Integration of the Clin-ToF into the VeriStrat® clinical testing workflow to generate serum protein profiles for prognosis and therapeutic guidance in NSCLC

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**Summary**
- The VeriStrat® test is a serum proteomic assay that is both prognostic and predictive for therapeutic benefit in NSCLC.\(^1\)\(^-\)\(^4\)
- Until recent clearances for microbiology applications, clinical assays in mass spectrometry have been run exclusively on platforms designed for use in research laboratories.
- In this study, Bioyong’s Chinese FDA (CFDA)-cleared MALDI-TOF device was integrated into the VeriStrat® assay workflow.
- A tiered qualification approach was taken by evaluating multiple sample sets. Key criteria evaluated were:
  - Manufacturer and Initial Performance Verification
  - Tuning and Verification with 67-sample set
  - Validation with independent 20-sample set

**Background**

The VeriStrat® Test Workflow

**Classification Scheme**
- Standard patient serum MALDI-TOF mass spectrum
- k-NN (k-nearest neighborhood) algorithm compares test spectra to indexed library of historical spectra to assign classification label
- MS Pre-processing:
  - Background subtraction
  - Alignment: PE normalization
- k-NN Classifier (6 peak areas)

**Clinical Performance**
- Prognostic for overall survival (OS) in first-line NSCLC patients treated with platinum doublet chemotherapy.\(^3\)
- Predictive of differential therapeutic benefit in second-line NSCLC comparing chemotherapy to EGFR tyrosine kinase inhibitors (e.g., erlotinib).\(^5\)

**Tuning, Verification and Validation**

67-Sample Verification

**Tiered Qualification Approach**
- New Instrument
- Major Maintenance
- Routine Maintenance
- Daily Qualification

**Performance Verification**
- Manufacturer Performance Verification
  - Resolution \(>5000\) for ACTH fragment (18-39), \(m/z = 2465.7\)
  - Sensitivity at \(S/N > 5\) of 500 fmol bovine serum albumin, \(m/z 66430\)

**Performance Verification with QC Serum Sample**

**References**

**Conclusions and Future Work**
- Clin-ToF generates spectra of sufficient quality for the VeriStrat® assay.
- The Clin-ToF has been validated for use in the VeriStrat® test workflow.
- Future work:
  - Additional development and analytical studies
  - Establish readiness for clinical trials to develop a version of the VeriStrat® test for the Chinese NSCLC management pathway