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Velafermin (CG53135-05 or recombinant human fibroblast growth factor-20) is under investigation for the prevention of oral mucositis (OM). OM is a common side effect in patients (pts) receiving high-dose chemotherapy (HDCT) with or without total body irradiation (TBI) as conditioning regimen for AHSCT. Preclinical studies have demonstrated that velafermin promotes epithelial and mesenchymal cell proliferation in vitro and that a single dose of velafermin had activities in reducing the severity and duration of OM as effective as multiple doses. Previous clinical data suggested that velafermin could be safely given at doses up to 0.2 mg/kg. The objectives of this phase II trial were to evaluate the safety and efficacy of velafermin in preventing severe OM from approximately 200 pts undergoing HDCT with or without TBI for an AHSCT in the US. Patients were equally randomized to one of four arms: placebo, or velafermin 0.03, 0.1 or 0.2 mg/kg. Pts received a single intravenous dose of velafermin or placebo 24-36 hrs after completion of the stem cell infusion and were monitored daily until they were discharged from the hospital or until neutrophil engraftment established (defined as first day of absolute neutrophil counts $\geq$500/μ in this study). The primary end point was the incidence of OM (World Health Organization (WHO) score of grade 3 or 4). Secondary end points included duration of severe OM, area under the curve of all OM, days with alternative nutrition, and narcotic analgesic use. Patient enrollment was completed with 212 pts randomized. Approximately 2/3 were multiple myeloma pts receiving high dose melphalan as conditioning regimen and 1/3 of them were lymphoma pts. Less than 10% of pts had TBI as part of their conditioning regimen. Preliminary blinded aggregate data from 160 pts indicated that study drug was generally well tolerated. 30% of pts did not develop any OM and 32% pts developed grade 3/4 OM with a duration of 4.8 $\pm$ 3.7 (mean $\pm$ sd) days among the pts with severe OM. Most adverse events (AE) were mild to moderate in severity with most frequent serious AEs being neutropenic fever, pneumonia and pyrexia. The trial was monitored by a Data Safety Monitoring Board (DSMB). The results of the primary end point of grade 3/4 OM from each treatment arm or placebo as well as 30-day safety information from all pts will be reported.

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INVASIVE ASPERGILLOSIS FOLLOWING HSCT: OUTCOMES AND PROGNOSTIC FACTORS ASSOCIATED WITH MORTALITY

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Invasive aspergillosis (IA) is a common cause of infection-related mortality in hematopoietic stem cell transplant (HSCT) recipients, despite appropriate therapy. Factors influencing outcomes have not been fully elucidated. To determine prognostic factors associated with mortality we retrospectively reviewed all cases of proven and probable IA diagnosed in HSCT recipients at the Fred Hutchinson Cancer Research Center (FHCRC) from 1st Jan 1990 to 31st Dec 2004. All-cause and attributable mortality were recorded. Prognostic factors identified in univariate analysis ($P <$ .10) were further analyzed using a Cox multiple regression model. All variables except those occurring before HSCT were modeled as time dependent. 408 cases were identified: 238 proven and 170 probable IA. The probability of overall mortality at 1 year after diagnosis was 70% in patients diagnosed from 2002 to 2004 versus 86% among those diagnosed prior to 2002 ($P <$ .0001). Cord blood as stem cell source (HR = 3.7 [1.0-13.2]), severe pulmonary function test abnormality pre-HSCT (2.3 [1.2-4.2]), increased creatinine (2.9 [1.9-4.3]) and bilirubin (6.2 [4.4-8.7]) at time of diagnosis of IA, monocytopenia (2.3 [1.6-3.2]), CMV disease (1.4 [1.0-1.8]), receipt of antithymocyte globulin (2.2 [1.5-3.3]), disseminated IA (2.0 [1.4-2.7]), and IA later after HSCT (>40 days) (2.8 [2.0-4.1]) were independently associated with increased all-cause mortality; receipt of non-myeloablative HSCT (0.5 [0.3-0.7]) was independently associated with decreased mortality. The probability of mortality attributable to IA at 1-year was 26% in patients diagnosed from 2002 to 2004 versus 49% among those diagnosed prior to 2002 (P = .007). Mismatched HSCT (2.1 [1.2-3.7]), increased creatinine (3.3 [1.8-6.1]) and bilirubin (5.5 [3.3-9.3]), receipt of antithymocyte globulin (2.3 [1.2-4.1]), disseminated IA (4.0 [2.5-6.3]) and IA later after HSCT (2.4 [1.2-4.0]) were independently associated with increased attributable mortality; non-myeloablative HSCT (0.3 [0.1-0.8]) and receipt of voriconazole therapy (0.4 [0.2-0.8]) were independently associated with decreased mortality. In this study we have demonstrated a significant decline in mortality in patients diagnosed with IA following HSCT in the time period 2002-2004, compared with prior to 2002. This finding has coincided with increased use of non-myeloablative conditioning regimens and voriconazole; two factors we have identified to be protective.