Dried blood spot sampling for therapeutic drug monitoring of pazopanib

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Introduction

Pazopanib is an oral multi-targeted tyrosine kinase inhibitor (TKI) used for the treatment of metastatic renal cell carcinoma (mRCC) and metastatic soft tissue sarcoma (STS).

The optimal therapeutic window for pazopanib in patients with mRCC lies between a Cmax of 20.5 - 36 mg/L.

Patients treated with pazopanib show a high variability in pharmacokinetics (PK).

Therapeutic drug monitoring (TDM) could therefore be useful to optimize the efficacy and minimize the toxicity of therapy.

At present, pazopanib concentrations are monitored in plasma collected by venous sampling.

Compared to venous sampling, dried blood spot (DBS) sampling is a convenient, simple, flexible and more patient friendly alternative to collect blood in an at home setting.

Methods

At day 14 of standard 800 mg once daily pazopanib therapy, patients were admitted to the hospital for pharmacokinetic sampling.

EDTA-blood samples were collected by venepuncture pre-dose and at 1, 2, 3, 4, 6, 8, 10 and 24 hours after pazopanib intake; 15 µL blood was collected into an EDTA capillary tube and spotted onto a pre-marked circle on a Whatman FTA® DBS card.

In addition, DBS sampling cards prepared by finger prick were collected pre-dose, and at 3 and 8 hours after pazopanib intake.

Finger prick DBS cards (n=3), venous DBS cards (n=9) and plasma samples (n=3) were all sent to GlaxoSmithKline, USA for further bio-analytical analysis with a validated LC-MS/MS method.

Plasma concentrations were calculated using the previously described formula: plasma concentration = DBS concentration / (1 - measured haematocrit).

Plasma concentrations were calculated using both patient specific measured haematocrit values and fixed haematocrit values of 0.40 and 0.45 for males and females.

Passing-Bablok regression and Bland-Altman analysis were used to determine the agreement between the two sampling methods.

We predefined the clinical acceptance limit of the Bland-Altman analysis at a 25% interval around the found ratio.

Results

The preparation of DBS cards by patients themselves should be validated, before the implementation of DBS into clinical practice.

To determine the agreement between pazopanib DBS- and plasma concentrations in order to facilitate the future implementation of DBS sampling into clinical practice.

Objective

Conclusions

At day 14 of standard 800 mg once daily pazopanib therapy, patients were admitted to the hospital for pharmacokinetic sampling.

EDTA-blood samples were collected by venepuncture pre-dose and at 1, 2, 3, 4, 6, 8, 10 and 24 hours after pazopanib intake; 15 µL blood was collected into an EDTA capillary tube and spotted onto a pre-marked circle on a Whatman FTA® DBS card.

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Figures 1A-B. Passing-Bablok regression

Figures 2. Bland-Altman analysis

Discussion

This makes validation of clinical utility with DBS sampling necessary.

In Table 1, it is shown that in 1 case (9.1%), there would have been a difference in decision making based on measured and calculated plasma concentrations. All other cases of clinical decision making would have been the same based on either the measured or calculated plasma concentration.

Table 1. Clinical decision making

In Table 1, it is shown that in 1 case (9.1%), there would have been a difference in decision making based on measured and calculated plasma concentrations. All other cases of clinical decision making would have been the same based on either the measured or calculated plasma concentration.

Conclusions

This study shows a good agreement between pazopanib levels measured in plasma and calculated plasma concentrations based on DBS sample collection.

DBS could therefore be a very useful and patient friendly approach to monitor pazopanib therapy.

The preparation of DBS cards by patients themselves should be validated, before the implementation of DBS into clinical practice.

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