# Bulletin: Europe's stellar decade in prostate cancer innovation

*by Robert Johnson, Alacrita LLP*

If, in 2001, you had hormone resistant metastatic prostate cancer, then your treatment options were severely limited. Nothing could extend your life and the focus was on providing you with symptomatic relief. The options comprised narcotic analgesics, radiotherapy to dominant sites of bone pain, treatment with bone seeking isotopes (strontium-89) and cytotoxic chemotherapy. Chemotherapy was only able to reduce PSA and relieve pain in some patients. Tolerability was a major concern; both patients and oncologists despaired. Prostate researchers were the poor relatives of their breast cancer colleagues - in 1997 NCI spending on prostate cancer was just $82m compared to $332m for breast. No new drugs had been approved for prostate cancer for 30 years.

Ten years later the urologic oncologist's toolbox has gained considerable weight, with five new drugs demonstrating substantial evidence of efficacy in Phase III trials. It is striking that 80% of these drugs were invented in Europe, despite a quadrupling of NCI spending on prostate cancer from 1997 to 2008.

**Drug:** Taxotere
**FDA approval:** October 2004
**Country of invention:** France

Breaking the therapeutic drought was docetaxel, approved by FDA in October 2004. The drug was already approved in breast, lung and gastric cancer and the pivotal trial in prostate cancer demonstrated a 2.4 month survival advantage. Oncologists celebrated, but observers questioned the risk/benefit ratio. Grade 3/4 side effects were common and advanced prostate cancer patients are often frail.

**Drug:** Provenge
**FDA approval:** April 2010
**Country of invention:** USA

After a billion dollars and a 10 year Phase III programme, Provenge was the first cancer immunotherapy to be approved by FDA. It was a landmark approval and may usher in a new era of low toxicity cancer therapeutics. It generated a survival benefit of 25.8 months vs. 21.7 months though uptake has been slow, with payors struggling to stomach the $93k price tag.

**Drug:** Jevtana
**FDA approval:** June 2010
**Country of invention:** France

Building on their taxane expertise, researchers at (what is now) Sanofi's Parisian labs developed Jevtana, a semisynthetic taxane that was selected due to its resistance to cancer's multi-drug resistance mechanisms (to which Taxotere is vulnerable). The drug was approved to treat Taxotere-resistant patients and provided patients with 15.1 months versus 12.7 of overall survival.

**Drug:** Zytiga
**FDA approval:** April 2011
**Country of invention:** England

Zytiga inhibits CYP17 which is required by the body to synthesise testosterone. By inhibiting this enzyme in all tissues in the body, Zytiga blocks testosterone production and slows prostate cancer growth. In Taxotere-resistant patients, this drug extended median survival to 14.8 months versus 11.2 months. It was discovered at ICR in London.

**Drug:** Alpharadin
**FDA approval:** Filing pending
**Country of invention:** Norway

In June 2011 the pivotal trial of Alpharadin was stopped early due to efficacy. In patients with bone pain, median overall survival was 14.0 vs. 11.2 months, with a remarkable safety profile. FDA has granted fast track status and filing is slated for mid-2012. The drug has a unique mechanism, emitting alpha particles to bone metastases. The technology was invented at the Norwegian Radium Hospital and the University of Oslo.