

**Point of Care PK Quantitation Device for Pharmacokinetic Guided Dosing of Paclitaxel as a Companion Diagnostic Device.**

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**Study Purpose:** Paclitaxel chemotherapy is the cornerstone of most anti-cancer regimens due to its potent cytotoxic activity against tumor cells. The variability of paclitaxel dosing can be as high as 10X across patients, therefore, dosing at a fixed dose even when adjusted for body weight will leave a significant portion of the patients underdosed – getting no benefit from the treatment- and another portion overdosed- getting undue toxicity. Therefore, paclitaxel therapy would benefit from Therapeutic Drug Monitoring (TDM) guided dosing. A full pharmacokinetic (PK) study is required to determine whether patients are getting the appropriate and efficient dosage. However, at the current state, a full PK requires not only multiple high-volume blood draws and extended stays in the hospital but also testing method by LC-MS/MS, which are both time-consuming and expensive. Here we describe the development of **Pac Flow™ system**, a Point of Care TDM device for PK guided dosing of paclitaxel as a companion diagnostic device.

**Methods:** The 8A10 and 3C6 mAbs (mAbs against paclitaxel) were purified from the antibody-rich harvested medium using MabSelect (GE Healthcare, Pittsburgh, PA). Commercial antibodies (29B7B3C and 69E4A8E; Santa Cruz Biotechnology Inc.) were also tested. To synthesize BSA-paclitaxel, we used the method of J-G Leu et al. as described in Cancer Res. (1993) 53:1388-1391. BSA-paclitaxel and mAbs were labeled with colloidal gold.

**Results:** Rapid test for paclitaxel based on the lateral flow system was developed. Of the mAbs tested, only 8A10 and 3C6 were useful. The assay requires the configuration of immobilizing BSA-paclitaxel onto the membrane followed by flowing the colloidal-gold labeled anti-paclitaxel mAb through in presence of test analyte. This resulted in a competitive assay for paclitaxel where the signal decreased as the concentration of paclitaxel analyte in blood increased. Coupled with the current lateral reader technology – especially the one developed by Qiagen- a rapid quantitative assay for paclitaxel is possible. The assay demonstrated good linearity and range suitable for paclitaxel TDM. The application of this assay in a preclinical pharmacokinetic study yield reasonably comparable result to LC/MS method.

**Conclusions:** **Pac Flow™ system**, a quantitative lateral flow platform coupled to a reader was developed to easily detect the paclitaxel concentrations in small amount of blood samples. Individual pharmacokinetic profiles can be obtained and used to determine the suitable treatments. In addition, the lateral flow PK quantitative assay can be deployed at point-of care (in home, doctor's office or central lab).