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Baseline Basophil and Basophil-to-Lymphocyte Status is Associated with Clinical Outcomes in Metastatic Hormone Sensitive Prostate Cancer

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Abstract

Background: Biomarkers have the potential to provide clinical guidance, but there is limited data for biomarkers in metastatic hormone sensitive prostate cancer (mHSPC).

Methods: We performed a retrospective multicenter review from Winship Cancer Institute at Emory University and Georgia Cancer Center for Excellence at Grady Memorial Hospital (2014 – 2020) in the United States of America (USA). We collected demographics, disease characteristics, and laboratory data, including complete blood counts (CBC) at the start of upfront therapy. We evaluated overall survival (OS) and progression-free survival (PFS) associated with baseline lab values.

Results: 165 patients were included with a median follow-up time of 33.5 months (mo). 105 (63.6%) had Gleason scores of 8–10 and 108 (65.9%) were classified as high-volume disease. 92 patients received upfront docetaxel (55.8%) and 73 received upfront abiraterone (44.2%). Univariate analyses (UVA) and multivariable analyses (MVA) identified worse clinical outcomes (CO) associated with elevated basophils and basophil-to-lymphocyte ratio (BLR). Based on MVA, elevated basophils (defined as ≥0.1, optimal cut) were associated with a hazard ratio (HR) of 3.51 (95% CI 1.65–7.43, p 0.001) for OS and HR of 1.88 (95% CI 1.05–3.38, p 0.034) for PFS. Our

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MVA also found that BLR ≥ 0.0142 was associated with HR 2.11 (95% CI 1.09–4.10, p 0.028) for OS; however, PFS was not statistically significant.

Conclusion: We conclude that elevated baseline basophils and BLR are associated with worse clinical outcomes in mHSPC. Although results require further validation, BLR is a potential prognostic biomarker.

Keywords

castration-sensitive prostate cancer; hormone-sensitive prostate cancer; biomarkers; basophils; basophil to lymphocyte ratio

1. Introduction

Prostate cancer (PCa) remains the most commonly diagnosed malignancy among men in the United States with an estimated 42% increase in new metastatic PCa cases from 2015 – 2025 [1–4]. Metastatic hormone sensitive prostate cancer (mHSPC) is a complex disease to manage due to a rapidly evolving treatment landscape in addition to the increasing incidence of disease. Current therapies include androgen deprivation therapy (ADT) with either upfront abiraterone (ABI), docetaxel (DOC), enzalutamide (ENZA), and apalutamide (APA), whereas ADT alone was the mainstay of treatment until 2015 [5–7].

Readily available data in routine labs, including complete blood counts (CBCs), can reflect inflammatory changes due to acute phase reactants that are associated with disease progression, serving as surrogates of the immune system-tumor interaction [8–12]. Studies in other subsets of PCa, such as metastatic castration resistant PCa (mCRPC) and in different malignancies have reported worse clinical outcomes (CO) with increases in leukocytes, such as neutrophils, and the neutrophil-to-lymphocyte ratio (NLR) [13–18]. Other leukocyte subsets, such as basophils, have not been studied as extensively. There is some data in other malignancies, specifically bladder and pancreatic cancer, showing that higher basophils are associated with tumor recurrence and decreased overall survival (OS), respectively [19–20].

To identify potential prognostic biomarkers in mHSPC, we compiled a demographically diverse patient database that included CBC data at initiation of upfront treatment in mHSPC, then evaluated for associations with CO, specifically OS and progression-free survival (PFS).

2. Material and Methods

2.1 Patients and Data

PCa patients' records were compiled from pharmacy databases at Winship Cancer Institute of Emory University and Grady Cancer Center for Excellence (2014 – 2020) in the United States of America (USA). Patients treated with either docetaxel (DOC) or abiraterone (ABI) in the upfront setting were identified and included in the study if they did not receive any other prior systemic therapy. Institutional Review Board approval was obtained. Data collected included demographics, treatments, outcomes, and labs. For labs, we focused on

baseline CBC, defined as the time prior to or just after starting upfront therapy. Based on the CBC, we calculated NLR and basophil-to-lymphocyte ratio (BLR). Each of those measurements were dichotomized as high vs. low at the location that maximized the log-rank test for OS using a bias-adjusted log-rank test searching algorithm [21]. The patient list was last reviewed in September 2021. At that time, the data was updated regarding disease progression and the last date of follow-up.

