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Fusion molecules as a new concept to take chemotherapy to the next level

Thomas Mehrling

Mundipharma EDO GmbH, Switzerland

Past attempts to improve treatment efficacy, by inventing various combinations of cytotoxic agents, have provided disappointing results. Patients, mostly treated in large cooperative trials, experienced little benefit from intensification of dose and schedule but instead suffered from frequent and severe adverse reactions. Classical chemotherapy now finds itself at a crossroad. In some cancers, treatment is increasingly reliant on just targeted therapies; whereas in others the demand for a less toxic combination of chemotherapy and targeted therapies creates the need for different drugs or 'smarter' ways to deliver chemotherapy to the tumor. As demand drives innovation chemotherapy is about to evolve, more effectively targeting tumor cells while reducing damage to healthy tissues. Two important trends are emerging: The development of antibody-drug conjugates (ADCs) and the exploitation of synergies of targeted and cytotoxic therapy through fusion molecules. Fusion molecules combine an established chemotherapy principle with a synergistic targeted mode of action in one molecule. By exerting their dual action simultaneously, fusion molecules may overcome the difficulties of combining single agents with different pharmacokinetics and other pharmacological factors. One fusion molecule, currently in development, combines the strong alkylating activity of bendamustine with the histone-deacetylase (HDAC) inhibitor vorinostat. The synergies of HDAC-inhibition and DNA-damaging agents, such as alkylators, provided the rationale for the synthesis of the first-in-class fusion molecule bendamustine-vorinostat. It is anticipated that this fusion molecule may have strong activity in various hematological malignancies and solid tumors.

Biography

Thomas Mehrling, MD, PhD, is Chief Executive Officer of the 2013 founded Mundipharma EDO GmbH in Basel, Switzerland. He is a Board Certified Pharmacist/Pharmacologist and obtained his PhD in Pharmacological Science based on pre-clinical research in serotonin-receptor antagonists for the treatment of nausea and vomiting caused by chemotherapy. This work provided the pathway to the market for tropisetron (Navoban®). He also is a Board Certified Physician and holds a Medical Doctor degree of the University of Frankfurt. He specialized and worked for several years in cardiology, hematology/oncology and pediatric oncology.

thomas.mehrling@mundipharma-edo.com

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