Venetoclax used as monotherapy or a doublet in combination with dexamethasone in 59% (n = 17) of patients and a triplet or quadruplet in 41% (n = 12) given at 800 mg (55%) or 400 mg (35%) daily. Triplet and quadruplet regimens combined venetoclax with a variety of proteasome inhibitors or daratumumab. One patient had a quadruplet of venetoclax, carfilzomib, pomalidomide and dexamethasone. 93% (n = 27) patients were refractory to at least one proteasome inhibitor and immunomodulatory drug. Dose titration and escalation was used in 31% (n = 9) of patients. None of the patients experienced tumor lysis syndrome. At last follow-up 35% (n = 16) of patients remain on venetoclax therapy. Overall response rate in the 24 patients evaluable for response was 46% (21% CR, 8% VGPR, 17% PR). Patients with t(11;14) had a numerically higher response rate than those without (50% vs 33%, p = 0.64). Patients with high risk cytogenetic abnormalities were less likely to respond (ORR 69% for standard risk vs 18% for high risk, p = 0.019). Median time to response was 2.6 months (range 1.1–6.9 months). Median duration of response was 5.2 months (range 2.2–12.9 months). After a median follow-up time of 7.2 months for the cohort, the median PFS and OS are 5.8 and 14.6 months, respectively, Figure 1A/B. High risk cytogenetic abnormalities were associated with a shorter PFS (median PFS 3 months vs 14 months for standard risk, p = 0.002). The outcomes with venetoclax monotherapy and combination therapies are reported separately in the Table.

Summary/Conclusion: Venetoclax is an effective oral agent in relapsed and/or refractory myeloma and can produce deep and durable responses in heavily pretreated patients. Further studies are needed to elucidate its role earlier in the disease and its effectiveness in combination with other anti-myeloma therapies.

Results:

Out of 11 patients who achieved CR or sCR, seven patients showed NGF MRD negativity (63.6%). Among 24 patients who failed to achieve CR, four patients (1 VGPR, 1 PR, 1 MR, and 1 SD) showed MRD negativity by NGF. In those four patients with discrepancy between IMWG treatment response and NGF results, we compared the results of IgH NGS on BM specimens at initial diagnosis with those after treatment. Of the four non-CR patients with NGF MRD negativity, all of the patients showed IgH rearrangement by NGS. NGS revealed a persistence of residual clone in one patient, an acquisition of new clones in two patients, and heterogeneous clones in one patient. Patient with PR had same dominant clone both initial diagnosis BM (87.13%; proportion of clone) and follow-up BM (19.38%). Two patients (one with MR, the other SD) acquired new clones after treatment. Patients with MR had a newly appeared clone (1.49%) carrying DJ rearrangement which was non-productive, whereas dominant clones found in the three other patients were productive VDJ rearrangement. Patient with SD had newly appeared clones in follow-up BM (5.24%, 4.72%, 3.11%, 2.09%) which were absent in initial BM. The last patient, with VGPR, showed heterogeneous clones without a dominant clone at follow-up BM by NGF. Results including laboratory tests are summarized in Table 1.

Summary/Conclusion: IgH rearrangement NGS revealed malignant clones in 100% of patients who did not achieve CR, but showed NGF MRD negativity. These results suggest that IgH rearrangement NGS can detect malignant clones which may not be identified by NGF. Immunophenotype switching may contribute to this escape of neoplastic plasma cells from NGF monitoring in non-CR patients. Complementary NGS test is needed to detect such drifting clones for monitoring of MRD in MM.

**PS1423 NEXT-GENERATION SEQUENCING STUDY OF V(D) J REARRANGEMENTS ON NON-CR PATIENTS SHOWING MRD NEGATIVITY BY NEXT-GENERATION FLOW**

S.-M. Kim1,*, N. Yang2, S. Ryu2, D. Jeong2, J. Yun3, K. Lim4, S. M. Hwang5, S.-S. Yoon1, D. S. Lee1,2

1Cancer Research institute, 2Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam, 3Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic Of

**Background:** International Myeloma Working Group (IMWG) evaluates the outcomes with venetoclax monotherapy and combination therapies are reported separately in the Table. Summary/Conclusion: Venetoclax is an effective oral agent in relapsed and/or refractory myeloma and can produce deep and durable responses in heavily pretreated patients. Further studies are needed to elucidate its role earlier in the disease and its effectiveness in combination with other anti-myeloma therapies.