2.2 Definitions

Patients were classified as high-volume disease based on the CHAARTED criteria of visceral metastases or ≥ 4 bone lesions with ≥1 beyond axial skeleton [22].

Normal labs were set at the following values: hemoglobin (hgb) 12.9 – 16.1 (gm/dl), platelets (plt) 150–400 (10_3/μL), neutrophils 0.67–6.41 (10_3/μL), lymphocytes 0.72–3.29 (10_3/μL), basophils 0–0.07 (10_3/μL).

Clinical outcomes included: OS (time from drug initiation to death) and PFS (time from drug initiation to biochemical progression, radiographic progression, or death; whichever occurred first). Patient deaths were confirmed by reviewing both the state of Georgia obituary database and electronic health record (EHR). Cases were censored at the last follow-up if there were no events. Biochemical progression was based on an increase in PSA on two consecutive measurements with the first measurement noted as time of progression, or if PSA nadir was <4 then the PSA >4 was used as time of progression.

2.3 Statistical Analysis

Statistical analysis was conducted using SAS Version 9.4, and SAS macros [23]. The significance level was set at $P < 0.05$. Descriptive statistics for each variable were reported. The univariate associations (UVA) and multivariable analyses (MVA) for OS or PFS was tested by Cox proportional hazard model with hazard ratio (HR) and its 95% confidence interval (CI) being reported. Variables controlled in the MVA were drug, race, age, Gleason score, disease volume, and ECOG status. Due to the limited number of events and total sample size, we focus on controlling with a few selected important confounders based on existing knowledge. The optimal cut off value for a continuous biomarker was derived relative to PFS using bias-adjusted log-rank test after examining all possible cuts in the data space. [24] The association of interest was also examined in subgroups by race and treatment using interaction terms in MVA model.

3. Results

3.1 Overview

165 patients were included with a median follow-up time of 33.5 months (mo) (95% CI 29.3 – 37.2 mo). 92 patients received upfront DOC (55.8%) and 73 received upfront ABI (44.2%). 105 (63.6%) had Gleason scores of 8–10 and 108 (65.9%) were classified as high-volume disease (per CHAARTED trial criteria) [Table 1]. The most significant results were an association of elevated basophils and BLR with worse clinical outcomes, notably OS [Tables 2 – 4, Figures 1 and 2]. Additionally, our results found decreased OS for low hgb

(<12.9 associated with HR of 2.33, 95% CI 1.18–4.62, p 0.015). There was no significant change in clinical outcomes based on platelets or NLR. The full UVAs can be found in Tables 2 and 3.

3.2 Overall Survival for Basophils and Basophil-To-Lymphocyte Ratio

UVA for OS shows decreased survival for patients with elevated basophils (defined as ≥ optimal cut of 0.1) (HR 3.69 95% CI 1.91–7.12, p <0.001) and high BLR (defined as ≥ optimal cut of 0.0142) (HR 1.35, 95% CI 0.73–2.50, p 0.338). These findings are confirmed in our MVA with elevated basophils having a HR of 3.51 (95% CI 1.65–7.43) p 0.001) and high BLR having HR of 2.11 (95% CI 1.09–4.10 p 0.028) (Tables 2 and 4).

3.3 Progression-Free Survival for Basophils and Basophil-To-Lymphocyte Ratio

UVA for PFS associated with elevated basophils had a HR 2.39 (95% CI 1.42–4.01 p 0.001) with MVA showing HR 1.88 (95% CI 1.05–3.38, p 0.034). High BLR was not statistically significant in either the UVA (HR 0.76, 95% CI 0.51–1.14, p 0.187) or MVA (HR 0.87, 95% CI 0.55–1.35, p 0.526) after controlling for drug, race, age at diagnosis, disease volume, ECOG status, and Gleason score (Tables 3 and 4, Figures 1 and 2).

