

HemoRANK™ -TKI Assay Service Package

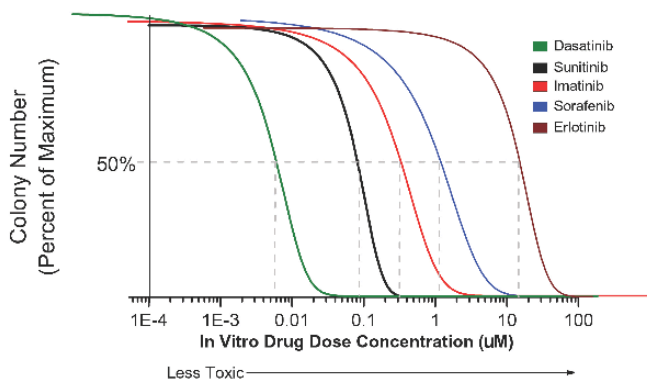
For Ranking Myelotoxic Potential of New Tyrosine Kinase Inhibitors

Myelotoxicity (neutropenia) is often a major dose-limiting side effect of Tyrosine Kinase Inhibitors (TKIs). Myelotoxicity / myelosuppression often occurs because the growth and/or differentiation of hematopoietic progenitors of the myeloid lineage in the bone marrow are affected by the administered TKI.

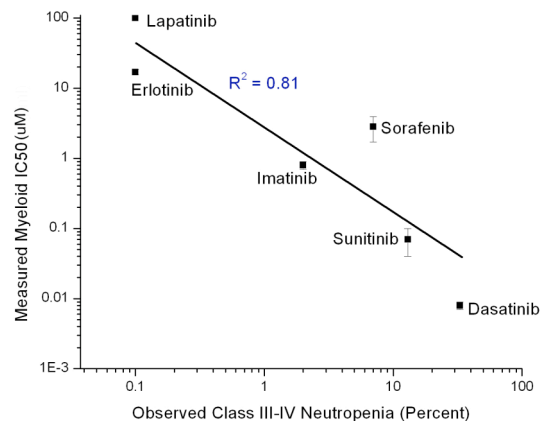
ReachBio's HemoRANK™-TKI Assay Service Package is a standardized test system in which one or more test TKIs provided by the client are run in *in vitro* hematopoietic progenitor (CFC) assays in parallel with a panel of 6 therapeutic TKIs with known levels of clinical myelotoxicity. The IC₅₀ values obtained for the test TKIs are ranked against the IC₅₀ values of the panel of control TKIs, and the clinical myelotoxicity potential is predicted from the results.

As shown in the figures below, expertly performed *in vitro* CFC assays can accurately predict the clinical myelotoxicity potential of TKIs. In ReachBio's hands, the rank order of IC₅₀ values of a number of therapeutic TKIs tested in *in vitro* CFU-GM assays correlated directly with the degree to which the TKIs were reported to cause Class III-IV neutropenia in the clinic. This high degree of correlation between *in vitro* results and clinical observation strongly suggests that the *in vitro* CFU-GM assay system can be used to predict* the level of myelotoxicity a new TKI compound will likely show in the clinic, when compared with a panel of known TKIs tested in parallel.

Ranking of TKIs Based on *In Vitro* Myeloid IC₅₀ Determination



Neutropenia for 6 Common Tyrosine Kinase Inhibitors



The HemoRANK™-TKI Assay Service Package Includes:

- Testing of your novel TKI compound(s) in *in vitro* CFC assays in parallel with a panel of 6 standard TKIs with known levels of clinical myelotoxicity
- Ranking of *in vitro* myelotoxicity of test TKI(s) compared to standards
- Prediction* of clinical myelotoxicity potential of test TKI(s)
- Full written report with data interpretation and statistical analysis
- Full confidentiality
- Standardized pricing

Customized *in vitro* assays for prediction of myelotoxicity of TKIs and other compounds are also available. Please contact us to discuss your unique requirements.

*Predictions are ReachBio's scientific estimates based upon *in vitro* assay results and the correlations with clinical observations of the TKIs in the control panel as described above. ReachBio does not guarantee that predictions based upon this system will always accurately reflect clinical myelotoxicity of new TKIs.