Towards Personalised and Mathematically Optimised Chemotherapy in Acute Myeloid Leukemia

F. Jost[1], **E. Schalk**[2], **K. Rinke**[1], **T. Fischer**[2], **and S. Sager**[1]

Abstract: The major obstacle in accurately predicting the outcome of a medical therapy is the vast variation in individual response patterns. A pertinent example of this is in the treatment of acute myeloid leukemia (AML) and involves the outcome of chemotherapy, kinase inhibitors, and immunotherapeutic approaches. It concerns both the subjective experience of the patient and the objectively measurable achievement of a clinical remission with restoration of normal blood counts.

Here we address AML-chemotherapy using cytarabine (Ara-C) as this drug is the most important component of AML-treatment. The considerable variation in patient response patterns can be partly explained by the wide spectrum of genetic and epigenetic aberrations involved in pathogenesis of AML. However, there is another facet of personalised medicine that awaits exploration of its full potential: a systematic, mathematical approach to understand and manipulate the dynamics of relevant biomarkers.

Here we are interested in the depth and duration of low white blood cell (WBC) counts after cytotoxic therapy in AML. In a comprehensive approach we extend the current gold-standard model of myelosuppression, analyse cross-validations and the impact of modelling assumptions (low) and of varying chemotherapy schedules (high) on prediction accuracy, and optimise schedules based on personalised mathematical models. Our numerical results confirm that dense schedules are superior and shed new light on the reasons why. We also optimise the time between two consecutive chemotherapy cycles. The optimal time and the predicted nadir strongly depend on the response patterns as specified by a novel dynamic stratification.

The application of these results in clinical practice may reduce complications arising from infection and thus avoid prolonged hospitalisation. Moreover, optimised and personalised chemotherapy schedules may be useful in enabling deeper remissions and therefore ultimately achieve improved survival rates.

---

[1] Institute of Mathematical Optimization,
Faculty of Mathematics,
Otto-von-Guericke University Magdeburg
Universitätsplatz 2, 39106 Magdeburg, Germany
felix.jost@ovgu.de

[2] Department of Hematology and Oncology,
Medical Faculty,
Otto-von-Guericke University Magdeburg
Leipziger Straße 44, 39120 Magdeburg, Germany