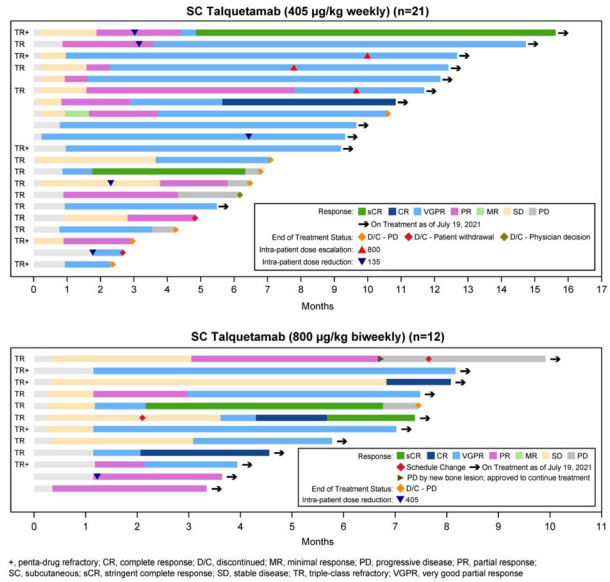
evaluation of talquetamab as monotherapy (phase 2; NCT04634552) and in combination with other therapies in patients with RRMM is underway.

Figure. Duration of Response



+, penta-drug refractory; CR, complete response; D/C, discontinued; MR, minimal response; PD, progressive disease; PR, partial response; SC, subcutaneous; sCR, stringent complete response; SD, stable disease; TR, triple-class refractory; VGPR, very good partial response

P11 IXAZOMIB WITH CYCLOPHOSPHAMIDE AND DEXAMETHASONE IN RELAPSED OR REFRACTORY MYELOMA: MUKEIGHT PHASE II RANDOMISED CONTROLLED TRIAL RESULTS

Auner, H; Brown, S; Walker, K; Kendall, J; Dawkins, B; Meads, D; Morgan, G; Kaiser, M; Cook, M; Roberts, S; Parrish, C; Cook, G

The Hugh and Josseline Langmuir Centre for Myeloma Research at Imperial College London, Clinical Trials Research Unit and Leeds Institute of Clinical Trials Research at University of Leeds, Academic Unit of Health Economics at Leeds Institute of Health Sciences at University of Leeds, Perlmutter Cancer Center at NYU Langone Health, The Institute of Cancer Research and The Royal Marsden Hospital NHS Foundation Trust, Centre for Clinical Haematology at Queen Elizabeth Hospital Birmingham, Department of Clinical Haematology at St James's University Hospital London, Leeds, New York, Birmingham

In the past two decades, treatment options for multiple myeloma (MM) have increased dramatically. While these developments hold great promise, many of the new treatment approaches will, for the foreseeable future, be inaccessible to large numbers of MM patients globally as they are costly and complex to deliver. The all-oral combination of ixazomib, cyclophosphamide, and dexamethasone (ICD) is well tolerated and effective in newly diagnosed and relapsed/refractory multiple myeloma (RRMM), and it is economically competitive.

We carried out MUKeight, a randomised, controlled, open, parallel group, multi-centre phase II trial in patients with RRMM after prior treatment with thalidomide, lenalidomide, and a proteasome inhibitor (ISRCTN58227268), with the primary objective to test whether ICD has improved clinical activity compared to cyclophosphamide and dexamethasone (CD) in terms of progression-free survival (PFS). Between January 2016 and December 2018, 112 participants were randomised between ICD (n=58) and CD (n=54) in 33 UK centres. Baseline characteristics were generally well balanced between the arms, with a median age of 70 years (range 46-82). In the entire study population, 73.6% (81/112) participants had a Charlson Comorbidity Index score of 0-2. More participants in the ICD arm had ECOG PS 1 or 2 (78.9% vs. 66.0%), and more were classed as frail (80.7% vs. 66.0%) by the modified IMWG frailty score. Overall, patients had a median of 4 (range 1-5+) prior lines of therapy, and median time from diagnosis to trial entry was 6.8 years (range 1.8-21.0). Median PFS in the ICD arm was 5.6 months, compared to 6.7 months with CD (hazard ratio (HR)=1.21, 80% CI 0.9-1.6, p=0.3634). Response rates were not significantly different between ICD and CD, with 24/57 participants (42.1%, 80% CI 33.2-51.5) in the ICD arm, and 21/53 (39.6%, 80% CI 30.5-49.4) in the CD arm, achieving at least PR. Median PFS in the ICD arm was 5.6 months (80% CI 4.1-7.2), compared to 6.7 months (80% CI 4.7-7.3) with CD (hazard ratio (HR)=1.21, 80% CI 0.9-1.6, p=0.3634). Overall survival (OS) was not significantly different between the arms, with a median OS of 14.1 months for ICD compared to 19.1 months for CD (HR=1.52, 80% CI 1.06-2.18, p=0.1346) Dose modifications or omissions, and serious adverse events (SAEs), occurred more often in the ICD arm. Of the 34 patients who discontinued CD due to disease progression, 20 crossed over to and received ICD. Median PFS from day 1 cycle 1 of crossover treatment was 4.6 months (80% CI 4.1-5.0). 5/20 participants (25.0%) achieved at least PR, including 3 VGPRs, with 10/20 (50.0%) participants achieving stable disease as their maximum response.

