of patients on dialysis, there is no significant difference between those receiving or not bortezomib. Median survival before 2008 was 54.82 months and rose to 82.30 months for patients treated after this date (p=0.95). Age (HR: 0.2819, CI 0.1375 to 0.5782), heart disease (HR: 0.3746, CI 0.1724 to 0.8141) and serum albumin (HR: 2.500 CI: 1.077 to 5.803) were identified as prognostic factors. Transplantation is a viable treatment option for good responders.
Summary/Conclusions: Prognosis of AL amyloidosis in dialysis is heterogeneous. Prognostic scoring integrating clinical biological data could identify the patient who may benefit the most dialysis. This results need to be matched by sex and age with non-dialysis and dialysis for another cause.

E1266

REAL-WORLD DATA ON THE TREATMENT OF RELAPSED/REFRACTORY MYELOMA WITH LENALIDOMIDE AND DEXAMETHASONE IN 2ND LINE (LEGEND STUDY): THE PROGNOSTIC SIGNIFICANCE OF BIOCHEMICAL VS. CLINICAL RELAPSE

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Background: The combination of lenalidomide/dexamethasone (LenDex) is an established treatment for relapsed/refractory Multiple Myeloma (MM) patients; however, apart from clinical trials, there is limited data for the efficacy of this combination as 2nd line treatment. Furthermore, the efficacy of LenDex when administered before evident clinical manifestations, namely in the case of biochemical relapse as compared to clinical relapse, has not yet been assessed.
Aims: In the current study, we evaluated response rates and progression-free survival (PFS) in patients treated with LenDex in 2nd line and we compared survival parameters for patients treated with LenDex at biochemical relapse *vs* those treated at clinical relapse.
Methods: Medical files of 207 patients with MM diagnosed between 2000-2013 in 18 Greek centers and treated with LenDex as 2nd line treatment from January 1st 2009, up to March 1st 2014, were retrospectively studied. Overall response and PFS were evaluated for all patients. Additionally, PFS was compared in patients treated at either biochemical relapse (group A) or at clinical relapse (group B). The prognostic significance of biochemical relapse adjusted with important patients' characteristics was also evaluated. Classical methods were used for statistical analysis.
Results: Two hundred and seven patient files were recorded and analyzed (M/F: 112/95, median age: 67.2y, range 31-91y, IgG: 115, IgA: 55, Light chain: 22, non-sectretory: 2, IgD: 5, IgM: 1, unknown: 7, ISS I: 54, ISS II: 74, ISS III: 77, high risk: 13%, standard risk: 87%). First line treatment included bortezomib-based regimens (63.3%), immunomodulatory drug-based combinations (34.8%) and chemotherapy (40.1%); 25% of patients underwent autologous stem cell transplantation; 2nd line treatment with LenDex was administered at biochemical relapse in 67.5% (95% CI: 61.1% >73.9%) of patients and at clinical relapse in 32.5% (95% CI: 26.1-38.9) of patients. The overall response rate (ORR) was 73.4%; 23.7% of patients achieved very good partial response (VGPR) and 17.8% complete response (CR). The number of patients that achieved at least VGPR did not differ between the 2 groups (p>0.05). The median time to best response was 6.7 months (range 0.6- 51.9). After a median follow-up of 52.8 months, 112 (54.1%) patients are alive and 95 (45.9%) patients are deceased; 131 patients (63.3%) have relapsed (biochemical relapse: 66.4%, clinical relapse: 33.6%). Median PFS and PFS rate at 12 months was 19.2 months (95% CI: 15.6-25.2) and 67.6% respectively. The median PFS was 24 months (95% CI: 18.0-34.8) for patients in group A *vs* 13.2 months (95% CI: 8.4-19.2) for patients in group B (HR: 0.63, p=0.006). When adjusted for important prognostic patients' characteristics (ISS, age, β2 microglobulin, and LDH), biochemical relapse maintained its prognostic significance for PFS (p<0.05).
Summary/Conclusions: Our data confirm that Lendex combination as 2nd line treatment leads to high overall response rates and prolonged PFS. Additionally, we have shown for the first time in routine clinical practice that MM patients who receive 2nd line therapy with LenDex at biochemical relapse have a significantly longer median PFS compared to patients treated at clinical relapse, underlining the importance of potentially starting treatment before evident clinical manifestations at the first relapse.

