal response, stabilization and progression of the disease in the group of patients treated by Bortezomibe were achieved faster than in the control group.

Keywords: lifetime analysis, censored data, regression models, cross-effect.

References

Bagdonavicius, V. and Nikulin, M. (2002). *Accelerated Life Models*. Boca Raton: Chapman and Hall/CRC.

Bagdonavicus, V., Levuliene, R. and Nikulin, M. (2009). Testing absence of hazard rates crossings, *Comptes Rendus de l'Academie des Sciences de Paris*, Ser. I, 346, 7-8, 445-450.

Hsieh, F. (2001). On heteroscedastic hazards regression models: theory and application. *Journal of the Royal Statistical Society*, B 63, 63-79.

Klein, J.P. and Moeschberger, M.L. (1997). *Survival Analysis*, New York: Springer.

Nikulin, M. and Wu, H.-D. (2006). Flexible regression models for carcinogenesis data. *Probability and Statistics, Steklov Mathematical Institute in St.Petersburg, RAS*, 78-101.

Piantadosi, S. (1997). *Clinical Trials*, J.Wiley : New York.

Zeng, D. and Lin, D.Y. (2007). Maximum likelihood estimation in semiparametric regression models with censored data. *Journal of Royal Statistical Society*, B 69, 1-30.