Pharmacogenetics of sunitinib in metastatic renal cell carcinoma

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Propositions

belonging to the thesis

Pharmacogenetics of sunitinib in metastatic renal cell carcinoma

1. *CYP3A4*22* carriers show a 22.5% decrease in the clearance of sunitinib, but this effect size is too small to guide individual sunitinib dosing in clinical practice.
   This thesis (Chapter 3)

2. Genetic polymorphisms in *CYP3A5* or *ABCB1* play an important role in predicting the need for dose reductions and the duration of progression-free survival in individuals treated with sunitinib.
   This thesis (Chapter 4)

3. Variant allele carriers of genetic polymorphisms in *CYP3A4*, *IL8* and *IL13* have a higher risk of developing sunitinib-induced toxicities.
   This thesis (Chapter 5+6)

4. PK/PD models provide a better understanding of the relationship between sunitinib exposure, pharmacological response and clinical outcome.
   This thesis (Chapter 8)

5. A Genome Wide Association Study (GWAS) is more informative than a candidate gene study.
   This thesis (Chapter 9)

6. The landscape for developing TKI therapy has changed, and "bench to bedside" must return to the bench.
   C.-H. Lee, R.J. Motzer. Urol Oncol. 2015;33(6);275–279

7. As is the case with any other biomarker, advancing from the research space into a clinical application requires that criteria of validity (analytical and clinical) and utility be met.
   Gillis N, Innocenti F. Clin Pharmacol Ther. 2014;96(6):655-657

8. While having contributed substantially to the understanding of genetic predisposition to drug response, current analyses of selected allelic variants do not accurately reflect the true interindividual variability in pharmacogenetic genes in specific patients.
   Lauschke VM, Trends Pharmacol. Sci. 2016;37(2):85-86

9. With TDM we can only adjust, while pharmacogenetics enables us to predict.

10. Seeking for the truth in science is as challenging as flying trough the ash clouds from the Eyjafjallajökull.

11. It is not the strongest of the species that survives, nor the most intelligent, but rather the one most adaptable to change.
    Charles Darwin (12 February 1809- 19 April 1882). In this thesis referring to resistance the tumor develops against sunitinib

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