multiple myeloma (MM) development. The wild allele of the *VEGF* C936T polymorphism and the *GSTM1* undeleted genotype were linked to a higher angiogenic phenotype compared to the respective variant genotypes in few reports, but their roles in MM is unclear. We tested herein whether the *VEGF* C936T, *GSTM1* and *GSTT1* genotypes altered the risk for MM.
Material and Methods: Genomic DNA from 117 MM patients (mean age: 55; range: 29−86; 95 Caucasians; 22 African-Americans; 55 females; 62 males) and 150 controls (mean age: 53; range: 25−60; 125 Caucasians; 25 African-Americans; 73 females; 77 males) was analysed by PCR-RFLP or multiplex-PCR.
Results: Patients' and controls' samples were in Hardy-Weinberg equilibrium for *VEGF* C936T ($\chi^2 = 0.35$, $P = 0.55$; $\chi^2 = 0.25$; $P = 0.61$). An excess of the undeleted *GSTM1* was seen in patients compared to controls (65.0% *vs* 52.0%, $P = 0.02$). Carriers of the *GSTM1* gene were under a 1.78-fold (95% CI: 1.07−2.96) increased risk for MM than others. Similar frequencies of the undeleted *GSTT1* (73.5% *vs* 79.3%, $P = 0.29$) and the undeleted *GSTM1+GSTT1* (49.6% *vs* 40.7%; $P = 0.86$) were seen in patients and controls. Individuals with the distinct genotypes of the *GSTT1* gene (OR = 0.73; 95% CI: 0.41−1.30) and the *GSTM1* and *GSTT1* combined genes (OR = 1.08; 95% CI: 0.46−2.52) were under similar risks for disease. Similar frequencies of the *VEGF* CC (76.9% *vs* 73.3%, $P = 0.51$) and the CC+CT genotypes (99.1% *vs* 97.3%, $P = 0.28$) were seen in patients and controls. Individuals with the CC (OR = 1.21, 95% CI: 0.68−2.15) and CC+CT (OR = 3.38, 95% CI: 0.36−31.55) genotypes were under similar risks for MM than others. Moreover, similar frequencies of the *GSTM1+GSTT1+VEGF CC* (41.0% *vs* 32.7%, $P = 0.86$) genotypes were found in patients and controls. Carriers of the *GSTM1+GSTT1+VEGF* CC (OR = 1.08, 95% CI: 0.45−2.61) combined genotypes were under similar risks for MM than others.
Conclusions: Our data suggests that the *GSTT1* and *VEGF* genotypes do not influence the risk for MM. However, the presence of *GSTM1* gene is associated with increased risk for disease in Brazilians. Additional studies about vascular microdensity in tumor samples from distinct genotypes individuals, as well as protein function studies, will elucidate if increased risk for disease results from stimulant effect of *GSTM1* gene into AG. Financial support: CNPq.

9234 POSTER

Clinical experience with vorinostat: collated safety and tolerability data from patients with solid or hematologic malignancies

D. Siegel[1], P.N. Munster[2], M. Iwamoto[3], S. van Belle[4], M. Hussein[5], C. Belani[6], F. Robert[7], E. Galanis[8], S. Rizvi[9], E.H. Rubin[10]. *[1]Hackensack University Medical Center, John Theurer Cancer Center, Hackensack NJ, USA; [2]H. Lee Moffitt Cancer Center, Medicine / Oncologic Sciences, Tampa FL, USA; [3]Merck & Co. Inc, Clinical Pharmacology, Upper Gwynedd PA, USA; [4]University of Ghent, Internal medicine, Ghent, Belgium; [5]H. Lee Moffitt Cancer Center, Malignant Hematology Program, Tampa FL, USA; [6]Penn State Cancer Institute, Penn State College of Medicine, Hershey PA, USA; [7]University of Alabama, Comprehensive Cancer Center, Birmingham AL, USA; [8]Mayo Clinic and Mayo Foundation, Oncology, Rochester MN, USA; [9]Merck & Co. Inc, Oncology Clinical Research, Upper Gwynedd, USA; [10]The Cancer Institute of New Jersey, Department of Medicine, New Brunswick NJ, USA*

