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Albumin-binding drugs as drug delivery systems in oncology

Albumin is playing an increasing role as a drug carrier in cancer therapy considering that numerous preclinical studies demonstrate an accumulation of albumin in experimental solid tumors. Principally, anticancer prodrugs can be covalently bound to exogenous or endogenous albumin, or antitumor agents are physically adsorbed to albumin forming nanoparticles as a galenic formulation. Clinically, the most advanced drug delivery system is an albumin-based nanoparticle with paclitaxel (Abraxane®) approved for the treatment of metastatic breast cancer, pancreatic cancer and NSCLC. An alternative to physically adsorbing drugs is to attach the latter covalently to albumin. Aldoxorubicin, an albumin-binding drug of doxorubicin with acid-sensitive properties, that has reached an advanced stage of clinical development with results from a registrational phase III trial against second-line soft-tissue sarcoma expected in Q2 2016 (www.cytrx.com). The underlying drug delivery strategy is a platform technology based on two features: (a) *in situ* binding of the prodrug to the cysteine-34 position of endogenous albumin after intravenous administration due to a thiol-reactive maleimide group in the molecule; (b) release of albumin-bound drug at the tumor site due to the incorporation of an acid-sensitive cleavable bond between the drug and the carrier. The acid-sensitive linker contains a hydrazone bond, and CytRx have developed a broad spectrum of linkers based on this release mechanism (LADRTM – linker activated drug release technology) that have resulted in promising albumin-binding drugs in the preclinical setting.

Biography

Felix Kratz is a medicinal chemist with more than 25 years of pertinent experience in the preclinical development of anticancer drugs, prodrugs and protein conjugation chemistry and profound knowledge of translational research from the laboratory to the clinic. He has successfully transferred aldoxorubicin, CytRx clinical lead compound, from bench to bedside that is based on an innovative drug delivery platform exploiting circulating albumin as a tumor-specific drug carrier. He has authored approximately 260 scientific publications, book articles and proceedings and is the inventor of over 20 patents and patent applications. As Vice President he heads the CytRx Drug Discovery Branch located in the Innovation Center Freiburg, Germany.

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