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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Prevalence of Monoclonal Gammopathy of Undetermined Significance in Eswatini: A Study of an African Population

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Multiple myeloma and its precursor, monoclonal gammopathy of undetermined significance (MGUS), both occur twice as often within Black populations compared to White populations, suggesting that racial factors may influence the development of MGUS, not the progression from MGUS to malignancy. The landmark epidemiologic study that described the natural history of MGUS was conducted among 21,463 of the 28,000 residents in Olmsted County, Minnesota, a 97% White population, and found the age-standardized prevalence (including light-chain, LC, MGUS) to be 4.2% (Dispenzieri, et al, *Lancet*, 2010). Although MGUS disproportionately affects Black individuals, few studies have been conducted on MGUS in Africa, and no prior study has evaluated MGUS in a Black African cohort inclusive of both sexes. Using a population-based biorepository from Eswatini, a small country in southern Africa, we further explored the racial disparities related to plasma cell dyscrasias. Our primary objective was to determine the prevalence of MGUS in Eswatini, as compared to that found in Olmsted County. Additionally, we aimed to determine the association between MGUS and HIV status.

From 2016 to 2017, over 15,000 individuals from a nationally representative selection of households participated in the Second Eswatini Population-based HIV Impact Assessment survey, SHIMS2 (phia.icap.columbia.edu/countries/eswatini). After providing informed consent, interviews were conducted and blood samples were collected. Samples were tested for HIV, and if positive, also for CD4+ cell counts and the serologic presence of antiretroviral therapy (ART). The remaining plasma aliquots were stored and linked to their de-identified corresponding survey data for future research endeavors. For our current study, all adults over the age of 35 years who had SHIMS2 specimens stored were included in the sampling frame. We randomly selected 515 plasma samples from the sampling frame, with the sample size determined to produce a two-sided 95% confidence interval (CI) with a width of 0.05 and power >80% for MGUS prevalence and comparison by HIV status. We performed protein electrophoresis with reflex immunofixation, as well as free light chain and creatinine quantification, and defined MGUS cases by the same criteria as the Olmsted County studies. If creatinine was greater than the upper limit of normal, then the renal reference range was used for free-light-chain ratios . Historical proportions and means were compared with z-tests and t-tests, respectively. To determine associations between categorical variables, odds ratios (OR) were calculated with logistic regressions or Fisher Exact tests.

The study cohort (n=515) was 60% female (n=309) with a median age of 50 years (range 35-80); 199 (38.6%) were HIV-positive, of whom 82.4% (n=164) were on ART, and 8.5% (n=17) had a CD4+ cell count of <200 cells/ul. These numbers reflected the overall national estimates (Kingdom of Eswatini, *SHIMS2 Final Report*, 2019). The MGUS prevalence (including LC-MGUS)

standardized for age and sex was 13.2% (95%CI: 10.5-16.5) (n=68), which was significantly greater than Olmsted County (RR 3.1, p<0.0001). Most (84%, n=57) MGUS cases were LC. Prevalence of non-light-chain (NLC) MGUS was 2.1% (n=11), which was similar to Olmsted County. Of the 11 participants with NLC MGUS, 4 were considered very low risk for progression to malignancy, 6 low risk, 1 intermediate risk, and 0 high risk by Mayo stratification (Rajkumar, et al., *Blood*, 2005). HIV status was not found to be significantly associated with MGUS (OR: 1.05, 95%CI: 0.62-1.77). However, within the HIV-positive cohort, the odds of MGUS were 69% lower among those on ART (OR: 0.31, 95%CI: 0.11-0.82) when adjusted for age, sex, and wealth quintile. Furthermore, MGUS was 2.8 times more frequent in those with untreated HIV when compared to those with treated HIV (95%CI: 1.1-7.2, *p*=0.031), and 2.3 times more frequent when compared to non-HIV (95%CI: 1.0-5.6, *p*=0.056); treated HIV was not significantly different from non-HIV (data not shown).
In conclusion, the MGUS prevalence in Eswatini was more than three-fold higher than that in Olmsted County, largely due to those with LC-MGUS. The high rate of HIV in Eswatini did not explain the high prevalence of MGUS, as the majority of those with HIV were on ART and only untreated HIV was significantly associated with MGUS.

