Session: 245. Molecular & Sequence Based Diagnostics Saturday, October 6, 2018: 12:30 PM

**Background.** Standard microbiological testing (MT) fails to identify a pathogen in most chemotherapy recipients with febrile neutropenia (FN), who therefore receive prolonged empiric courses of broad-spectrum antimicrobials (AM). We evaluated the ability of the Karius next-generation sequencing plasma test (KT) to identify infectious etiologies of FN and its impact on AM management.

**Methods.** This prospective, observational study enrolled 57 patients with ≤500 neutrophils/mm^3. Samples were collected within 24 hours of fever onset (TO) and every 2–3 days. Cell-free plasma DNA was prepared and sequenced in a CLIA/CAP laboratory; human reads excluded, and remaining sequences aligned to curated pathogens and parasites. Positive agreement (PA) was defined as KT identification of ≥1 isolate also seen by blood culture (BC). Discordant results were adjudicated by 3 infectious disease specialists as: Definite: KT isolated ≥1 organism also seen by MT; Probable: KT result was a likely cause of FN compatible with clinical diagnosis; Possible: KT result was consistent with an infection but not a common cause of FN.

**Results.** 56 results (55 subjects) with valid KT and BC results were analyzed. Compared with BC, KT had a PA of 90% (9/10) and negative agreement of 31% (14/45). KT identified ≥1 organism in 61% (25/41) of the cases. Definite (13), Probable (24) and Possible (4) cases were classified as True Positives. Using clinical adjudication, KT had a sensitivity of 98% (41/42) and specificity of 100% (14/14). The committee would have changed AM therapy 68% (27/40) of the time, had the KT results been available in real-time (∼T2–10h). In 8/19 cases (42%) vancomycin was stopped; in 6/27 cases (22%) and in 5/27 cases (19%), anaerobic coverage or antivirals would have been added earlier. Serial analysis of a *Pneumocystis jirovecii* infection indicated that earlier diagnosis and treatment may have prevented morbidity and eventual ICU transfer.

**Conclusion.** The absence of infectious etiology in FN often leads to broad AM therapy or delay of targeted treatment. Given its sensitivity and ability to detect a breadth of pathogens, the KT can provide useful data for diagnosis and management of FN and may allow for optimization of AM therapy.

**Disclosures.** H. Seng, Karius, Inc.: Employee, Salary. R. Aquino, Karius, Inc.: Employee, Salary. D. Boulton, Karius, Inc.: Employee, Salary. D. Hong, Karius, Inc.: Employee, Salary. T. Blaukamp, Karius, Inc.: Board Member, Employee and Shareholder. S. Kertesz, Karius, Inc.: Board Member, Employee and Shareholder. L. Blair, Karius, Inc.: Employee, Salary. S. Zompi, Karius, Inc.: Employee, Salary.