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.

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**E1267**

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


**Aims:** The aim of this study was to evaluate the predictive role of DTP 18F-FDG PET/CT imaging in assessing response to chemotherapy in multiple myeloma (MM).

**Methods:** Patients with MM (21 male, aged 53-75 years) underwent 18F-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).

**Summary/Conclusions:** 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. Complete 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 analyses 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).

**Background:** To our knowledge, this is the first study to analyze the correlation between focal lesion SUVMean and SUVMax in the post-treatment scan and the response to chemotherapy in MM.

**Conclusions:** Our data confirm that Lendex combination as 2nd line treatment is a viable treatment option for good responders.

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**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**


**Aims:** 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.

**Methods:** 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: 77, high risk: 13%, standard risk: 87%). First line treatment included bortezomib-based regimens (63.3%), immunomodulatory drug-based combinations (22, non-secretory: 2, IgD: 5, IgM: 1, unknown: 7, ISS I: 54, ISS II: 74, ISS III: 1). The overall response rate to stem cell transplantation; 2nd line treatment with LenDex was administered at zomib-based regimens (63.3%), immunomodulatory drug-based combinations (27.7%). Median survival for patients treated with LenDex at biochemical relapse vs those treated at clinical relapse.

**Summary/Conclusions:** 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.
**Methods:** We established two MM cell lines stably retaining the doxycycline-inducible pTREPIR vector containing anti-Jagged1 and Jagged2 shRNAs and a BM mesenchymal stromal cell line (BMSC) 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 performed by western 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 proliferation of pro-tumor factors by BMSCs (i.e. SDF-1α), promoting their ability 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 control cultures. 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-aggregated BM niche represent the rationale for a Notch-directed therapy aiming to uncouple the crosstalk of MM with the surrounding microenvironment by inhibiting Notch signaling.

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**E1269**

**THE USE OF CARFILZOMIB AND BORTZEOMIB 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 on the real-world utilization of therapy include 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 and received index therapy (first-line treatment) with an IMiD, PI or IMiD+PD within 90 days before to 30 days after study entry. 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 ≤120mg/m2 (285/55; 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 37% at 33 mo for any bort-based therapy (6/86; 7%) when most were 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 pom-based regimens (n=23/34; 68%). 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 thrombocyto-penia and diarrhea (each 14%).