E1267

FDG-PET IN MULTIPLE MYELOMA: DUAL TIME POINT FDG UPTAKE IN FOCAL LESIONS CORRELATE TO RESPONSE TO CHEMOTHERAPY

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Background: Dual Time Point (DTP) ^{18}F-FDG PET imaging has been shown to be useful in differentiating malignant from benign lesions in that increasing uptake from 1 to 3 hours is a characteristic feature of malignancy in contrast to inflammation.
Aims: The aim of this study was to evaluate the predictive role of DTP ^{18}F-FDG PET/CT imaging in assessing response to chemotherapy in multiple myeloma (MM).
Methods: 23 patients with MM (21 male, aged 53-75 years) underwent ^{18}F-FDG PET/CT in a prospective study (NCT02187731) before start of treatment and two months after high dose chemotherapy with stem cell support. All scans were performed at 60 and 180 minutes after tracer injection at Odense University Hospital and Vejle Hospital. Thirteen patients with ≥ 3 focal lesions of at least 10 mm were selected for analysis. Images were analyzed using an adaptive thresholding algorithm (ROVER software; ABX GmbH, Radeberg, Germany). Focal malignant lesions were localized in pre-treatment scans; maximum standard uptake value (SUVmax) and mean SUV (SUVmean) and partial volume corrected SUVmean (pvcSUVmean) were obtained for each lesion. Lesional response to chemotherapy was classified as complete or partial in the post-treatment scan. A complete response was defined as a complete resolution of the lesion in the post-treatment scan. Lesions with partial response were present in the post-treatment scan. All statistical analyzes were done in SPSS 24 using repeated measurements-ANOVA.
Results: Three-five focal lesions were evaluated in each patient. In the pre-treatment PET studies, the increase in SUVmean from 1 to 3 hours was significantly higher for lesions with partial response compared to those with complete response (27.7% *vs* 11.4%; P=0.050). Additionally, the increase in pvcSUVmean was more significant than the increase in SUVmean (+42.23% *vs* +12.0%; P=0.003). The increase in SUVmax of delayed scans was not significant (P =0.082).
Summary/Conclusions: These preliminary data show that a more significant increase of FDG uptake in delayed scans of DTP PET before treatment correlates with a poor response of focal malignant lesions to chemotherapy in MM. The increase in pvcSUVmean is a better index than those of SUVmean and SUVmax for this purpose.

E1268

UNDERSTANDING THE CONTRIBUTE OF THE NOTCH PATHWAY IN MULTIPLE MYELOMA BONE MARROW NICHE: A FOCUS ON EXTRACELLULAR VESICLES-MEDIATED COMMUNICATION

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Background: Multiple myeloma (MM) is an incurable cancer stemming from malignant plasma cells. MM is characterized by a strong tropism to the bone marrow (BM), where tumor cells accumulate and establish complex interactions with the normal stroma, which in turn promotes tumour survival, drug resistance and the development of bone disease. The Notch oncogenic pathway provides a key contribute to the ability of MM cells to shape the BM niche, affecting both MM cell biology and the interplay with the surrounding normal cells. Recently, extracellular vesicles (EVs) have been reported as novel mediators in creating a supportive milieu for MM. Here we investigate the role of the activated Notch signaling in EV-mediated cross-talk.
Aims: The aim of this work was to further elucidate the role played by the Notch pathway in the shaping of the BM microenvironment to provide a supportive milieu for MM cells, with a focus on the contribute of EVs to the crosstalk between MM cells and the BM stromal cells.

Methods: We established two MM cell lines stably retaining the doxycycline-inducible pTRIPZ vector containing anti-Jagged1 and Jagged2 shRNAs and a BM mesenchymal stromal cell (BMSC) line expressing shRNAs for Notch1 and Notch2. EVs were isolated by ultracentrifugation and used for functional assays and molecular analysis. qPCR was performed using SYBR Green. Apoptosis analysis was performed by flow cytometry; evaluation of protein expression was achieved by flow cytometry or western blot.
Results: We present evidences that EVs play a crucial role in the dysregulated interactions of MM cells with the BM microenvironment and that Notch regulates their release. Indeed, BMSCs knockdown for Notch1/2 results in a decrease in EVs release and reduce their ability to induce Bortezomib resistance in MM cells and to stimulate their migration. On the other side, MM-derived EVs are able to increase the production of pro-tumor factors by BMSCs (*i.e.* SDF1α), promoting their ablity to boost tumor growth; interestingly, this effect is lost when EVs are isolated from MM cells where the Notch pathway was inhibited. Finally, EVs released by co-cultures of BMSCs and MM cells where the Notch pathway is blocked display a reduced ability to increase osteoclastogenesis compared with EVs from the control culture. This is particularly relevant due to the crucial role played by bone disease in MM progression.
Summary/Conclusions: These new insights in the pathophysiology of the de-arranged BM niche represent the rationale for a Notch-directerd therapy aiming to uncouple the crosstalk of MM with the surrounding microenvironment by inhibiting Notch signaling.

