Interim Safety Analysis of Cancer Immunotherapy Trials Network – 12 (CITN-12): A Phase 1 Study of Pembrolizumab in Patients with HIV and Cancer

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Background:
Anti-PD-1 and anti-PD-L1 antibodies are becoming mainstays of cancer therapy. The safety of pembrolizumab, an anti-PD-1 humanized monoclonal antibody, is being evaluated in patients with HIV and cancer. The effect of anti-PD-1 therapy on HIV reservoirs is unknown.

Methods:
CITN-12 is a multicenter study of pembrolizumab in patients with HIV and advanced cancers. Three CD4 defined cohorts (C) are accruing; C1: 100-199, C2: 200-350, and C3: >350 cells/uL. Eligibility: >4 weeks antiretroviral therapy (ART), HIV viral load <200 copies/mL. Treatment: pembrolizumab 200mg intravenously every 3 weeks for up to 2 years. Primary objective: assess safety and tolerability by summarizing CTCAEv4 graded adverse events (AEs) and evaluating HIV viral load (VL) and CD4 counts. Immune mediated AEs are managed using standard guidelines. We performed an interim analysis of treatment emergent adverse events at least possibly related to pembrolizumab (rTEAEs), serious AEs, and CD4 counts on therapy. Plasma HIV VL was measured by an HIV gag single copy assay (SCA).

Results:
17 patients were accrued starting April 2016 and followed through May 2017. Characteristics: 1 woman, 16 men; median age 56 years (range 43-77); Cancers: lymphoma (3), Kaposi sarcoma (1), anal (5), tonsil (1), lung (2), bladder (1), hepatocellular (1), pancreatic (1), cholangiocarcinoma (1). Safety was observed over 100 total cycles, median 4 (range 1-20). 82 rTEAEs were observed and comparable between cohorts. 93% were grade 1-2. Ten primary serious AEs were observed, 2 possibly attributable to pembrolizumab, both in the setting of progressive malignancy. Immune mediated AEs: subclinical hypothyroidism 6 (35%), pneumonitis (2) and liver test elevations (2). Median CD4 increased over time, changes did not reach statistical significance. HIV remained suppressed on ART in all patients. In a subset of 14 patients, baseline median HIV VL by SCA was 0.8 copies/mL (range: <0.3-9.9); no significant increases between noted.

Conclusions:
Pembrolizumab has an acceptable safety profile to date in patients with cancer and suppressed HIV on CITN-12, with no evidence of increased HIV VL over 6 weeks of therapy. Anti-PD1 therapy is appropriate for FDA approved indications in HIV-infected patients. Studies evaluating HIV latency reversal and HIV-specific immunity are underway.