3.4 Overall Survival and Progression Free Survival for Baseline Basophils and Basophil-To-Lymphocyte Ratio: Subgroup Analyses

3.4.1. Stratified by Race—Given the diversity of our patient population, we decided to stratify our results based on race. MVA for OS showed worse survival in Black patients with high BLR compared to low BLR (HR 2.23, 95% CI 1.02–4.89, p 0.045). OS was also worse in Black patients with elevated basophils (HR 3.70 (1.62–8.45), p 0.002). There was no significant difference in PFS in Black patients with high vs low BLR or normal vs elevated basophils. There was also no significant difference in OS or PFS in non-Black patients with elevated basophils or high BLR (Supplemental Materials).

3.4.2. Stratified by Upfront Therapy—MVA for OS showed survival was worse in patients who had high BLR and were treated with DOC (HR 2.64 (95% CI 1.08–6.41, p 0.032) as well as patients with elevated basophils treated with DOC (HR 3.95 (95% CI 1.49–10.51, p 0.006). There was no association with abiraterone on basophil or BLR status and survival outcomes (Supplemental Materials).

4. Discussion

Our study evaluated potential biomarkers in a diverse population of mHSPC patients within readily available clinical labs. We found that elevated basophils and BLR are associated with worse clinical outcomes (Figure 1, Table 4). MVA data revealed that patients with elevated baseline basophils were more than three times as likely to have shorter survival compared to those with normal baseline values (Table 4). Utilizing prognostic markers, such as baseline basophils and BLR, can aid in navigating the evolving treatment landscape of mHSPC by helping predict more aggressive, high-volume disease.

We further stratified results based on race and choice of upfront therapy. Elevated basophils and BLR is associated with worse OS more often for Black patients compared to Non-Black patients (supplemental table B1 and B2). Additionally, elevated basophils and BLR is associated with worse OS more often for patients treated with upfront DOC compared to ABI (supplemental table D1 and D2). These results may be due to a higher incidence of high-volume disease in Black patients and high-volume disease being treated more often with DOC.

Current literature regarding basophils and BLR in prostate cancer is limited with one study reporting no association of basophils with Gleason score [26]. At the time of publication, there was no literature discussing basophils or BLR specifically in mHSPC. However, basophils have been evaluated as a biomarker in other malignancies. In bladder cancer, higher basophils were associated with recurrence after tumor resection and bacillus Calmette-Guerin (BCG) administration [19]. In pancreatic cancer, a higher percentage of basophils in tumor-draining lymph nodes were associated with worse OS (HR 8.51, 95% CI 1.04–69.33, p 0.04) and PFS (HR 11.07, 95% CI 1.38–88.60, p 0.02) [20]. Additionally, the same study from De Monte el al. found that basophil-deficient mice do not fully develop pancreatic tumors after orthotopic transplantation of pancreatic tumor cells. Although these findings are consistent with our results in mHSPC showing that patients have worse CO with higher basophils and BLR, basophils are not always associated with worse outcomes in all malignancies. For example, melanoma patients with higher basophils who were receiving immune checkpoint inhibitors (ICIs) had improved OS (HR 2.33 for basophils <0.06, 95% CI 1.30 – 4.19, p 0.005) [27]. In non-metastatic colorectal cancer, low baseline basophils are associated with more aggressive disease and worse survival outcomes [28, 29]. These differences in outcomes associated with basophils compared to our data may be related to tumor type, extent of disease, and types of prior treatments such as ICIs.

Other components of the CBC, such as NLR, have more data for use as biomarkers. High NLR has been associated with worse clinical outcomes in most solid tumors, including PCa [10, 16–18, 30, 31]. Within mCRPC, NLR has been used in prognostic scoring models and for predicting response to ABI and ENZA [16–18, 31]. In a study of all metastatic PCa without specification for subtype, a higher pretreatment NLR was associated with disease progression and decreased survival [32]. For our study population of mHSPC, NLR was not associated with any significant changes to OS or PFS.