E1269

THE USE OF CARFILZOMIB AND BORTEZOMIB IN ROUTINE CLINICAL PRACTICE: RESULTS FROM PREAMBLE, AN ONGOING, OBSERVATIONAL COHORT STUDY IN MULTIPLE MYELOMA

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Background: Multiple myeloma (MM) remains largely incurable despite improvements in clinical outcomes following the approval of immunomodulatory drugs (IMiDs) and proteasome inhibitors (PIs) (Rajkumar et al 2010). Previous findings from PREAMBLE indicated shorter median duration of therapy (DoT) with PIs and IMiDs (5 and 9 mo, respectively; Palumbo et al 2016) *vs* clinical trials (Stewart et al 2014). Understanding real-world use of therapies for relapsed/refractory (RR) MM is important to determine their position in the treatment paradigm.
Aims: In this subsequent PREAMBLE analysis, treatment patterns in patients (pts) with RRMM receiving bortezomib (bort) and carfilzomib (carf) were evaluated to better understand the use of PIs in routine clinical practice.
Methods: PREAMBLE (NCT01838512) is an ongoing, observational, international cohort study exploring real-world treatment patterns and outcomes in pts with MM. Eligible pts were aged ≥18 yrs with diagnosis of RRMM, ≥1 prior therapy and initiated treatment (index therapy) with an IMiD, PI or IMiD+PI within 90 days before to 30 days after study enrollment. Treatment patterns, DoT and time to next treatment (TTNT; for pts who switched or died) were assessed. Informed consent was obtained for all pts.
Results: At data cut-off (Sept 1, 2016), data were available for 924 pts, of which 326 (35%) pts had bort-based index therapy and 86 pts (9%) received carf-based index therapy (63/72 [88%] were enrolled in North America). The most common bort-based combination was bort + dexamethasone (dex; n=99, 30%). The most common carf-based therapies were carf alone (n=40, 47%), followed by carf+dex (n=21, 24%). The most widely used bort dose per 21 days for any bort-based therapy was ≤4.0mg/m^2 (98/151; 65%). The most common carf dose per 28 days received for any carf-based therapy was ≤120mg/m^2 (28/55; 51%). Switch from carf-based index therapy occurred after a median (Q1, Q3) DoT of 3.4 (1.9, 9.5) mo (n=34); most pts switched to pomalidomide (pom)-based regimens (23/34; 68%). Switch rates increased from 17% at 3 mo to 54% at 15 mo, and then to 57% at 24 mo. Median (Q1, Q3) TTNT from index therapy was 5.6 (2.3, 9.0) mo (n=53). Median (Q1, Q3) DoT (n=113) and TTNT (n=173) for bort-based index therapy was 4.5 (2.4, 7.1) and 7.0 (3.7, 12.3) mo, respectively; most pts switched to lenalidomide (43/113; 38%) or pom (33/113; 29%). Switch rates increased from 10% at 3 mo to 57% at 33 mo. Dose reductions on carf-based therapies (6/86; 7%) were mostly determined by clinical decision (67%), whereas for bort+dex (24/99; 24%) adverse events (AEs) were the main reason (63%). Discontinuation/switching from carf-based index therapy was reported for 80% (69/86) of pts, driven mainly by disease progression (39%) and AEs (14%). Similarly, disease progression (27%) and AEs (21%) were also the main reasons for pts discontinuation/switching from bort+dex therapy (84/99; 85%). AEs were reported for 45% (39/86) of pts with carf-based index therapy, most commonly fatigue (12%) and anemia (9%); 70% (69/99) of pts receiving bort+dex had AEs, most commonly thrombocytopenia and diarrhea (each 14%).
Summary/Conclusions: Treatment duration observed for PIs in the real-world clinical practice setting was shorter than reported in clinical trials. As patient enrollment and follow-up continues for PREAMBLE, additional analyses will be conducted to evaluate the impact of these patterns on efficacy outcomes.
Study funding: BMS.

