GLOSSARY

RECIST CRITERIA

Criteria for measuring tumor shrinkage as an indicator of antitumor activity, as evaluated by the Response Evaluation Criteria in Solid Tumors Group (RECIST)

definition was the most specific of the three definitions, had equal or greater positive predictive value than the other definitions, and had the best overall accuracy. In addition, the nadir plus 2 ng definition identified more cases of BF than the unmodified ASTRO definition in the first 2 years of follow-up.

The results show that the nadir plus 2 ng/ml definition is the best predictor of sustained BF and is not affected by combined treatment with ADT or length of follow-up. The authors conclude that this definition should be used when comparing therapeutic regimes in prospective or retrospective studies.

Kate Matthews

Original article Buyyounouski MK *et al.* (2005) Defining biochemical failure after radiotherapy with and without androgen deprivation for prostate cancer. *Int J Radiat Oncol Biol Phys* 63: 1455–1462

Androgen deprivation therapy and BMD loss

Several studies have suggested that androgen deprivation therapy (ADT), often used in the treatment of prostate cancer, is associated with loss of BMD. Greenspan *et al.* have conducted a 12-month, prospective, US study comparing the rate of bone loss in men with prostate cancer versus healthy men, and in men initiating ADT versus men who had received chronic ADT (for ≥ 6 months).

The nonrandomized study enrolled 152 men (mean age 68 years) with nonmetastatic prostate cancer and 43 healthy, age-matched controls. The men with cancer were categorized as having no ADT ($n=72$), acute ADT (mean duration 2.9 ± 1.5 months, $n=30$) or chronic ADT (mean duration 33.2 ± 33.4 months, $n=50$). BMD of the hip, wrist, total body, and spine was measured at baseline and at 6 and 12 months, by dual-energy X-ray absorptiometry.

At 12 months, men in the acute ADT group showed a statistically significant reduction in BMD of the total hip, trochanter, wrist, spine and total body (all $P < 0.05$), compared with baseline BMDs. Men in the age-matched control and chronic ADT group showed a reduction in BMD only of the wrist ($P < 0.05$), and men in the no-ADT group showed no reductions in BMD.

Bone loss was greatest in the first year of ADT, indicating that men initiating treatment are at the highest risk for bone fracture. The

authors suggest that antiresorptive therapy might be most effective in this period.

Katherine Sole

Original article Greenspan SL *et al.* (2005) Bone loss after initiation of androgen deprivation therapy in patients with prostate cancer. *J Clin Endocrinol Metab* 90: 6410–6417

Use of SU11248 to inhibit proangiogenic growth factors in renal cell carcinoma patients

Renal cell carcinoma (RCC) is a highly resistant malignancy in which there is high expression of proangiogenic vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) due to loss of von Hippel–Lindau tumor suppressor gene activity. Blockade of VEGF and PDGF signaling pathways might inhibit tumor growth. In a multicenter phase II study, Motzer *et al.* tested whether SU11248 (sunitinib malate), which selectively inhibits tyrosine kinases required for signaling by VEGF and PDGF receptors, had antitumor activity in metastatic RCC.

Patients with metastatic RCC ($n=63$) that had not responded to cytokine-based therapy were treated with repeated cycles of 50 mg SU11248 daily for 4 weeks, followed by 2 weeks off treatment, until disease progressed, the patient withdrew consent or unacceptable toxic effects occurred. Median duration of treatment was 9 months; median time to progression was 8.7 months. Analysis using RECIST CRITERIA showed partial responses (observed in lesions at multiple sites) in 25 patients (40%) and stable disease lasting more than 3 months in an additional 17 patients (27%). Of the 25 patients with partial responses, 2 discontinued treatment, 15 experienced progression and 8 remained progression-free more than 20 months from the initiation of therapy.

In summary, selective inhibition of VEGF and PDGF receptor tyrosine kinases using SU11248 as second-line therapy results in antitumor activity in patients with metastatic RCC. These results hold promise for the development of additional therapies that target VEGF and PDGF receptors in RCC patients.

Kate Matthews

Original article Motzer RJ *et al.* (2006) Activity of SU11248, a multitargeted inhibitor of vascular endothelial growth factor receptor and platelet-derived growth factor receptor, in patients with metastatic renal cell carcinoma. *J Clin Oncol* 24: 16–24