Background: Vorinostat is an orally active histone deacetylase inhibitor approved in the United States for the treatment of cutaneous manifestations of progressive, persistent or recurrent cutaneous T-cell lymphoma (CTCL), and has been widely investigated in other malignancies in a clinical trial program.
Methods: Safety and tolerability data were collated from patients who received vorinostat as monotherapy or in combination therapy for solid or hematologic malignancies in Phase I and II trials.
Results: Collated safety and tolerability data are available for 341 patients who received vorinostat monotherapy (107 CTCL, 105 other hematologic malignancies, 129 solid tumors) and 157 patients who received vorinostat combination therapy (with pemetrexed/cisplatin for advanced cancer [n = 46], bortezomib for multiple myeloma [n = 34], bexarotene for CTCL [n = 23], and erlotinib [n = 30], gemcitabine/platin [n = 21] or carboplatin/paclitaxel [n = 3] for non-small-cell lung cancer). With monotherapy, common drug-related adverse events (AEs) were fatigue (61.9%), nausea (55.7%), diarrhea (49.3%), anorexia (48.1%), and vomiting (32.8%); Grade 3/4 AEs included fatigue (12.0%) and thrombocytopenia (10.6%), and 3 drug-related deaths (ischemic stroke, tumor hemorrhage, unspecified) occurred. Thirty-eight patients (11.1%) discontinued due to drug-related AEs, 71 patients (20.8%) required dose modifications, and 1 patient (0.3%) discontinued due to Grade 2 chest pain. With combination therapy, common drug-related AEs were nausea (48.4%), diarrhea (40.8%), fatigue (34.4%), and vomiting (31.2%); the most common Grade 3/4 AE was fatigue (13.4%), and 1 drug-related death (hemoptysis) occurred. Thirty-one patients (19.7%) discontinued due to drug-related AEs and 27 patients (17.2%) required dose modifications. In 24 patients with advanced cancer, a single supratherapeutic 800 mg dose of vorinostat did not prolong the QTcF interval (monitored over 24 hours). The upper limit of the 90% confidence interval for the placebo-adjusted mean change-from-baseline of vorinostat was 30 msec, and 1 patient had a QTcF interval >450 msec (after both vorinostat and placebo administration).
Conclusions: Vorinostat was generally well tolerated, with the majority of AEs ⩽Grade 2 and no prolongation of the QTc interval observed, when administered as monotherapy or in a combination regimen in cancer patients.

9235 POSTER

First-line therapy for patients (pts) with newly diagnosed multiple myeloma (MM) ineligible for stem cell transplantation (SCT): a systematic review and meta-analysis (Hemo-ONCOLGroup Study)

M.L. Rodríguez[1], J.F. Combariza[1], C.P. Casas[1], C. Alarcón[1], L. Reveiz[2], J. Buendía[2], A. Martí-Carvajal[3], A.F. Cardona[4]. *[1]Instituto Nacional de Cancerología E.S.E. (INC), Hematology and Bone Marrow Therapy Department, Bogotá, Colombia; [2]National University of Colombia, Clinical Research Institute and Health Technology Assessment Unit, Bogotá, Colombia; [3]University of Carabobo, Clinical Epidemiology and Public Health Unit Iberoamerican Cochrane Network, Valencia, Venezuela; [4]Catalan Institute of Oncology Hospital Germans Trias i Pujol, Medical Oncology, Barcelona, Spain*

Background: Treatment for newly diagnosed MM is predicated on eligibility for SCT. Pts not eligible for SCT have been treated with melphalan (M) plus prednisone (P); however, the standard of care has shifted to MP plus thalidomide (T) due to its survival benefit. Bortezomib (B) and lenalidomide have emerged as effective agents.
Methods: Randomized clinical trials (RCTs) were identified from the Cochrane Library, PUBMED, LILACS, EMBASE and Scirus. Only RCTs comparing MP vs. any other regimen were considered in the analysis.
Results: 22 RCTs were included from 2.159 potentially eligible references. *MP vs. M+dexamethasone (MD):* 3 RCTs. No differences were found between the two combinations in overall survival (OS), complete response (CR), or hematological toxicity. MD was superior in partial response (PR) (RR 1.54, 1.32−1.80; I2 = 17%) and non-hematological toxicity (RR 2.15; 1.36−3.41; I2 = 42%). *MP vs. T regimens:* 4 RCTs. Significant differences favoring T regimens were found in CR (RR 3.44; 1.86−6.39; I2 = 53%) and PR (RR 1.67; 1.28−2.17; I2 = 72%) Although the meta-analysis of 3 RCTs showed a significant difference in OS favoring T regimens (HR 0.79; 0.66−0.96; $I^2$86%), heterogeneity was high. Progression-free survival (PFS) was superior in the T group in 4 RCTs; estimated PFS at 24 mo. was 41% and 48% in pts treated with TD and MP, respectively (p = 0.02). A significant difference was found in non-hematological toxicities (RR 0.79; RR 2.14 1.80−2.55; I2 = 0%). *MP vs. B regimens:* 1 RCT. Significant differences in OS (HR 0.61; 0.42−0.89), TTP (HR 0.48; 0.41−0.56), CR (RR 8.35; 4.68−14.89) and PR (RR 1.30; 1.06−1.59) favored B according to the EBMT criteria. No significant differences were found as regards treatment-related deaths, overall toxicity or hematological toxicity. However, peripheral neuropathy was more frequent with B (RR 88.22; 5.45−1426.63). *MP vs. chemotherapy regimens without M:* 3 RCTs. No differences in CR or OS were observed between P+bendamustine (BP) and MP, but a significantly higher number of patients treated with BP achieved a CR (RR 2.55; 1.22−5.30). TTP was also significantly longer in BP-treated pts (p < 0.02). *MP vs. polychemotherapy regimens:* 13 RCTs. No significant differences in PR or OS were observed between MP and the other chemotherapy regimens. When pooling RCTs, no significant difference was noted in hematological grade 3−4 toxicity or non-hematological G3−4 toxicity.
Conclusions: MM patients ineligible for SCT should receive as a first line treatment a combination of the standard treatment (MP) plus B or T; these regimens are associated with greater toxicity. More homogeneous RCTs using a cytogenetic risk approach are required.