

PROVE3 Study Finds Benefit of Sustained Virologic Response With Telaprevir-based Regimen in Hepatitis C Genotype 1-infected Patients Who Failed Prior Treatment

PROVE3 is a randomized phase II study assessing the efficacy and safety of telaprevir (VX-950, Vertex/Johnson & Johnson) plus peginterferon alfa-2a (P; Pegasys, Genentech) with or without ribavirin (R) in hepatitis C virus (HCV) genotype 1 patients who failed previous PR treatment. Patients were randomized to receive 1 of 4 protocols: telaprevir/PR for 24 weeks followed by PR for 24 weeks; telaprevir/P for 24 weeks followed by PR for 24 weeks; telaprevir/P for 24 weeks or placebo/PR for 24 weeks followed by PR for 24 weeks; or PR for 48 weeks. Overall, the sustained virologic response (SVR) rates in groups receiving telaprevir treatment were significantly higher than in those not receiving it. All patients who completed a telaprevir regimen and achieved SVR maintained virologic response 48 weeks after the end of treatment, except for 1 patient who was lost to follow-up. The safety profile in this population was similar to that observed in treatment-naive patients.

CD44 Polymorphisms Aid in Determining Risk of Recurrence in Gastric Cancer

According to researchers who analyzed blood and tissue samples from 137 patients, polymorphisms of the CD44 gene could help detect gastric cancer patients who have an increased risk of tumor relapse. Dr. Thomas Winder, who presented these findings at the American Society of Clinical Oncology Gastrointestinal (ASCO GI) Cancers Symposium, analyzed blood or formalin-fixed, paraffin-embedded tissue samples from patients with local stage II and III gastric cancer. Over a median of 3.3 years, tumor recurrence was observed in 45% of patients; the 3-year probability of recurrence was 0.52. In a univariate analysis, median time to recurrence for patients with the G allele (GG; AG) at the CD44 +4883G>A gene locus was 2.1 years and 7 years for patients without the G allele ($P=.022$). Overall survival (OS) for patients with and without the G allele was 4.1 years and 7 years, respectively ($P=.079$). For patients with the A allele (AA; AG) at the CD44 +779G>A gene locus, median time to recurrence was 2.2 years compared to 7 years in those without the A allele; OS in patients with and without the A allele was

3.8 years and 7.3 years, respectively ($P=.018$). In patients with at least 1 favorable allele, the median time to recurrence was 7 years compared to 1.7 years in those with no favorable alleles. Median OS was 7.3 years for patients with at least 1 favorable allele, and 3.6 years for those with no favorable alleles. The findings demonstrated that patients with either of the 2 alleles relapsed almost 5 years earlier than patients without these alleles.

Mitotic Index, Tumor Size, and Small Bowel Location Are Predictors of Relapse in Gastrointestinal Stromal Tumor

A retrospective multivariate analysis of data from a phase III, double-blind, placebo-controlled study of 700 patients with localized, primary gastrointestinal stromal tumor (GIST) found that high mitotic rate, tumor size, and small bowel location were predictors of relapse and thus should be examined before choosing appropriate therapy. These prognostic factors were discussed by Dr. Martin Blackstein at the 2010 ASCO GI. The study enrolled patients with KIT-positive primary GIST and randomized them to either adjuvant imatinib ($n=359$) or placebo ($n=354$) for 1 year. Both arms were similar at baseline. Mitotic scoring was performed retrospectively in tumors from 620 patients. The researchers used the Miettinen classification system to classify patients as being at low, medium, or high risk for relapse. In the 270 low-risk patients, relapse rates were similar between imatinib and placebo. In the 148 moderate-risk patients, the relapse rates showed a trend, albeit non-significant, favoring imatinib (14% with placebo vs 5% with imatinib; hazard ratio, 3.183; $P=.0509$). However, in the 201 high-risk patients, there was a major benefit for patients receiving imatinib (47% with placebo vs 19% with imatinib; hazard ratio, 3.108; $P<.0001$).

Decrease in Plasma Levels of Epidermal Growth Factor Seen With Minimally Invasive Colorectal Resection

In the March 31 issue of *Surgical Endoscopy*, Dr. Michael J. Grieco and colleagues presented a study conducted to evaluate the effect of minimally invasive colorectal resection (MICR) on postoperative plasma epidermal growth factor (EGF) levels in colorectal cancer (CRC) and benign disease settings and to determine

whether preoperative (preop) EGF levels are altered in cancer patients. Blood samples were obtained preop and postoperatively (postop; days 1 and 3) from patients with benign pathology (n=40) and patients with CRC (n=48); in some patients, samples were taken between postop day 7 and 60 and were grouped into 7-day blocks and analyzed as single time points. EGF levels were determined by enzyme-linked immunosorbent assay. The cancer and benign groups were comparable except for age. Study findings revealed that the mean preop plasma EGF level was significantly higher in the CRC group compared to the benign group (122.9±75.9 pg/mL vs 85.3±38.5 pg/mL; $P=.015$). In the CRC group, EGF levels were significantly reduced on postop day 1 and 3 and for the postop day 31–55 time point (mean EGF level, 63.1±42.2 pg/mL). In the benign group, the postop day 3 and day 7–14 EGF levels were significantly lower compared to the preop levels. Researchers concluded that the plasma EGF levels are significantly higher in cancer patients and that MICR corresponds with significant decreases in EGF levels postop in CRC and benign settings. In the CRC group—but not the benign group—EGF levels remained low in the second postop month. A larger study is needed to corroborate the findings of this study.

1-g Mesalamine Suppository Once Daily Is As Efficacious As a 500-mg Suppository Thrice-Daily in Ulcerative Proctitis

In a single-blinded, randomized, multicenter, comparative, phase III study, published ahead of print in *Inflammatory Bowel Diseases*, once-daily administration of a 1-g mesalamine suppository was compared to thrice-daily administration of a 0.5-g mesalamine suppository. Patients who had mild to moderately active ulcerative proctitis inserted either a 1-g suppository at bedtime or a 0.5-g suppository three times per day over a 6-week period. The primary endpoint was rate of remission. A total of 354 patients were included in the safety and per-protocol analysis. Remission was observed in 87.9% of patients receiving the once-daily 1-g suppository and 90.7% of patients receiving the thrice-daily 0.5-g suppository. The primary objective, which was to show noninferiority in once-daily administration, was met. Patient preference was once-daily administration of the suppository. Study findings demonstrated that once-daily administration of a 1-g mesalamine suppository was safe, effective, and more convenient than the standard of treatment—thrice-daily administration of 0.5 g of a mesalamine suppository—in patients with ulcerative proctitis.