The biological rationale for the association of improved clinical outcomes with changes in leukocytes and lymphocytes is likely related to tumor-driven systemic inflammation. Acute phase reactants are upregulated leading to elevated leukocytes and platelets while decreasing hemoglobin and lymphocytes [15]. Neutrophils activate the innate and adaptive immune system to promote macrophage recruitment and differentiation, angiogenesis, and tumorigenesis [14]. Monocytes are also recruited to tumors and differentiate to tumor-associated macrophages, which then contribute to tumor growth, local immune suppression, and ultimately metastasis [33]. Lymphocytes are involved in immunosurveillance, so decreased lymphocytes, which contribute to higher NLR or monocyte to lymphocyte ratio (MLR), could indicate an ineffective immune response to the tumor leading to evasion of immunosurveillance resulting in unchecked progression [11–13, 16, 30, 34]. We suspect

that similar mechanisms involving changes in acute phase reactants also lead to elevated basophils and BLR, but the exact role of basophils in disease progression is not well defined.

Our study is the first to identify baseline basophils and BLR as promising prognostic biomarkers in mHSPC, a disease that has minimal biomarker data, and is unique in that our patient population included 54% Black patients and 46% non-Black patients. However, there are some limitations to our study. Our patient population lacked additional diversity from other racial or ethnic groups such as Hispanic and Asian groups. We also did not include data on patients treated with ENZA or APA due to limited sample size given these therapies have recently been approved in mHSPC. Additionally, preliminary findings of the PEACE trial suggest better outcomes in high volume mHSPC treated with docetaxel, abiraterone, and ADT [25]. Other limitations are inherent to a retrospective study, such as, working within the confines with the electronic medical records (EMR), evaluating real world data, and being unable to control all confounding factors in our analyses. Further study is needed to validate our findings in a larger population, with additional ethnicities, inclusive of all approved upfront therapies, and with a longer follow up time.

5. Conclusions

Elevated baseline basophils and BLR were associated with worse OS and PFS in a demographically diverse population of patients with mHSPC treated with upfront DOC or ABI. Our study is the first to identify baseline basophils and BLR as prognostic biomarkers. This is one of few studies evaluating biomarkers in mHSPC. Although our findings require further validation, basophils and BLR may have the potential to help guide prognostication in mHSPC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest:

M.A. Bilen has acted as a paid consultant for and/or as a member of the advisory boards of Exelixis, Bayer, BMS, Eisai, Pfizer, AstraZeneca, Janssen, Calithera Biosciences, Genomic Health, Nektar, and Sanofi and has received grants to his institution from Xencor, Bayer, Bristol-Myers Squibb, Genentech/Roche, Seattle Genetics, Incyte, Nektar, AstraZeneca, Tricon Pharmaceuticals, Genome & Company, AAA, Peloton Therapeutics, and Pfizer for work performed as outside of the current study.

