CP201

CP201 is an orally available enantiomer of the alkyl-lysophospholipid (ALP) edelfosine. It is a synthetic etherlipid. The asset is owned by RDP Pharma AG, Romanshorn, Switzerland. CP201 is close to entering phase 1 in healthy male volunteers.

Racemic edelfosine, the parent compound of CP201, was used in more than 1,300 cancer patients in phase 1 and 2 studies conducted in the 1980s/1990s. It revealed encouraging signs of clinical activity in various cancers (e.g. lung cancer, brain cancer) and in patients with multiple sclerosis, whilst showing a favorable toxicity profile (mainly mild to moderate and reversible gastro-intestinal adverse events, e.g. nausea). Multiple long-term administrations of edelfosine over 2 years are documented.
Other compounds belonging to the class of ALPs were also intensively tested in clinical trials (e.g. perifosine and miltefosine) and even miltefosine got marketing approvals in USA and European countries for the treatment of the parasitic disease leishmaniasis under the trade name of Impavido®.
Edelfosine is the most potent of all anti-cancer ALPs and is the best characterized representative of this compound class. To date, more than 1,400 papers have been published on edelfosine, mainly dealing with its multifarious mode of action.

ALPs such as edelfosine and CP201 are predominantly incorporated in the cholesterol/sphingolipid-rich bilayer cell membrane domains, known as lipid rafts, of malignant or inflamed cells whilst sparing healthy cells. In addition, ALPs are inserted in the intracellular membranes of the endoplasmatic reticulum (ER) and mitochondria, thereby inducing biophysical alterations in their organization. Lipid rafts play a critical role in membrane domain organization. Lipid rafts serve as sorting platforms and hubs for signal transduction proteins. Upon insertion, ALPs disrupt lipid rafts and normal signal transduction by up- or downregulation or modification of membrane-based receptors and ion channels, affecting growth regulatory cascades and signals that require a particular lipid domain used as scaffold for assembly and/or function. Among other things, this leads to apoptosis of the malignant cell, and expression of signaling molecules (e.g. cytokines, sexual hormones) and their membrane-based receptors can be modified. Prominent examples are the interference with the CD95 (FAS) and the PI3K-Akt pathways.

In addition, ALPs were reported to have direct effects on the transcription of genes known to promote carcinogenesis and/or inflammation.

A non-clinical toxicology package compliant with current regulatory standards for CP201 was compiled. CP201 is ready for phase 1 in healthy volunteers which is planned to start in the near future.

Edelfosine and CP201 showed strong anticancer activity in numerous preclinical in vitro and in vivo models in both hematological and solid tumors. ALPs strongly enhance the cytotoxic effect of radiation in preclinical models making these compounds attractive candidates as clinical radiosensitizers. It was also demonstrated that they can prevent or reduce the formation of metastases. Moreover, edelfosine revealed anti-inflammatory activity in in vitro and in vivo models of autoimmune diseases, including multiple sclerosis (MS), arthritis and colitis. Among other things, in these models the drug demonstrated a beneficial impact on critical effectors and suppressors of the immune system.

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The available initial data include encouraging in vitro single-agent activity against HIV-1, bovine herpes virus, human papilloma virus, Chikungunya virus, hepatitis B virus, MERS virus, and corona virus HCoV-229E.

Based on the initial evidence of anti-viral activity of ALPs including edelfosine and CP201 and numerous considerations related to their mode of action suggesting benefits of these drugs in Covid-19, we propose that CP201, being under development as anti-cancer agent, should be investigated as anti-viral drug, too. It should undergo intensive in vitro and in vivo testing to elucidate its full potential as anti-viral medication, both as single agent and in combination with other promising drugs, including protease inhibitors (e.g. lopinavir/ritonavir, camostat mesylate) or RNA polymerase inhibitors (e.g. remesdivir, favipiravir). The combination with other drugs is considered being of particular interest, since CP201 represents a novel mode of action which may result in synergistic anti-viral activity and since its parent drug edelfosine was tolerated well in a large number of cancer patients. Most of the a.m. compounds are associated with significant adverse events. If these non-clinical experiments are successful, clinical studies with CP201 could be initiated relatively fast because appropriate clinical trial material and the regulatory package of toxicity studies is available.