TARGETED THERAPIES

A new success for an antiangiogenic?

The field of prostate cancer therapy has been one of the most fast moving over the past year or so, with new treatment options against novel drug targets being developed and approved. This has led to an aura of optimism for this disease.

Despite all these advances, it is also generally agreed that more treatment options are necessary, especially for those patients with advanced-stage disease. One place to look for novel targets is in preclinical models. For example, tumor growth is impaired in S100A9 knockout mice, pointing the way to a potential novel clinical target.

S100A9 is an immunomodulatory protein that is expressed in cells that are present in the tumor microenvironment and that stimulate angiogenesis. Roberto Pili and coworkers have been involved in the clinical development of an inhibitor of S100A9. “Tasquinimod is a linomide analog that showed antitumor and antiangiogenic effects in preclinical models of prostate cancer. The immunomodulatory and antiangiogenic activity of this agent represented a novel

therapeutic approach for the treatment of prostate cancer,” explains Pili.

Promising phase I clinical results led to a phase II trial assessing tasquinimod in 201 patients with metastatic castration-resistant prostate cancer. Pili describes the study as, “a randomized placebo-controlled study design with a 2:1 ratio and possibility of crossover that offered the opportunity to show robust difference in the primary end point of progression-free survival.” Indeed, progression-free survival was shown to be significantly longer in the patients who received tasquinimod, when compared with the placebo arm: 7.6 months versus 3.3 months.

Given that other novel drugs have recently become available for this patient population, it is not only important to show that there is a progression-free survival advantage associated with the therapy, but it is also crucial to establish the safety profile of the new drug. Unsurprisingly, there were some adverse events noted in the patients receiving therapy, that were not seen in the placebo population. These included

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gastrointestinal disorders, fatigue, musculoskeletal pain and elevated pancreatic and inflammatory biomarkers. However, the overall adverse-event profile was deemed to be acceptable.

“A phase III clinical trial with a similar study design is currently accruing patients,” outlines Pili. However, going forward, it seems clear that this therapy will need to be compared with the current standard of care.

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Original article Pili, R. *et al.* Phase II randomized, double-blind, placebo-controlled study of tasquinimod in men with minimally symptomatic metastatic castrate-resistant prostate cancer. *J. Clin. Oncol.* doi:10.1200/JCO.2011.35.6295