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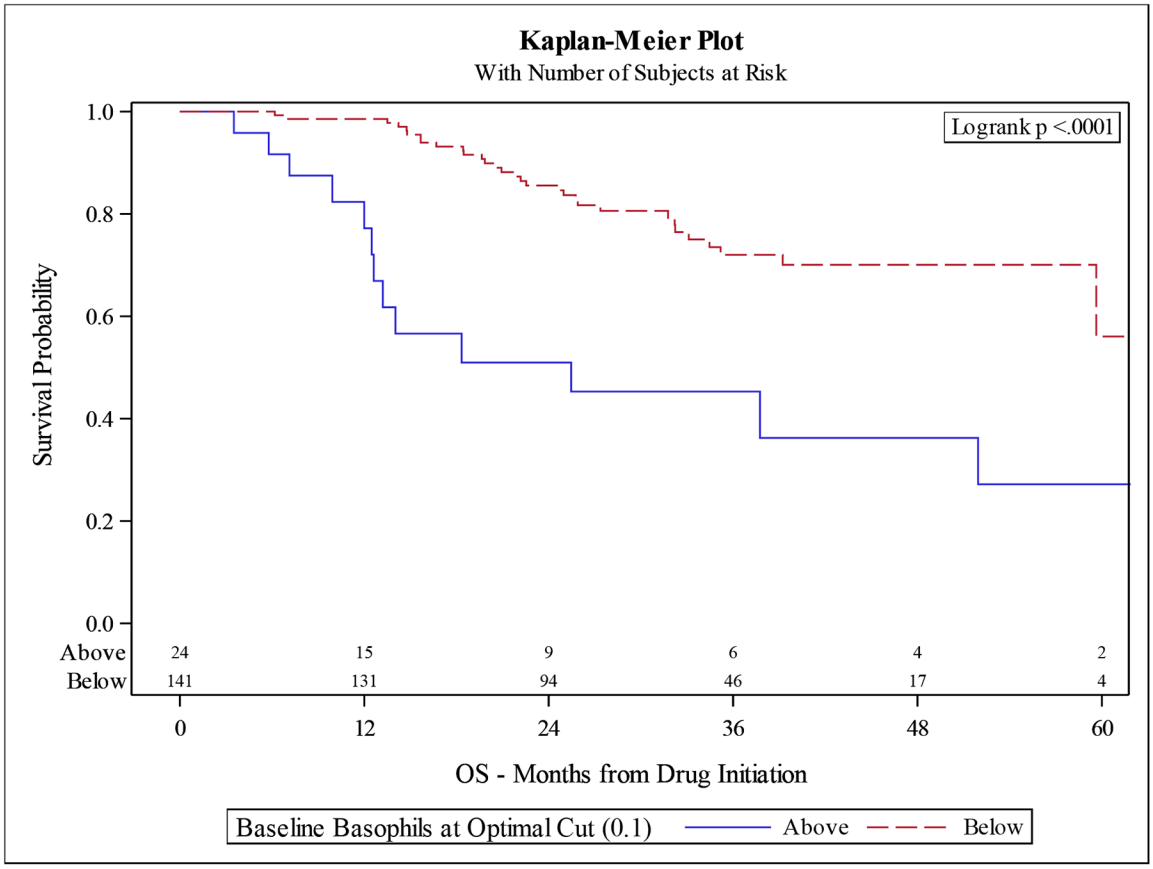
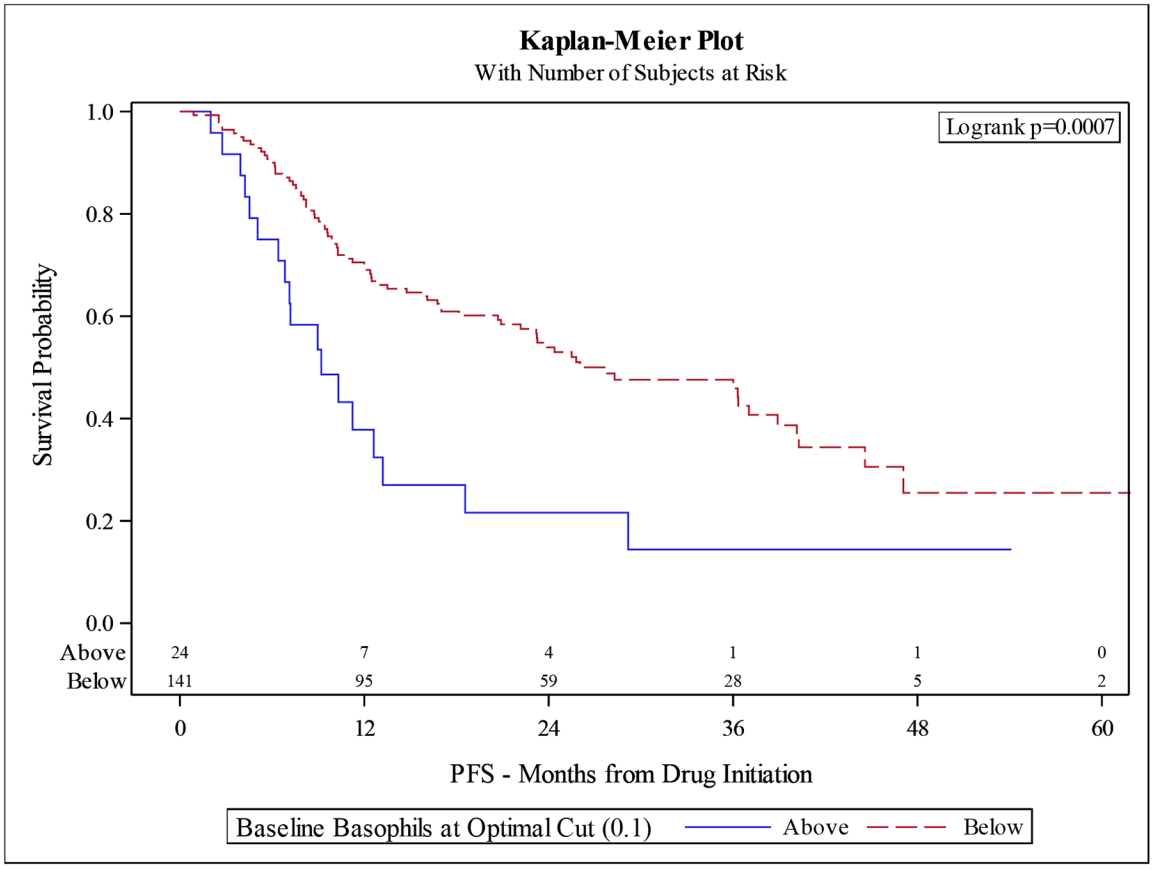
Highlights