**Results:** Out of 11 patients who achieved CR or sCR, seven patients showed NGF MRD negativity (63.6%). Among 24 patients who failed to achieve CR, four patients (1 VGPR, 1 PR, 1 MR, and 1 SD) showed MRD negativity by NGF. In those four patients with discrepancy between IMWG treatment response and NGF results, we compared the results of IgH NGS on BM specimens at initial diagnosis with those after treatment. Of the four non-CR patients with NGF MRD negativity, all of the patients showed IgH rearrangement by NGS. NGS revealed a persistence of residual clone in one patient, an acquisition of new clones in two patients, and heterogeneous clones in one patient. Patient with PR had same dominant clone both initial diagnosis BM (87.13%; proportion of clone) and follow-up BM (19.38%). Two patients (one with MR, the other SD) acquired new clones after treatment. Patients with MR had a newly appeared clone (1.49%) carrying DJ rearrangement which was non-productive, whereas dominant clones found in the three other patients were productive VDJ rearrangement. Patient with SD had newly appeared clones in follow-up BM (5.24%, 4.72%, 3.11%, 2.09%) which were absent in initial BM. The last patient, with VGPR, showed heterogeneous clones without a dominant clone at follow-up BM by NGF. Results including laboratory tests are summarized in Table 1.

**Summary/Conclusion:** IgH rearrangement NGS revealed malignant clones in 100% of patients who did not achieve CR, but showed NGF MRD negativity. These results suggest that IgH rearrangement NGS can detect malignant clones which may not be identified by NGF. Immunophenotype switching may contribute to this escape of neoplastic plasma cells from NGF monitoring in non-CR patients. Complementary NGS test is needed to detect such drifting clones for monitoring of MRD in MM.
Methods: We examined a combined database of clinical and survival information for 314 patients from Brighton and Worthing, Sussex, UK, over a 6-year period, who were newly diagnosed with myeloma, and represent real-world clinical experience. To determine the presence of a CRAB feature, the cut-off values previously defined by the International Myeloma Working Group (IMWG) were used; serum calcium ≥2.75 mmol/L, serum creatinine >177 μmol/L, haemoglobin <10 g/L (or ≥20 g/L below lower limit of normal), and one or more osteolytic lesion on skeletal radiography, CT, PET-CT or MRI.

 Patients were stratified into five CRAB score groups by having either 0, 1, 2, 3 or 4 CRAB features at initial presentation, with a score of 0 denoting a diagnosis of smouldering myeloma. We then studied the relationship between CRAB score and overall survival using Kaplan Meier curves plotted by the statistics programme SPSS.

 Results: Our analysis reveals that each additional CRAB feature confers a stepwise statistically significant poorer outcome in terms of overall survival as shown in Figure 1a. This result was regardless of the treatment regimen the patient received and gave 5-year survival percentages of 81%, 58%, 41%, 22% and 0% for patients with CRAB scores 0–4, respectively. We also found CRAB score to have coherence with the current International Staging System (ISS) scoring system, which combines serum albumin as a measure of general health with β2-microglobulin as a measure of tumour bulk to estimate risk.

 Cytogenetic data required for the revised ISS score was not undertaken for the majority of patients, highlighting the lack of feasibility of this system in practice, although we did observe higher CRAB scores for those patients identified with poor risk chromosomal abnormalities. A trend for higher ISS score with higher CRAB score was observed, further validating the CRAB scoring system (figure 1b).

 Summary/Conclusion: Our study shows that the CRAB score yields accurate prognostic predictions for patients with newly diagnosed multiple myeloma based on simple clinical criteria. It has more prognostic categories than the currently used ISS score (5 versus 3) and superior clinical utility than expensive and time-consuming cytogenetic-based scoring systems that have been recently described. These results indicate that the CRAB score may provide a useful and reliable tool to guide prognostic evaluation in newly diagnosed myeloma patients, requiring only routine laboratory testing to be undertaken, and therefore greater availability to patients in diverse clinical settings.

