Poster

[P25-9] P25-9: Oncologic drugs (1)

Chair: Ryuji Ikeda, Japan

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[P25-9-10] Utility of therapeutic drug monitoring of sunitinib in patients with metastatic Renal Cell Carcinoma

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Background

Sunitinib (SU) is used for the first line treatment of metastatic renal cell carcinoma (mRCC). SU is associated with distinct pattern of toxicities that require frequent monitoring and management. Common adverse reactions include fatigue, hypertension, diarrhea, hand-foot syndrome, mucositis, vomiting and neutropenia. Therapeutic drug monitoring (TDM) for SU is not routinely practiced clinically, due to lack of evidence and guidelines. The present study was designed to develop a TDM strategy for SU in mRCC.

Methods

Adult patients aged 18 and above receiving SU as first line treatment for mRCC were enrolled in the study. Eligible patients were administered SU at a starting dose of 50mg OD. Each cycle comprised of 4 weeks of treatment with SU followed by 2 weeks rest (4/2). All patients had response evaluation by PET-CT at 3 months (end of 2 cycles). Response was categorized as Stable Disease (SD) or Progressive Disease (PD) using Response Evaluation Criteria In Solid Tumors (RECIST 1.1). Toxicity was graded as per CTCAEv4.03. Trough samples for determination of SU and its active metabolite (SU 012662) were collected on cycle 1 day 14. Drug levels were measured using a validated HPLC assay.

Results

Twenty five patients were enrolled of whom 22 were evaluable for response (SD=18, PD=4) and 23 for toxicity (Gr2=17, Gr3=6). Mean (±SD) age was 49±12 yrs; M=19, F=6. Trough levels were highly variable (CV = 45%, 57% and 47% for SU, SU 012662 and total drug respectively). There was no difference in trough levels in patients with SD versus PD. Receiver Operating Curve (ROC) characteristics showed that threshold trough concentrations of 62.8, 26.55 and 80.95 ng/mL for SU, SU 012662 and total drug respectively could discriminate between occurrence of Gr-3 toxicity versus not. The odds ratio for occurrence of Gr-3 toxicities at these thresholds was 23.33 (1.95-279.43) for SU and total drug and 15.0 (1.58-142.17) for SU 012662 ($P<0.01$).

Conclusions

In our cohort of patients, SU exhibited high pharmacokinetic variability. No concentration-response relationship was observed. However, trough levels at steady state were highly predictive of Gr-3 toxicity, suggesting TDM based dosing could significantly reduce the morbidity associated with SU treatment.