- We found that metastatic hormone sensitive prostate cancer patients with high baseline basophils and basophil-to-lymphocyte ratios (BLR) had worse outcomes.
- Basophils ≥ 0.1 has a hazard ratio (HR) of 3.51 for OS and HR of 1.88 for PFS
- BLR ≥ 0.0142 has a HR 2.11 for OS. There was no significant difference for PFS.
- We conclude that basophils may help predict patient outcomes and could serve as a prognostic biomarker.



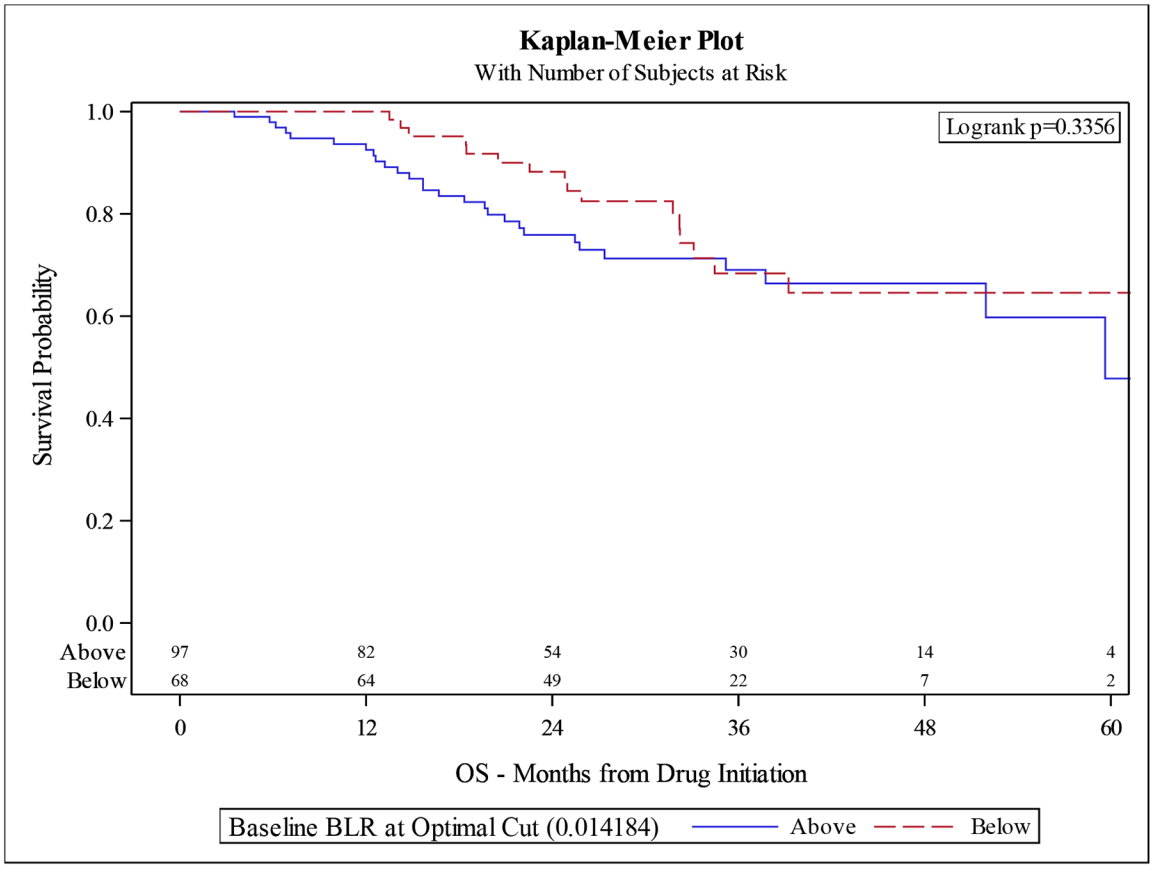
Baseline Basophils at Optimal Cut (0.1)	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	24 Mo Survival
Above	24	13 (54%)	11 (46%)	25.5 (12.5, NA)	77.2% (53.3%, 89.9%)	51.0% (27.7%, 70.2%)
Below	141	31 (22%)	110 (78%)	NA (59.6, NA)	98.6% (94.3%, 99.6%)	85.6% (78.0%, 90.7%)



