Tyrosine kinase inhibitors (TKIs) are multi-targeted anticancer drugs with high activity towards several families of receptor and non-receptor tyrosine kinases involved in angiogenesis, tumor growth and metastatic progression of cancer. Many of these will be running off-patent, sequentially, in the next few years. Bioequivalence (BE) studies are needed for the development and regulatory approval of generic products of TKIs.

**RESULTS**

Oral absorption of TKIs spanned from very fast (1.3 h Tmax for dasatinib) to fast 3.5 h (Tmax for axitinib, erlotinib and regorafenib) to relatively slow absorption 6 h (gefitinib) & 8 h (sunitinib).

Under fed state, there was a slight delay in Tmax and a relatively higher variability compared to the fasting state for the same drug (results not shown).

The inter-subject variability can be indicated by the error bars (for SD) in the profiles below.

**CONCLUSIONS**

The studied TKIs exhibited different PK profiles and plasma exposure.

The variability of TKIs was shown to be diverse: ranging from high (dasatinib, medium (axitinib, erlotinib, gefitinib, regorafenib, imatinib) to very low (sunitinib).

**METHODS**

BE studies (fast/fed) as follows:

- NHV (total≈1360)
- Well-controlled standardized conditions.
- BE study design shown below.

**OBJECTIVES**

The objectives of this work is to:

- Highlight the prominent pharmacokinetic (PK) properties of TKIs.
- Assess the variability of TKIs in BE clinical trials.
- Discuss the reasons for the high variability of some TKIs.
- Identify the safety profiles (in terms of AEs) observed in clinical trials.
- Suggest an optimized study design for BE studies of this class of drugs.

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