 PS1425 RESULTS OF THE DARATUMUMAB MONOTHERAPY EARLY ACCESS TREATMENT PROTOCOL (EAP) IN PATIENTS FROM EUROPE AND RUSSIA WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA

 G. Cook1,2, A. Corso3, M. Streety4, L.P. Mendelleva5, V.V. Pushkin5, C. Couturier6, E. Chan7, W. Iraqi8, A. Al-Akabawi9, H. Pei9, M. Gaudig10, M.T. Petrucci11, A. Alegre12, M. Victoria Mateos13

 1St James Institute of Oncology, Leeds Teaching Hospitals NHS Trust and University of Leeds, Leeds, United Kingdom, 2Division of Hematology, Ospedale di Legnano, Milano, Italy, 3Department of Haematology, Guys and St Thomas’ Hospital, London, United Kingdom, 4National Research Center for Hematology of the Ministry of Healthcare of the Russian Federation, 5The City Clinical Hospital named after S.P. Botkin Moscow Department of Health, Moscow, Russian Federation, 6Janssen-Cilag, Iasy les Moureaux, France, 7Janssen Medical Affairs, London, United Kingdom, 8Janssen Medical Affairs, Paris, France, 9Janssen Research & Development, Horsham, PA, United States, 10Janssen-Cilag, Neuss, Germany, 11Division of Hematology, Sapienza University of Rome, Rome, Italy, 12Hospital Universitario de La Princesa, Madrid, 13University Hospital of Salamanca/BSSL, Salamanca, Spain

 Background: Daratumumab (DARA) is a human IgGκ monoclonal antibody targeting CD38 that is approved for monotherapy as relapsed or refractory MM (RRMM) and in combination with standard-of-care regimens for RRMM and transplant-ineligible newly diagnosed MM. Despite the demonstrated benefit of DARA in patients with MM, not all patients are eligible for inclusion in clinical trials or have access to commercially available DARA.

 Aim: The purpose of this multicenter, open-label, EAP was to provide early access to DARA monotherapy to eligible patients with RRMM, while collecting safety and patient-reported outcomes (PRO) data. We report results from a pooled analysis of patients enrolled in 4 countries: Spain, Italy, Russia, and the United Kingdom.

 Methods: Patients eligible for study inclusion had to have ≥3 prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), or were double refractory to both a PI and IMiD. Patients received DARA 16 mg/kg intravenously weekly for 8 weeks, every 2 weeks for 16 weeks, and every 4 weeks until disease progression, unacceptable toxicity, study conclusion, or if DARA became available with reimbursement. Grade ≥3 treatment-emergent adverse events (TEAEs), serious TEAEs (SAEs), infusion-related reactions (IRRs), PRO, investigator-assessed best response, and progression-free survival (PFS) data were collected.

 Results: A total of 293 patients (median [range] age: 64 [32–83] years) were enrolled and received ≥1 dose of DARA. Baseline Eastern Cooperative Oncology Group score was 0, 1, and 2 for 38.2%, 50.5%, and 11.3% of patients, respectively. The median duration of treatment was 4.2 months (range: 0.03–24.08), with a median number of 13 infusions (range: 1–37). Median duration of infusions was 7.1, 4.3, and 3.5 hours for the first, second, and all subsequent infusions, respectively. Grade 3/4 TEAEs were reported in 176 (60.1%) patients; the most common (>10%) included thrombocytopenia (18.8%), anemia (11.9%), and neutropenia (11.6%). Common (>3%) SAEs included pneumonia (4.4%), pyrexia (4.1%), lower respiratory tract infection (3.8%), general physical health deterioration (3.8%), hypercalcaemia (3.8%), and thrombocytopenia (3.4%). Primary reasons for treatment discontinuation included progressive disease (64.8%) and market authorization/reimbursement (16.7%), AE (11.3%), and death (2.7%). Sixty-one (20.8%) patients discontinued treatment due to TEAEs (3.8% drug-related). Forty (13.7%) patients had a fatal TEAE (none were drug-related). IRRs occurred in 132 (45.1%) patients, including 10 (3.4%) with grade 3/4 IRRs (grade 3, n = 9 [3.1%]; grade 4, n = 1 [0.3%]). IRRs occurred in 44.4%, 1.8%, and 1.5% of patients during the first, second, and all subsequent infusions, respectively. The most common (≥5%) any grade IRRs were dyspnea (8.9%), nasal congestion (8.9%), and cough (5.1%). A total of 97 (33.1%) patients achieved a partial response or better, with 36 (12.3%) patients achieving a very good partial response or better. Median PFS was 4.63 months (95% confidence interval [CI], 3.75–5.75), and the 12-month PFS rate was 20.8% (95% CI, 15.9–26.2). The median change from baseline in all domains of the EQ-5D-5L, EORTC QLQ-C30, and EORTC QLQ-MY20 questionnaires was 0 or close to 0, which indicates no clinically significant changes.

 Summary/Conclusion: These EAP results are consistent with previously reported trials of daratumumab monotherapy, and confirm the safety of daratumumab in patients from Europe and Russia with heavily pretreated RRMM. ClinicalTrials.gov identifier: NCT02477891.