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Nano-amorphous abiraterone acetate formulation with improved bioavailability and eliminated food effect

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Abiraterone Acetate (AA) is a poorly water soluble drug molecule indicated for patients with metastatic castration resistant prostate cancer. It is a prodrug, which is converted to abiraterone *in vivo*. The oral dose is high; 1,000 mg which is administered once daily as 4x250 mg Zytiga® tablets. The absolute bioavailability of abiraterone following the administration of Zytiga® is estimated to be below 10% in the fasted state with a 10-fold (AUC) and up to a 17-fold (C_{max}) increase following a high-fat meal. We have developed a nano-amorphous AA formulation prepared by controlled precipitation followed by lyophilization. The formulation exhibited higher apparent solubility and passive permeability when compared to either the crystalline AA or Zytiga. In beagle dog studies, this resulted in a >10-fold increase in bioavailability in the fasted state when compared to the marketed drug and the elimination of the food effect. After the preclinical investigation a first-in-human clinical trial was conducted. Based on the analysis of pharmacokinetic data~250 mg oral dose of the nano-amorphous formulation is expected to result in the same exposure as 1,000 mg Zytiga® in the fasted state. The substantial positive food effect seen for Zytiga® was eliminated. This might allow the reduction of the dose and could eliminate the requirement of taking the drug on an empty stomach. Also, the novel formulation is expected to exhibit smaller variability when compared to Zytiga®. In conclusion we have developed a novel nano-amorphous AA formulation that significantly outperformed the marketed product in *in vitro* and *in vivo* tests. Ultimately, the formulation might allow a 75% dose reduction and negate the restriction of a food label.

Biography

Tamás Jordán holds a MSc Degree in Pharmaceutical Engineering and is currently writing his PhD thesis. He has been working at NanGenex Inc for 5 years, gaining experience in the formulation of poorly water soluble active ingredients. He is interested in the physicochemical background of nanoformulation and bioavailability increasing technologies.

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