6th Annual Meeting Of The European Haematology Association - Frankfurt, Germany, 21-24 June 2001

A NEW METHOD FOR PREDICTING AND OPTIMIZING THROMBOPOIETIN (TPO) THERAPEUTIC PROTOCOLS IN THROMBOCYTOPENIC PATIENTS AND IN PLATELET DONORS

Kirill Skomorovski[1] , Zvia Agur[1,2]

Abstract category: Developmental haematopoiesis

***Background*:** Thrombocytopenia is a common hazardous blood condition, which may appear in different clinical situations, including cancer chemotherapy, where it represents a major dose limiting side effect. A thrombopoiesis-controlling cytokine, thrombopoietin (TPO), isolated in 1994, has shown to dramatically increase blood platelet counts, thus improving a patient's ability to withstand chemotherapy. In addition, TPO is shown to aid in the treatment of other conditions, and in harvesting platelets from donors. In the last few years an extensive experimental research has been dedicated to the search for effective TPO dosing.

Aims: In this work we describe a new biomathematical method for predicting and optimizing TPO protocols.

***Methods*:** We simulated TPO and cytotoxic drugs' effects on thrombopoiesis, by translating the driving biological, pharmacological and clinical interactions into a very elaborate computation system. The result is an "*In silico*" Bone Marrow model, which predicts treatment effects on the dynamics of human thrombopoiesis. This model was evaluated by its ability to retrieve published data from clinical trials involving TPO administration.

***Results*:** The model has been shown to quickly and efficiently retrieve diverse published clinical experiments involving different TPO protocols.
When presented with previously untested protocols, the model yields elaborate results that are biologically and medically sound, and are in harmony with known clinical information. The different thrombopoiesis lineage cell counts, as well as the TPO concentration can be graphically and numerically presented in various time resolutions, and relevant medical thresholds (e.g. thrombocytopenia, thrombocytosis, transfusion indicating levels etc.), can be alerted online during the simulation process.

***Conclusions*:** In this work we have shown that a computerized model of biological-medical-pharmacological processes can accurately retrieve clinical results. The use of such "*In Silico*" methods at the research level can accelerate the design of effective treatment protocols, thus reducing the number of experiments needed, the number of patients and laboratory animals that are subject to potential hazards, and finally, the cost and duration of trials. At the level of aspired medical goals, our "*In Silico*" methods enable developing optimal drug administration protocols for maximized efficacy and minimized toxicity. In particular, the "*In Silico*" Bone Marrow model can help define optimal protocols that minimize post-chemotherapy thrombocytopenia, maximize platelet harvest in platelet donations and reduce treatment cost. Our methods are now being generalized for implementation in different therapeutic areas, and with different drug candidates.

1. Institute for Medical Biomathematics, 10 Ha'Teena St. , Beney Ataroth, 6099, Israel.
2. Optimata Ltd., Tel Aviv, Israel. agurz@optimata.com