CriPec® nanomedicines: academic to industry and preclinical to clinical translation

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Introduction
Cristal Therapeutics is a clinical stage pharmaceutical company developing next generation nanomedicines based on its proprietary CriPec® platform to treat various diseases, including cancer. CriPec® is perfectly suited for the rational design of (targeted) nanomedicines with superior efficacy and safety profiles. The most advanced product in development is CPC634 (CriPec® docetaxel) for treatment of solid tumours, while other CriPec® products are in preclinical development.

Methods
CriPec® is a pioneering approach to transform a broad range of therapeutic compounds into rationally designed nanomedicines to assure optimal treatment of various diseases.

Results
CriPec® has been successfully combined with small molecules, peptides or oligonucleotides, thereby generating monodisperse CriPec® nanoparticles with tuneable sizes between 30 and 100 nm with high drug entrapment efficiencies and predetermined drug release kinetics. The surface can be modified by targeting ligands. CriPec® products are customisable and biocompatible, with a robust manufacturability at clinical scale.

CPC634 is a 65 nm sized nanoparticle entrapping docetaxel designed which improves tumour accumulation and tolerability compared to conventional docetaxel by taking advantage of the presumed enhanced permeability and retention (EPR) effect. In preclinical models, an enhanced therapeutic index is observed due to an improved pharmacokinetic profile, increased tumour uptake and superior tolerability.

The first-in-human study demonstrated a favourable plasma PK profile of CPC634. Safety evaluation specifically demonstrated less neutropenia. One partial response and sixteen cases of stable disease (RECIST 1.1) were confirmed. The RP2D was set at 60 mg/m2 with dexamethasone premedication. In a randomized cross-over study, tumour biopsies were taken after intravenous administration of CPC634 and conventional docetaxel (or vice versa). CPC634 generated higher intratumoural total docetaxel (323%, p < 0.001) and comparable released docetaxel levels relative to conventional docetaxel.

Next, CPC634 was labelled with zirconium-89 to facilitate non-invasive PET imaging of its biological fate. Tumour retention showed intra- and interpatient heterogeneity with the highest intensity at 96h post injection and with a mean %ID/kg of 3.43 [1.14-9.32], confirming the EPR effect in patients.
Conclusion
The clinical results of CPC634 illustrate the improved safety profile and increased tumour uptake. A phase II efficacy study of CPC634 in patients with platinum resistant ovarian cancer (NCT03742713) is currently ongoing.

The innovative CriPec® platform allows for the rational design of nanomedicines of a variety of drug molecules with an anticipated superior therapeutic performance.

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