cycle use of growth factors. A study of patients with breast cancer receiving docetaxel 100 mg/m² Q3W (expected FN incidence of 20% without growth factor support) demonstrated that patients receiving pegfilgrastim experienced a significant reduction in FN compared with placebo (1% versus 17%; p<0.0001). Additionally, pegfilgrastim significantly reduced the incidence of FN-associated hospitalizations and IV anti-infective use. Lyman has shown ~50% of initial neutropenic events occur in cycle 1 for non-Hodgkin's lymphoma patients. We analyzed our study to determine if breast cancer patients also experience neutropenic events early in therapy.
METHODS: Breast cancer patients (ECOG 0 to 2) received either pegfilgrastim 6mg (n=463) or placebo (n=465) on the day after docetaxel for up to 4 cycles. FN was defined as temperature ≥38.2°C and absolute neutrophil count <0.5x10⁹/L (within 1 day after temperature ≥38.2°C).
RESULTS: For patients receiving placebo, most neutropenic events occurred in cycle 1. For patients receiving pegfilgrastim, few FN events occurred and a pattern could not be discerned.

		Placebo (n=465)	Pegfilgrastim (n=463)
Febrile Neutropenia, % (95% CL)	Cycle 1	11 (8.5, 14.4)	<1 (<0.1, 1.6)
	Cycles 2 to 4	6 (3.7, 8.1)	<1 (0.2, 2.2)
FN-associated hospitalizations, % (95% CL)	Cycle 1	9 (6.8, 12.3)	1 (0.4, 2.5)
	Cycles 2 to 4	5 (2.8, 6.8)	<1 (<0.1, 1.2)
FN-associated IV anti-infective use, % (95% CL)	Cycle 1	6 (4.4, 9.1)	1 (0.4, 2.5)
	Cycles 2 to 4	4 (2.5, 6.3)	<1 (0.1, 1.9)

CONCLUSIONS: Patients receiving moderately myelosuppresive chemotherapy with no growth factor support experienced two-thirds of neutropenic events in cycle 1. Patients receiving first and subsequent cycle pegfilgrastim were generally protected from experiencing neutropenic events.

233. Hematologic outcomes and costs in epoetin alfa (EPO) and darbepoetin alfa (DARB) treated cancer patients with anemia: results of the Dosing and Outcomes Study of Erythropoiesis Stimulating Therapies (D.O.S.E. Registry). Asli Memisoglu, ScD[1], Cyrus Peake, MS[1], Radha Vichare, MS[1], R. Scott McKenzie, MD[2], *Jamie Howell, PharmD, MS*[2], Catherine Tak Piech, MBA[2]; (1)Abt Associates–HERQuLES, Lexington, MA; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: EPO and DARB, two erythropoietic stimulating therapies (ESTs), are FDA approved for the treatment of chemotherapy-related anemia. D.O.S.E. is an ongoing prospective, observational registry collecting data on real-world practice and outcomes associated with these ESTs in cancer patients.
METHODS: Data were drawn from hospital and community-based outpatient practices during 1/04–4/05. Adult patients were required to have diagnosis of a non-myeloid malignancy, baseline hemoglobin (Hb) <11g/dL, and received at least 2 doses of either EPO or DARB. Outcomes assessed included treatment duration; mean weekly and cumulative doses; Hb change from baseline at weeks 4, 8, 12; and proportion of patients receiving transfusions. Cost was based on 2004 wholesale acquisition cost.
RESULTS: 361 patients (149 EPO, 212 DARB) from 24 sites were identified. Baseline characteristics were similar between groups and reported for the entire 361 patients cohort: mean age 62.7 years, mean weight 74.6 kg, gender 65% female, and mean baseline Hb 10.0 g/dL. Breast and lung cancer were the most common malignancies in both groups. Both groups had identical mean treatment duration (56 days) and number of Hb measurements (8.5). The proportion of patients requiring blood transfusion (21%) was similar. The mean weekly doses were EPO 38,010 units and DARB 112 µg. The mean cumulative doses, or overall treatment doses, for EPO 348,910 units and DARB 1,124 µg were associated with a drug cost of $4,100 for EPO and $4,755 for DARB, a 16% difference. Mean Hb changes (g/dL) from baseline were similar at weeks 4 (0.8), 8 (0.9), and 12 (0.9).
CONCLUSIONS: Results of this prospective observational study suggest similar hematological outcomes with 16% higher drug cost in the DARB group compared to the EPO group. The similar number of Hb measurements suggest a comparable number of office visits for both treatment groups over the relatively brief treatment duration.

234. Greater area under the hemoglobin change curve is associated with improved outcomes in patients receiving epoetin alfa (EPO) or darbepoetin alfa (DARB) for chemotherapy-related anemia (CRA). Patrick Lefebvre, MA[1], Mei-Sheng Duh, MPH, Sc.D.[2], *R. Scott McKenzie, MD*[3], Samir H. Mody, PharmD, MBA[3], Richard C. Woodman, MD[3], Denise Williams, MD[4]; (1)Groupe d'Analyse, LtÉe., Montreal, QC, Canada; (2)Analysis Group, Inc, Boston, MA; (3)Ortho Biotech Clinical Affairs, LLC, Dallas, TX; (4)Johnson and Johnson Pharmaceutical Research and Development, Raritan, NJ.