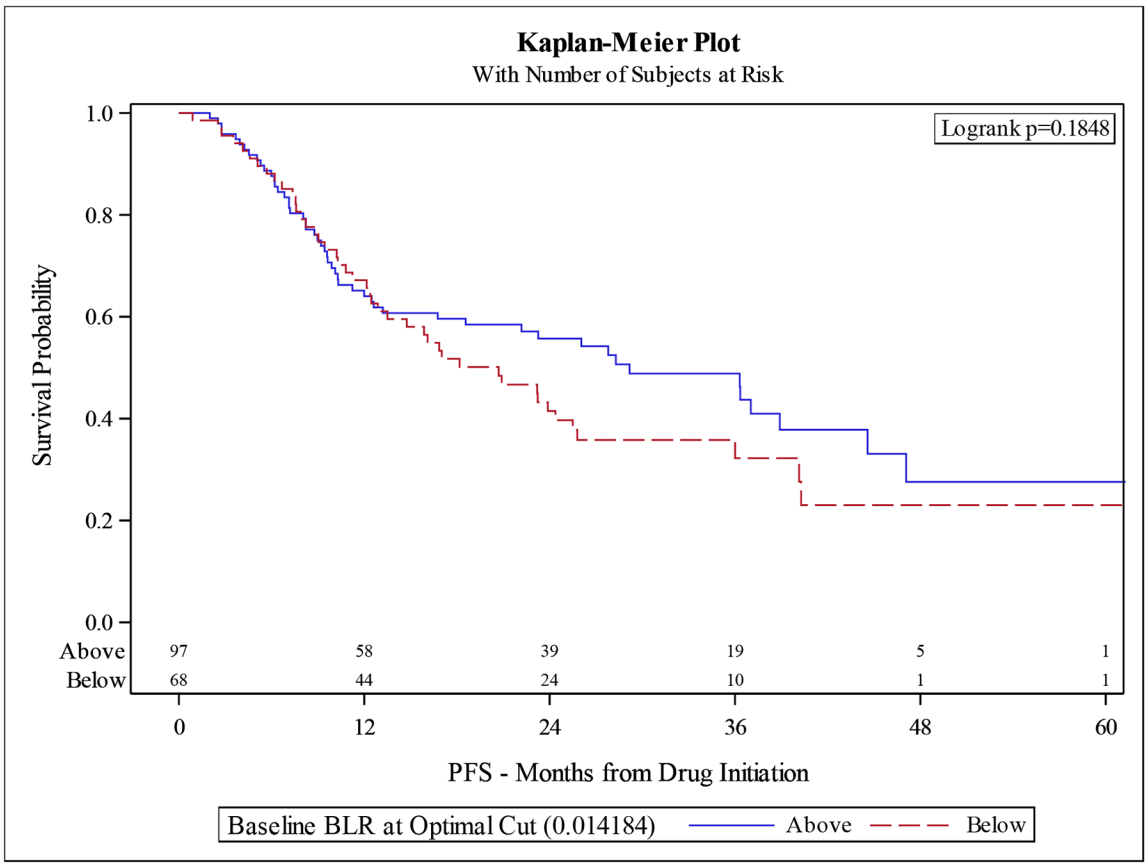
Baseline Basophils at Optimal Cut (0.1)	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	24 Mo Survival
Above	24	18 (75%)	6 (25%)	9.2 (6.4, 13.2)	37.8% (18.1%, 57.5%)	21.6% (7.0%, 41.3%)
Below	141	77 (55%)	64 (45%)	26.1 (20.9, 38.9)	69.8% (61.4%, 76.7%)	53.9% (45.0%, 62.0%)