E1270

ROLE OF SERUM FREE LIGHT CHAIN *VS* BENCE JONES MEASUREMENT IN LIGHT CHAIN MULTIPLE MYELOMA (LCMM) AT DIAGNOSIS, DURING TREATMENT AND FOLLOW-UP FOR RESPONSE EVALUATION AND RELAPSE DETECTION

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Background: According to IMWG recommendations for response assessment in multiple myeloma (MM), serum free light chain (sFLC) measurement should be used to define a "stringent" complete response in symptomatic MM and, only in cases when Bence Jones protein (BJP) is deemed as not quantifiable (<200mg/24h), in light chain multiple myeloma (LCMM). However, data are available suggesting that sFLC could be a more sensitive tool than BJP for minimal residual disease assessment and an earlier indicator of progressive disease (PD). BJP measurement requires to perform both urinary electrophoresis and immunofixation, it is time-consuming for tecnicians and could be limited by poor patient compliance.
Aims: Aim of our study was to retrospectively compare sFLC and BJP results in LCMM patients (pts) at diagnosis, during treatment and follow-up.
Methods: Serum and urine samples were collected from pts affected with plasma cell dyscrasia referring to the Azienda Ospedaliero-Universitaria Careggi between 1st February 2012 and 31 December 2013. Serum and urine protein electrophoresis was performed using Capillarys II, serum and urine immunofixation using Hydrasys II (both from Sebia), sFLC were measured on Immage 800 nephelometer (Beckman Coulter) using Freelite reagents (The Binding Site).
Results: We analized samples from 387 pts having positive serum and/or positive urinary immunofixation and/or abnormal sFLC ratio. Among them, 43 symptomatic LCMM pts were identified having both sFLC and BJP measurement at baseline (at MM diagnosis or first relapse). Serum and urine lab tests results were evaluated at baseline, monthly during therapy and every 3 months during follow-up. Median duration of laboratory monitoring for the whole group was 42 months (range 3-120). Autologous stem cell transplantation was performed in 30% of pts previously treated with proteasome inhibitors (81%) and/or immunomodulating agents (40%) or chemotherapy (9%). sFLC or BJP were not available in 10% of 872 pair of samples from 43 pts. In 10% of cases (68/696 pair of samples) sFLC ratio was abnormal with increased involved FLC without any detectable BJP (FLCr+;iFLC+;BJP-); the opposite (FLCr-;iFLC-;BJP+) occurred in 1% of cases (8/696 pair of samples). Renal failure was found in 9% *vs* 13% of discrepant cases. At baseline, of the 43 LCMM pts, 6 had "measurable disease" only by sFLC due to BJP<200mg/24h and were therefore considered not evaluable for response assessment. Median time to BOR was 3 months by both sFLC and BJP (range FLC: 1-11 mesi; range BJP: 1-10 mesi). Among the remaining 37 pts evaluable for best overall response, 6/37 had complete response according to BJP but not to sFLC; interestingly 5/6 progressed after 2-8 months. Twenty-one pts progressed during follow-up: PD was detected only by sFLC in 4, only by BJP in 1. Both tests were able to detect PD in 16 pts: at the same time in 5, with sFLC-PD occurring earlier in 7 and BJP-PD occurring earlier in 4 pts.
Summary/Conclusions: Both sFLC and BJP measurement are useful in LCMM pts for disease monitoring, however, sFLC assessment appears to be more sensitive in MRD and early relapse identification. These data suggest that BJP could be substituted by sFLC assessment in LCMM. In our series only 1 case showed BJP-PD according to IMWG occurring earlier than sFLC-PD but was considered not clinically significant. On the contrary 5 pts in BJP-CR clinically progressed within few months without having reached FLC-CR. Limits of our study are a small number of pts, inhomogeneous duration of therapy and follow-up and retrospective analysis.

E1271

SUPPRESSION OF THE NON-MONOCLONAL PAIR AS NEW BIOMARKER OF POOR PROGNOSIS IN MULTIPLE MYELOMA PATIENTS AT DIAGNOSIS AND AFTER AUTOLOGOUS STEM CELL TRANSPLANT

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Background: The outcome for patients with Multiple Myeloma (MM) is highly