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Preeclampsia like syndrome induced by the multi-targeted kinase inhibitors, sorafenib and sunitinib treatment for advanced hepatocellular carcinoma

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Introduction: Orally administered multitargeted kinase inhibitors (MTKI) by targeting receptors for VEGF, sorafenib was approved for the treatment of hepatocellular carcinoma (HCC) in 2007. Sunitinib is under investigation. They are generally well tolerable, but have been associated with renal toxicity in some patients. There has been no report of heavy proteinuria in anti VEGF treated patients with HCC. **Case report:** A 64-year-old man with chronic B-viral hepatitis inactive carrier was diagnosed with HCC in 2007. He had no hypertension and renal disease. Initial therapy was wedge resection of primary HCC, then intraoperative RFA with laparoscopic abdominal lymph node sampling followed by 5040 centigray radiotherapy on paraaortic lymph node metastasis. Aortocaval lymph node metastasis was found 6 months later and he started taking sorafenib (400 mg twice daily). After 18 month therapy of sorafenib, the tumor progressed. Sunitinib (Scheduled as 50 mg/day for 4 weeks, followed by 2 weeks off) was started. He showed progressive hypertension, heavy proteinuria, pitting edema and azotemia two weeks later. Laboratory finding was serum creatinine of 1.87 mg/dl, 24 hour urine protein 2011.62 mg, random urine P/Cr ratio of 8.6 hemoglobin 8.3g/dl, platelet 43000/ul and occasional schistocytes in blood smear. Sunitinib was immediately discontinued. Proteinuria was slowly improved after about 3 weeks and completely disappeared 6 months after sunitinib withdrawal with conservative management. **Discussion:** VEGF is expressed by podocytes and essential for glomerular endothelial function. Disrupted glomerular VEGF signaling is strongly implicated in the pathogenesis of preeclampsia, suggesting that inhibition of glomerular VEGF receptor signaling by MTKI is plausible mechanism to account for the renal toxic effects we observed. Clinicians should monitor all patients starting MTKIs a baseline urinalysis with regular checkup of renal function throughout the course of therapy.

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A difference of HER2 amplification between ER+ and ER- subgroup in HER2 positive breast cancer

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Background: Expression profiling studies have suggested that HER2-amplified breast cancers constitute a heterogeneous group that may be subdivided according to their ER status. Here we have compared the amount of HER2 gene amplification of ER-positive (luminal B subgroup) and ER-negative HER2-amplified (HER2 subgroup) breast cancers using FISH. **Methods:** From Jan 2004 to Dec 2009, 753 patients with HER2-amplified breast cancer were tested by FISH and 224 patients were available for this study. Two molecular subtypes were defined from the immunohistochemical results of hormone status and HER2 amplification confirmed by FISH. A difference of HER2 amplification index was analyzed between luminal B and HER2 subgroup. HER2 amplification was defined as HER2/CEP17 ratio of >2.0 by FISH. Clinicopathologic parameters were analyzed. **Results:** The proportions of luminal B and HER2 breast cancer were 53.5% (N=120) and 46.5% (N=104). According to the stage, the proportions of early breast cancer were 84.8% (N=190) and metastatic breast cancer were 15.2% (N=34). HER2 amplification index of luminal B group and HER2 enriched group were 4.99 and 5.84, which values showed the quantitative difference statistically significant ($p=0.003$). However, increasing value of HER2 amplification was not associated with a better overall survival or progression free survival. **Conclusions:** The magnitude of HER2 amplification was different between luminal B and HER2-enriched subgroup statistically significant. It was not clear exactly whether the extent of overexpression of this gene relates to the survival benefit of treatment in HER2-positive breast cancer.