

EMERGING TAXANE THERAPIES

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In 1963 the National Cancer Institute began research on an extract from the Yew tree that had anticancer properties. In 1992 the first taxane, paclitaxel, was approved for use in women with metastatic, refractory ovarian cancer. Today, the taxanes are used for a wide variety of malignancies both in the adjuvant and therapeutic setting.

There are however, many challenges with traditional taxanes. The molecules require solvents to go into solution for administration and stability. Paclitaxel requires Cremophor EL and docitaxel requires Tween 80. These solvents have their own toxicity profiles including hypersensitivity reactions, myelosuppression, peripheral neuropathy and leaching of plasticizers. Also, the taxane can get trapped in the Cremophor micelle which does not allow drug to enter the tumor cell in therapeutic doses. Therefore, the ideal taxane would deliver drug selectively to the tumor cells without the additional toxicity of solvents which would allow for greater efficacy.

Currently, there are many formulations of taxanes in clinical trials. There is one novel approach that was approved in January 2005. Nab paclitaxel is paclitaxel that is bound to human albumin, thereby eliminating the need for solvents. There is greater tumor uptake of this formulation due to the small nano particles of albumin bound paclitaxel which capitalize on the leaking vasculature of tumors, transcytosis of albumin through endothelial walls due to increased GP 60 receptors and increased expression of SPARC albumin binding protein in certain cancers.

Nab-paclitaxel or Abraxane therapy is approved for the treatment of metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. The recommended dose is 260 mg/m² given intravenously over 30 minutes every three weeks and there are no recommended pre-medications. Research is ongoing to develop new agents that are efficacious and less toxic in the care of individuals with cancer. Clinical trials are underway for the use of nab taxanes in other tumor types.

