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Performance Characteristics of Cell Free DNA

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DNA is constantly released from injured cells into the peripheral blood circulation. When an allograft is present in the human body, the injured cells of the allograft also release DNA into the host recipient's circulation, known as donor-derived cellfreeDNA (dd-cfDNA). This dd-cfDNA can be detected and measured separately from host-derived cfDNA, even without knowledge of the donor's DNA alleles. Typically the dd-cfDNA represents a very small portion of the circulating total DNA, 0.2% or less. In allograft injury states such as acute rejection, the dd-cfDNA percentage may rise. In the DART study, Bloom et al demonstrated in kidney transplant recipients that a rise above 1% was strongly associated to acute rejection of both types, more strongly to antibody-mediated rejection. Subsequent longitudinal work in the ADMIRAL study by Bu et al showed that elevations in dd-cfDNA preceded the development of donor-specific antibodies by about 90 days. More than 2 dd-cfDNA results > 0.5% predicted a 25% decline in the estimated glomerular filtration rate over the next 3 years. Other studies have since demonstrated the utility of dd-cfDNA in other populations, such as non-kidney solid organs (heart, liver, lung), in pediatric populations or in other injury conditions such as BK virus replication. Some studies have evaluated the value of absolute copy number rather than the percentage of dd-cfDNA. More recent studies have assessed the accuracy of combined peripheral blood dd-cfDNA and gene expression panels to detect overt or subclinical acute rejection. The speaker will present data from these various studies.

Keywords: -