



## Successful metronomic chemotherapy for castration resistant prostate cancer with bone- and lymph node metastases

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The patient is a 68-year old man who was diagnosed in January 2005 with prostate cancer with a Gleasonscore of 9. The patient had his prostate removed, was treated with extended radiotherapy and removal of the testicles (orchiectomy). He was also treated with Casodex, but a year later he progressed with multiple bone metastases and lymph node metastases. The patient now had 6 treatments with Taxotere, which initially reduced the PSA, but then it increased again. After 6 treatments, the patient developed a polyneuropathy (nerve inflammation) grade II. PSA continued to rise after Taxotere. Treatment with Zometa began in August 2006 and anti-hormone therapy was continued.

Trofosfamide was started in August 2007 with 150 mg daily, but after four weeks of treatment it was necessary to reduce the dose to 100 mg daily due to a facial rash and paresthesia in the legs, which could come from the Taxotere treatment. The neuropathy came under fine control by a treatment with Lyrica. During treatment with trofosfamide PSA decreased from 46.6 to 2.1, and the treatment was now tolerated well without side effects. PET-CT scan was performed both before and after treatment with trofosfamide and 10 months after starting treatment showed partial remission of all bone metastases and regression of all lymph nodes except one.

The treatment took place at the university hospital of Ulm in Germany, and this case story is mentioned as an example of how the metronomic chemotherapy affects not only PSA but also gives visible reduction of the metastases.

Other studies confirm the effect of low dose metronomic trofosfamide on prostate cancer and for example lung cancer, and the late Dr. Nieper in Hannover always used 50 mg trofosfamide daily for his cancer patients, even though the working principle was not known at that time.

There is an additional advantage to using low dose trofosfamide. It has been shown that conventional high dose trofosfamide leads to a reactive stimulation of CEPS - the circulating precursors of endothelial cells (cells in the blood vessel wall) that promote angiogenesis (new formation of blood vessels) in the tumor, while low dose trofosfamide do the opposite: reduce the number of CEPS and thereby impairs angiogenesis and thus growth of the cancer.