PURPOSE: Previous research with erythropoiesis-stimulating therapies has shown area under the 16-week Hb change curve (Hb AUC_{16}) is a more sensitive and comprehensive efficacy measure versus traditional single time-point or threshold-based measurements such as hematopoietic response. To date, Hb AUC has not been validated within a randomized controlled trial of anemia treatments.
METHODS: Data were retrospectively analyzed from a randomized controlled clinical trial (n= 358) designed to compare the hematologic outcomes of EPO and DARB in solid tumor patients with CRA. Inclusion criteria were a baseline Hb ≤11g/dL and receiving chemotherapy. Hb AUC_{16} was calculated using sequential trapezoidal methodology based on Hb changes over 16 weeks of treatment and was stratified into quartiles to assess correlation with clinical and drug utilization outcomes. Trend tests were performed on the individual EPO and DARB groups, as well as the combined group, to determine if the following outcomes had significant linear trends across the Hb AUC_{16} quartiles: proportion of patients receiving transfusion, time to hematopoietic response (Hb rise ≥2 g/dL from baseline or Hb ≥12 g/dL during study), and average weekly EPO or DARB dose.
RESULTS: Mean Hb AUC_{16} values were higher for the EPO group versus the DARB group (EPO: 14.2g/dL; DARB: 7.9g/dL, p<0.001). Greater Hb AUC16 values had a strong linear association with decreasing proportions of patients transfused (p<0.0001), decreasing time to hematopoietic response (p<. 0001), and decreasing average weekly EPO or DARB doses (p<. 0001). These results were observed in the EPO and DARB groups separately, as well as in the two groups combined.
CONCLUSIONS: Hb AUC_{16} is associated with clinical outcomes and drug utilization benefits in patients with CRA receiving either EPO or DARB. These features should make it a preferred comprehensive efficacy measure in the assessment of comparative treatment responses.

235. Stability and compatibility of paclitaxel infusion under replicated clinical use conditions to facilitate dose-banding. *Asha Kattige, Ph.D*[1], Graham J. Sewell, Ph.D.[2]; (1)University of Bath, Bath, United Kingdom; (2)Kingston University, Kingston-upon-Thames, United Kingdom.

PURPOSE: To investigate the stability and compatibility of paclitaxel infusion at concentrations 0.3(mg/ml), 0.75(mg/ml) and 1.2(mg/ml), in Freeflex infusion bags containing 0.9% sodium chloride or 5% glucose under refrigerated storage and clinical use conditions to facilitate an outpatient chemotherapy dose-banding scheme.
METHODS: Dose-banding is widely used in UK and offers advantage of patient convenience but needs stability data to permit batch manufacturing. Stability and compatibility of paclitaxel infusion stored in Freeflex infusion bags was evaluated by incubating at 2-8°C or 25°C to represent refrigerated storage and clinical use conditions. Samples were withdrawn at selected time intervals and analysed for physical stability (visible and sub-visual particulates, pH, % weight loss) and chemical stability using a validated stability-indicating HPLC method.
RESULTS: Results indicated that in all cases, paclitaxel is chemically stable with variation in assay values within ± 5% but exhibited precipitation on prolonged storage at 2-8°C and 25°C. The stability of 0.3(mg/ml), 0.75(mg/ml) and 1.2(mg/ml) paclitaxel infusions at 2-8°C in 5% glucose was 28, 16 and 12 days respectively. There was a negligible change in pH and the variation over 28-day study period was less than 0.6 pH units. Similarly moisture diffusion across the infusion bag was minimal with less than 1% weight loss.
CONCLUSION: Stability timescale for various paclitaxel infusions varied and was a function of paclitaxel concentration in the infusion, diluents used and the storage temperature. In all cases, physical stability of the infusion was the limiting factor influencing the stability of the infusion. Maximum stability period of 28 days was observed for paclitaxel (0.3mg/ml) infusion prepared in 5% glucose and stored at 2-8°C. Given the increased popularity of the 90mg/m² weekly regimen in the UK, the 0.3(mg/ml) concentration would be appropriate for most patients and the 28-day shelf life would facilitate a dose-banding scheme.

236. Determination of paclitaxel in rabbit plasma using liquid chromatography tandem mass spectrometry: comparison of liquid liquid extraction (LLE) with solid phase extraction (SPE). *Armaghan Emami, Pharm.D., Ph.D.*[1], Noble Nemieboka, B.S.[2], Kenneth S. Bauer, Pharm.D., Ph.D.[1]; (1)Department of Pharmacy Practice and Science, School of Pharmacy, University of Maryland, Baltimore, MD; (2)University of Maryland Greenbaum Cancer Center, Baltimore, MD.

PURPOSE: Clinical application of a continuous low dose of paclitaxel as an anti-angiogenic agent has been recommended for treatment of cancer. Liquid chromatography tandem mass spectrometry (LC-MS/MS) has been used for the quantification of low concentration of paclitaxel in plasma samples. Both solid phase extraction (SPE) and liquid-liquid extraction (LLE) have been used as sample preparation methods. We have compared SPE and LLE as methods of sample extraction to quantify low concentration of paclitaxel based on the use of small sample volumes (200µl plasma).
METHODS: Rabbit plasma spiked with known amounts of paclitaxel was