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617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Establishment of a PML-RARa Copy Number Estimator for Prototype Xpert ® PML-RARa Assay

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Statement of the Problem: Acute Promyelocytic Leukemia (APL) represents 10-15% of Acute Myeloid Leukemia (AML). The PML-RARa fusion transcript is expressed in more than 95% of APL patients. Three PML-RARa isoforms (bcr1, bcr2, and bcr3) are identified in 90-95% of PML-RARa positive cases. Prototype Xpert ® PML-RARa, an automated cartridge-based assay for measuring PML-RARa fusion transcript levels (bcr1, bcr2, and bcr3), is standardized to quantify the amount of PML-RARA relative to ABL1 control gene based on delta Ct in peripheral blood. Since PML-RARa level is crucial for diagnosis and ongoing therapeutic monitoring in APL, it can be useful to obtain the PML-RARa copy number (CN). The aim of this work is to develop PML-RARa CN estimator and to compare %PML-RARa/ABL1 reporting between delta Ct-based and CN-based methods. **Methodology & Theoretical Orientation:** Four levels of PML-RARa (bcr1, bcr2, and bcr3) and ABL1 IVT-RNA panels as well as two lots of prototype Xpert ® PML-RARa assay were used to generate standard curves for CN and %CN reporting. The samples with spiked-in bcr1 IVT-RNA and APL clinical samples containing PML-RARa fusion transcript were examined to evaluate the CN and %CN between two lots of the prototype Xpert ® PML-RARa assay and to compare the delta Ct-based and CN-based methods for reporting %PML-RARa/ABL1. **Findings:** Linearity was demonstrated in Ct vs CN input for PML-RARa ($R^2 > 0.98$) and ABL1 ($R^2 > 0.97$). Less than 2-fold difference was exhibited for CN and %CN across two different lots. Less than 2-fold difference was observed in %PML-RARa/ABL1 reporting between delta Ct-based and CN-based approaches. **Conclusion & Significance:** A PML-RARa copy number estimator for prototype Xpert® PML-RARa assay was established, which will provide helpful information for diagnosis and prognosis of APL. (Product in development. Not for use in diagnostic procedures. Not reviewed by any regulatory body.)

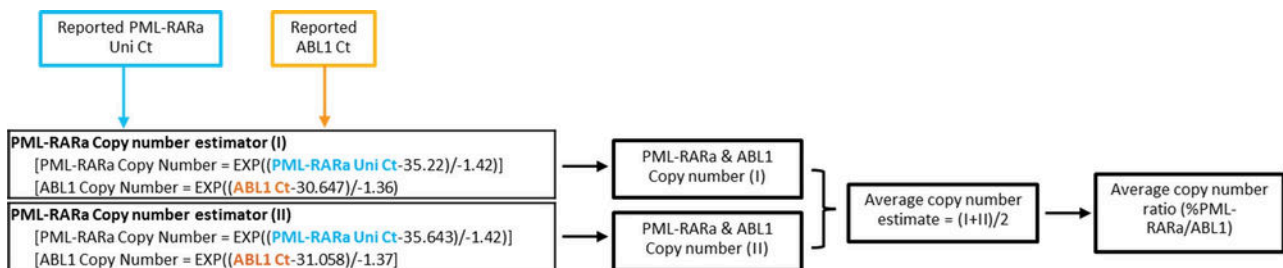**Disclosures Yuan:** *Cepheid:* Current Employment.

Figure 1: Two sets of PML-RARa copy number estimator for prototype Xpert® PML-RARa assay, which will provide diagnostic and prognostic values for APL. Enter reported PML-RARa Uni Ct and ABL1 Ct into the formulas (I) and (II) to calculate the copy number. Average copy number of PML-RARa and ABL1 from both formulas will be utilized in obtaining averaged %PML-RARa/ABL1.

Figure 1