In summary, the addition of ixazomib to cyclophosphamide and dexamethasone did not improve key outcomes in the comparatively frail, old, and heavily pre-treated RRMM patients enrolled in the MUKeight trial. The results also suggest that the inexpensive and all-oral combination of CD can be associated with satisfactory responses, a finding that is particularly relevant for MM patients who do not have access to costly or complex novel drug combinations, or those with impaired access to healthcare facilities for reasons such as geographical remoteness, frailty, or public health concerns.

P12 TREATMENTS IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: RETROSPECTIVE CHART REVIEW OF REAL-WORLD OUTCOMES FOR STANDARD OF CARE

Vekemans, M-C[1]; Delforge, M[2]; Anguille, S[3,4]; Depaus, J[5]; Meuleman, N[6]; Van de Velde, A[4,7]; Vande Broek, I[8]; Strens, D[9]; Van Hoorenbeeck, S[10]; Moorkens, EJ[10]; Diels, J[11]; Ghilotti, F[12]; Dalhuisen, S[13]; Vandervennet, S[10]

[1]Cliniques Universitaires Saint-Luc, Brussels (BE); [2]Universitaire Ziekenhuizen Leuven, Leuven (BE); [3]Laboratory of Experimental Hematology, Vaccine and Infectious Disease Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp (BE); [4]Division of Hematology and Center for Cell Therapy & Regenerative Medicine, Antwerp University Hospital, Edegem (BE); [5]Department of Haematology, Université catholique de Louvain, CHU UCL Namur, Yvoir (BE); [6]Institut Jules Bordet, Université Libre de Bruxelles, Brussels (BE); [7]Heilig Hartziekenhuis, Lier (BE); [8]AZ Nikolaas, Haematology, Sint-Niklaas (BE); [9]Realidad bvba, Grimbergen (BE); [10]Janssen-Cilag NV, Beerse (BE); [11]Janssen Pharmaceutica NV, Beerse (BE); [12]Janssen-Cilag SpA, Cologno Monzese (IT); [13]Janssen-Cilag BV, Breda (NL)

Introduction: The prognosis of patients with multiple myeloma has improved considerably with the introduction of immunomodulatory agents (IMiDs), proteasome inhibitors (PIs), and anti-CD38 monoclonal antibodies (mAbs). However, most patients relapse and require further therapy, with no clear standard of care (SOC). Data on how patients with relapsed/refractory multiple myeloma (RRMM) are treated in clinical practice and outcomes to these treatments in the real-world setting are lacking. This study aimed to evaluate the outcomes of patients with triple-class (IMiD, PI, and anti-CD38 mAb) and triple-line exposed RRMM using real-world data from patients in Belgium.

Methods: This multicenter (7 non-academic and academic Belgian centers), observational study was conducted based on a retrospective chart review of adult patients with RRMM who had received ≥3 lines (IMiD, PI, anti-CD38-directed) of therapies (tri-exposed) and started subsequent treatment from March 2017 through May 2021. In patients meeting eligibility criteria, all treatment lines utilized were considered for analysis (as separate observations for patients who met the eligibility criteria more than once during the follow-up), with date of treatment initiation as specific baseline for each treatment line. Prognostic value with overall survival (OS), progression-free survival (PFS), and time-to-next therapy (TTNT) was evaluated using Cox proportional hazards models.

Results: A total of 112 patients with 237 eligible treatment-lines were included; median follow-up was 16.6 months. In 45% of initiated treatment lines, patients were refractory to 4 or 5 therapies, 62% had ≥5 prior lines, 22% had extramedullary disease; in 48% of observations, time-to-progression (TTP) in prior line was <4 months. After patients were tri-exposed, >50 unique regimens were initiated, with the most common being carfilzomib + dexamethasone (14%), pomalidomide + dexamethasone + chemotherapy (8%), and ixazomib + lenalidomide + dexamethasone (6%). Among included observations, 4% were exposed to anti-BCMA agents. The most frequently initiated therapies were: PI only (19%), PI + IMiD combinations (17%), and regimens that included