OBJECTIVES: The introduction of pegylated interferons has led to improved treatment of hepatitis C virus (HCV) over the past 4 years. These agents have shown higher rates of sustained virological response compared to non-pegylated interferons. Although efficacy has been shown, the safety of these agents must be better characterized. The purpose of this phase of the study is to evaluate the safety profile of HCV therapy in Veterans Administration (VA) patients. Specifically, to evaluate and compare the rates of hemolytic anemia, neutropenia, thrombocytopenia and new onset major depression following initiation of (1) pegylated interferon alfa 2A, (2) pegylated interferon alfa 2A/ribavirin, (3) pegylated interferon alfa 2B or (4) pegylated interferon alfa 2B/ribavirin. The secondary objective is to compare discontinuation rates of the four therapies.

METHODOLOGY: A new-user (inception) cohorts study was conducted among VA patients initiating HCV therapy with pegylated interferons, with or without ribavirin, from 10/02-9/03. Data were obtained from national VA prescription and patient care (inpatient and outpatient) databases. Patients with at least 1 diagnostic code for HCV (ICD-9-CM 70.4,70.5,V26.2) and a VA prescription for one of the four HCV medications were studied. Patients with incident hemolytic anemia, neutropenia, thrombocytopenia, and depression following initiation of HCV therapy were identified using ICD-9-CM codes from inpatient and outpatient care, after excluding those with codes for the condition in the preceding 2 year period. The analysis was restricted to patients with a first prescription following a period of at least 1 year in which they did not receive the HCV therapy. The incidence rates within 180 days from first use of HCV therapy and discontinuation rates were estimated and differences among the groups are tested by chi-square test, analysis also evaluated time to event using Cox proportional Hazard models with covariable adjustments (age, gender, race).

RESULTS: Rates of new events expressed as % event within 180 days after the first use of Hep C medication are for medications (1) - (4) for hemolytic anemia - 0%, 1.8%, 0.4%, 0.9%, respectively; for thrombocytopenia - 1.7%, 3.1%, 1.7%, 1.4%, respectively; for neutropenia - 0%, 3.6%, 0.4%, 3.1 %, respectively; for major depression - 1.8%, 16.2%, 12.4%, 17.2%, respectively. Discontinuation rates for the 4 medications are 13.3%, 12.1%, 30.6% and 21.5%, respectively. Adjustments using hazard rates of peg alpha 2A/ribavirin and peg alpha 2b/ribavirin (reference group) are 3.0 (hemolytic anemia), 2.6 (thrombocytopenia), 1.5 (neutropenia) (p<0.01).

Conclusions: Increased rates of hemolytic anemia, neutropenia and thrombocytopenia are shown for pegylated alpha 2A when compared with alpha 2B, with ribavirin.

Impact Statement: Results have potential implications for future therapeutic treatment of Hepatitis C in the VA.