Disclosures Cicero: *BMS:* Research Funding; *Novartis:* Research Funding. **Low:** *BioMarin:* Current Employment. **Lentzsch:** *Takeda:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Research Funding; *Regeneron:* Honoraria; *Pfizer:* Consultancy; *Oncopeptide:* Membership on an entity's Board of Directors or advisory committees; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Clinical Care Options:* Honoraria; *Celgene:* Research Funding; *Caelum Biosciences:* Membership on an entity's Board of Directors or advisory committees, Patents & Royalties; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Alexion:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Adaptive:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Neugut:** *Otsuka:* Consultancy, Research Funding; *United Bioscience Corp:* Consultancy; *GSK:* Consultancy; *Value Analytics:* Consultancy; *EHE:* Membership on an entity's Board of Directors or advisory committees.

ALL PARTICIPANTS	MGUS+ *n*=68 (%)	MGUS- *n*=447 (%)	Univariable OR [95% CI]	P	Multivariable OR [95% CI]	Adjusted P
Median Age (Q1, Q3)	56.5 (45, 63.5)	50 (41, 60)	1.024 [1.00, 1.044]	0.02	1.026 [1.01, 1.05]	0.02
Sex				0.96	1.05 [0.62, 1.78]	0.85
Male	27 (39.7)	179 (40.0)	0.986 [0.59, 1.66]			
Female	41 (60.3)	268 (60.0)	ref			
Mean Wealth Quintile (SD)	2.57 (1.26)	2.79 (1.36)	0.88 [0.73, 1.08]	0.22	0.92 [0.75, 1.78]	0.37
HIV Status				0.85	1.32 [0.75, 2.32]	0.34
Positive	27 (39.7)	172 (38.5)	1.05 [0.62, 1.77]			
Negative	41 (60.3)	275 (61.5)	ref			

Table 1 (Panel A). Associations for MGUS with demographic characteristics collected as part of the Second Eswatini Population-based HIV Impact Assessment survey (SHIMS2).

CI, confidence interval; MGUS, monoclonal gammopathy of undetermined significance; OR, odds ratio; Q, quartile; SD, standard deviation

HIV-POSITIVE PARTICIPANTS	MGUS+ *n*=27 (%)	MGUS- *n*=172 (%)	Univariable OR [95% CI]	P	Adjusted* OR [95% CI]	Adjusted P
CD4 >500	12 (44.4)	107 (62.2)	0.84 [0.17, 4.13]	0.83	0.89 [0.17, 4.69]	0.89
CD4 200-500	13 (48.1)	50 (29.1)	1.95 [0.40, 9.6]	0.41	1.68 [0.32, 8.82]	0.54
CD4 <200	2 (7.4)	15 (8.7)	ref		ref	
On ART	18 (66.7)	146 (84.9)	0.36 [0.13, 1.06]	0.04	0.31 [0.11, 0.82]	0.02
Not on ART	8 (29.6)	23 (13.4)	ref		ref	
VL suppressed	20 (74.1)	144 (83.7)	0.56 [0.20, 1.71]	0.27	0.46 [0.17, 1.24]	0.13
VL not suppressed	7 (25.9)	28 (16.3)	ref		ref	

Table 1 (Panel B). Associations for MGUS in the HIV-positive cohort from the Second Eswatini Population-based HIV Impact Assessment survey (SHIMS2).

ART, antiretroviral therapy; CI, confidence interval; MGUS, monoclonal gammopathy of undetermined significance; OR, odds ratio; VL, HIV viral load

*Adjusted for age, sex, and wealth quintile

Figure 1

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