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## The combination of photodynamic therapy with anti-angiogenic therapy for the effective control of local prostatic tumor and distant metastasis

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he Combination of anti-angiogenic therapy with cytotoxic therapy has shown positive outcome in various preclinical studies. However, these promising results did not always translate to clinical efficacy, demonstrating the complexity of combination strategies. As a result, there are ongoing efforts to combine existing cytotoxic therapy with anti-angiogenic therapy to enhance the efficacy of cancer treatment. However, the optimal scheduling of anti-angiogenic therapy with cytotoxic therapy, although crucial for maximizing treatment efficacy remains unclear. The aim of this study is to investigate VEGF regulation following cytotoxic therapy as a basis for the efficacy of combination anti-angiogenic therapy. Materials and methods: Orthotopic prostate tumors were implanted in the prostate of 6-week-old male severe combined immunodeficient mice. In particular, we investigated the effect of the combination treatment strategy on the two major patterns of metastasis: hematogenous as well as lymphatic metastasis. Here, we investigated an optimal

protocol for combining Avastin anti-angiongenic therapy with photodynamic therapy (PDT), a cytotoxic therapy for various diseases including cancer. We demonstrate that PDT leads to a temporally transient regulation of vascular endothelial growth factor (VEGF) following treatment. More importantly, combination Avastin therapy was most effective in inhibiting lung metastasis when delivered around the peak of VEGF response following PDT. Considering that temporally transient VEGF regulation was observed following PDT, radiotherapy and chemotherapy. In conclusion, PDT lead to a temporally transient regulation of vascular endothelial growth factor (VEGF) following treatment. Considering that temporally transient VEGF regulation was observed following PDT, radiotherapy and chemotherapy, optimal scheduling of combination anti-angiogenic therapy based on temporal dynamics of the VEGF response has implications in a wide range of cancer treatments.

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