Pill Burden & Treatment Length Reduce Adherence To IFN-Free Hepatitis C Therapy in an Urban Cohort

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Background: Potent orally directly acting antiviral (DAA) HCV therapy with low pill burdens and short therapeutic courses are promising replacements for interferon and ribavirin based regimens. The impact of these improvements on patient adherence and virologic outcomes has not been described.

Methodology: Sixty HCV infected, treatment naïve, genotype 1 patients were enrolled into 3 arms of a phase 2 clinical trial and received: sofosbuvir + ledipasvir (400/90mg one pill once daily in a fixed dose combination (FDC)) for 12 weeks, FDC + GS-9451 (80mg/day), two pills, once daily for 6 weeks, or FDC + GS-9669 (500mg/day), three pills, once daily for 6 weeks. Serial measurements of virologic correlates (HCV RNA; deep sequencing of viral mutations) were performed. Adherence was measured using three tools: MEMS caps (MEMS), pill counts (PC) and patient report (PR). Demographics and modified ACTG questionnaires were used to determine risk factors for non-adherence. Adherence tools, treatment arms, and risk factors were compared using Pearson correlations, T-tests/ANOVA and Chi-squared tests respectively.

Results: Patients enrolled were African American (88%), male (72%) with ≤ 12th grade education (61%). Psychiatric disease (43%) and recent history of drug/ETOH abuse (37.5%) were common.

Adherence to DAA regimens declined with increasing pill burden (99.3 ± 1.6% vs. 97.2 ± 3.6% vs. 94.8 ± 7.4%, one, two & three pills/day respectively, p=0.02 (Fig 1A)). Adherence to therapy declined significantly during the 12-week treatment course (98.1 ± 0.9% vs. 95.0 ± 1.2% weeks 0-4 vs. weeks 8-12, p=0.04 (Fig1B).) Missed doses by MEMS correlated with PC (R2=0.24, p<0.0002), but neither with PR (p=0.14 & p=0.84 respectively). Three patients missed ≥2 consecutive doses. Adherence was similar in patients with and without early viral suppression (<LLOQ at week 4) and time to viral suppression similar between adherent and non-adherent (defined as 0.05). Risk factors for non-adherence were feeling inconvenienced (p=0.03) and children living at home (p=0.01). Common reasons for non-adherence were feeling that drugs were working (39%), forgetting (35%) and absence from home (32%).

Conclusions: Adherence to short courses of DAA therapy with 1-3 pills once a day was excellent in an urban population with multiple risk factors for non-adherence. Increased pill burden and duration of treatment decreased adherence. Continued education regarding adherence despite on-therapy viral load decline may improve outcomes.