observed in 4 recipients and resolved after steroid treatment. Four patients received prophylactic donor lymphocyte infusion (DLI) because of mixed chimerism (RIC conditioning) in the post-transplantation period. After a median follow-up of 40 months (range 1–115 months), 16 patients (73%) are still alive; 12 are in CR and 3 have limited chronic GVHD. One patient died (day +720) of chronic hepatitis. Progression of CLL was diagnosed in 4 patients; 1 was treated effectively with chemotherapy plus rituximab and DLI, and 3 died of resistant disease at 6 months and 2 and 5 years after allo-HSCT. **Conclusions:** Although allo-HSCT is recommended in CLL as a selected clinical option, it seems to be safe and effective in special cases.

5.23

Phase 2 Study of Navitoclax (ABT-263) Safety and Efficacy in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia: Interim Results

John F. Seymour,[1] Andrew W. Roberts,[2] Dennis A. Carney,[1] Martin J.S. Dyer,[3] Thomas J. Kipps,[4] Michael Hallek,[5] R. Gregory Bociek,[6] Jennifer R. Brown,[7] William G. Wierda,[8] Kanti Rai,[9] Moacyr Ribeiro de Oliveira,[10] Evelyn McKeegan,[11] Brenda Chyla,[11] Todd Busman,[11] Andrew Krivoshik,[12] Sari Enschede,[11] Rod Humerickhouse[11]

[1]Peter MacCallum Cancer Center, Victoria, Australia; [2]The Royal Melbourne Hospital, Parkville, Australia; [3]Leicester University, Leicester, United Kingdom; [4]Moores UCSD Cancer Center, CLL Research Consortium, La Jolla, CA; [5]University of Cologne, Cologne, Germany; [6]University of Nebraska Medical Center, Omaha, NE; [7]Dana-Farber Cancer Institute, Boston, MA; [8]The University of Texas M.D. Anderson Cancer Center, Houston, TX; [9]Long Island Jewish Medical Center, New Hyde Park, NY; [10]Northwest Medical Specialties, PLLC, Tacoma, WA; [11]Abbott, Abbott Park, IL; [12]Astellas Pharma Global Development, Inc., Deerfield, IL

Background: Despite available, effective treatments, most patients with chronic lymphocytic leukemia (CLL) will experience multiple relapses and become refractory to standard therapy. Bcl-2 is universally overexpressed in CLL cells; thus, suppression of Bcl-2 is an attractive therapeutic target. Navitoclax, a novel BH3 mimetic, binds with high affinity (Ki ≤ 1nM) and inhibits multiple antiapoptotic Bcl-2 family proteins. Our earlier phase 1 trial established that single-agent navitoclax 250 mg/day achieved predicted pharmacokinetic parameters, was well tolerated, and provided a signal of activity in previously treated patients with relapsed/refractory CLL, justifying phase 2 evaluation at this dose. **Methods:** This multicenter international trial assessed the safety, efficacy, and pharmacokinetics of oral navitoclax in patients with relapsed/refractory CLL, Eastern Cooperative Oncology Group status 1 or less, and platelet count 75,000/mm^3 or greater who had received 5 or fewer prior regimens. Patients from the phase 1 study were excluded. After a 7-day lead-in at 100 mg/day, navitoclax was dosed at 250 mg/day on a 21-day cycle until PD or intolerable toxicity. Preliminary efficacy end points included tumor response (according to the 1996 criteria of the National Cancer Institute-sponsored Working Group) and progression-free survival (PFS). Disease was assessed at the end of cycles 2 and 4, every 4 cycles through cycle 20, and every 8 subsequent cycles. Adverse events (AEs) were graded by NCI CTCAE v3.0. **Results:** Thirty-one patients, median age 70 years (range 44-82), were enrolled; 7 of 19 with available data were fludarabine-refractory. Median number of prior therapies was 2.5 (range 1-6). So far, 13 patients have cytogenetic data; 9 were high-risk (5 with 11q–, 2 with 17p–, and 2 with both), and 4 had neither deletion. Median time on study is 5.6 months (range 3.8 to > 14.5 months), with 10 patients still receiving drug. Twenty-six patients are evaluable for response (too early for 5 patients): 10 (38%) have partial remission (PR), 14 (54%) have stable disease (SD), and 2 (8%) have progressive disease. Median PFS [95% CI] for 29 patients was 8.7 months [6.0 to not reached]. On serial computed tomography, 12 patients (46%) had greater than 50% nodal regression. Of 27 patients with baseline lymphocytosis, 24 (89%) had more than 50% reduction (median reduction 78.4%). Seventeen patients (55%) had bulky disease (adenopathy > 5 cm); of the 13 evaluable patients, all showed antitumor activity (6 with PR and 7 with SD). pharmacokinetic analysis of trough concentrations suggested consistent exposure across cycles. The most common navitoclax-related AEs (all grades) were diarrhea (57%) and nausea (43%), both of which are most likely attributable to the formulation; Grade 3/4 AEs included thrombocytopenia (27%) and neutropenia (17%). One patient each had a serious, navitoclax-related AE: pyrexia (grade 1/2), tumor lysis syndrome (grade 3), dizziness (grade 1/2). Three patients had AEs leading to discontinuation of therapy, and 9 leading to dose reduction, mainly thrombocytopenia. Nineteen patients discontinued therapy: 6 owing to PD, 6 owing to AEs, 5 because of withdrawal of consent, and 2 for other reasons (lack of response, investigator decision based on low-trending platelets). Two of 4 patients with 17p– achieved PR; patients with 11q– (n = 5) seemed to have favorable outcome versus patients with 17p– (n = 4) or those with normal cytogenetics (n = 4) (PFS 183 days vs not reached, p = 0.0376). **Conclusions:** These data confirm that navitoclax has an acceptable safety profile at 250 mg/day and significant antitumor activity in patients with heavily pretreated CLL, including those with 17p– and other high-risk cytogenetic characteristics. Updated results will be presented.

5.24

Pentostatin, Alemtuzumab, and Low-Dose Rituximab Is Effective Therapy for Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Clive S. Zent,[1] Betsy R. LaPlant,[2] Brian Link,[3] Timothy G. Call,[1] Tait D. Shanafelt,[1] Deborah A. Bowen,[1] Neil E. Kay,[1] George Weiner,[3] Thomas Witzig[1]

[1]Division of Hematology, Mayo Clinic, Rochester, MN; [2]Biostatistics, Mayo Clinic, Rochester, MN; [3]Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA