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Drug Delivery and Targeting: Poster Presentations - Proffered Abstracts

Abstract #5622

Comparison of physicochemical characteristics and stability of three novel formulations of paclitaxel: Abraxane, Nanoxel, and Genexol PM

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Background: Abraxane (Abraxis BioScience, Inc., Los Angeles, CA, approved in USA and Canada), Nanoxel (Dabur Pharma, H.P., India, approved in India), and Genexol PM (Samyang Pharmaceuticals, Seoul, Korea, approved in Korea) are 3 commercially approved, novel formulations of paclitaxel. Abraxane consists of albumin-bound injectable nanoparticles of paclitaxel, while Genexol and Nanoxel (utilizing cosolvents) are polymeric-micelle formulations. Abraxane and Genexol are lyophilized products approved for 25°C ± 2°C storage, while Nanoxel is a liquid formulation approved for 2-8°C storage. This study investigated the physicochemical characteristics and short-term stability of the 3 products under recommended clinical use conditions and under accelerated conditions.

Methods: The drugs were reconstituted and prepared per the instructions provided in the respective package inserts. Abraxane and Genexol were reconstituted using the recommended saline diluent, while Nanoxel was mixed and diluted in 10% dextrose. Each drug was reconstituted to 0.7 mg/mL and 5 mg/mL. Physical stability was monitored both visually and microscopically; particle size was measured and monitored over time at room temperature (RT, measured to be 23°C) and 40°C using photon correlation spectroscopy (PCS) (Zetasizer 3000, Malvern, UK). Chemical purity was measured by reduced reversed-phase HPLC (Shimadzu Scientific Instruments, MD).

Results: Following reconstitution, Abraxane was determined to be stable both physically and chemically

at RT and 40°C over 24 hrs, with no evidence of nanoparticle size growth at either 0.7 mg/mL or 5 mg/mL. While reconstituted Genexol was stable at RT over 24 hrs, micelle instability resulting in precipitation of paclitaxel in the form of large needle-like crystals for both 0.7 mg/mL and 5 mg/mL formulations was seen between 2 to 4 hrs at 40°C. These observations were confirmed using orthogonal techniques, visual assessment from photomicrographs, and PCS particle size measurement. For Nanoxel at 0.7 mg/mL, a minor, but consistent, increase in particle size was observed at RT over 24 hrs. However, significant aggregation, particle-size growth, and crystallization were seen within 4 hrs at 40° C. HPLC data comparing pre- and post-filtration confirmed that the crystal formation for both Nanoxel and Genexol resulted from paclitaxel precipitation and aggregation. In addition, analytical results showed that Nanoxel had slightly lower paclitaxel purity as compared to either Abraxane or Genexol. **Conclusions:** Nanoparticle albumin-bound paclitaxel, Abraxane, showed excellent physicochemical stability as compared to the micellar formulations, Nanoxel and Genexol. Particle size growth and crystal formation were readily apparent in Nanoxel and Genexol, especially in the short term under accelerated conditions.