Figure 1. Kaplan-Meier (KM) Plots for overall survival (OS) and progression free survival (PFS) for Baseline Basophils at Optimal Cut.

A) OS improved for patients with lower baseline basophils (p <0.0001). B) PFS improved for patients with lower baseline basophils (p 0.0007).



Baseline BLR at Optimal Cut (0.014184)	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	24 Mo Survival
Above	97	28 (29%)	69 (71%)	59.6 (51.9, NA)	92.5% (84.9%, 96.4%)	75.9% (65.4%, 83.6%)
Below	68	16 (24%)	52 (76%)	NA (39.2, NA)	100.0% (NA, NA)	88.2% (76.9%, 94.2%)



Baseline BLR at Optimal Cut (0.014184)	No. of Subject	Event	Censored	Median Survival (95% CI)	12 Mo Survival	24 Mo Survival
Above	97	51 (53%)	46 (47%)	29.2 (16.8, 44.6)	64.0% (53.4%, 72.8%)	55.7% (44.9%, 65.2%)
Below	68	44 (65%)	24 (35%)	20.7 (12.5, 25.5)	67.2% (54.6%, 77.0%)	41.5% (29.3%, 53.2%)

Figure 2. Kaplan-Meier (KM) Plots for overall survival (OS) and progression free survival (PFS) for Basophil-to-Lymphocyte Ratio (BLR) at Optimal Cut.

A) OS is not statistically different between BLR high vs low groups (p 0.3356). B) PFS is not statistically different based on BLR (p 0.1848).

Table 1.

Baseline Characteristics by Baseline BLR and Baseline Basophils at Optimal Cut.

		Baseline Basophils at optimal cut [Ψ]			Baseline BLR at optimal cut [Ω]		
Variable	**Level**	**Below N=68**	**Above N=97**	**p-value***	**Below N=141**	**Above N=24**	**p-value***
Drug under investigation	Docetaxel	76 (53.90)	16 (66.67)	0.244	38 (55.88)	54 (55.67)	0.978
	Abiraterone	65 (46.10)	8 (33.33)		30 (44.12)	43 (44.33)	
Race	Black	68 (48.23)	21 (87.50)	**<0.001**	51 (75.00)	38 (39.18)	**<0.001**
	Non-Black	73 (51.77)	3 (12.50)		17 (25.00)	59 (60.82)	
Age at diagnosis	<65	73 (51.77)	16 (66.67)	**0.176**	40 (58.82)	49 (50.52)	0.292
	>=65	68 (48.23)	8 (33.33)		28 (41.18)	48 (49.48)	
PSA at diagnosis at	Above	73 (52.9)	18 (75)	**0.044**	44 (64.71)	47 (50)	0.063
optimal cut 37.2 (ng/mL)	Below	65 (47.1)	6 (25)		24 (35.29)	47 (50)	
Total Gleason score	7	22 (15.60)	1 (4.17)	0.282	10 (14.71)	13 (13.4)	0.743
	8–10	89 (63.12)	16 (66.67)		41 (60.29)	64 (65.98)	
	Unknown	30 (21.28)	7 (29.17)		17 (25.00)	20 (20.62)	
ECOG at time of starting treatment [a]	0	71 (50.35)	4 (16.67)	0.002	29 (42.65)	46 (47.42)	0.829
	1	53 (37.59)	12 (50.00)		28 (41.18)	37 (38.14)	
	2	17 (12.06)	8 (33.33)		11 (16.18)	14 (14.43)	
Number of distant metastases [b]	0–1	41 (29.08)	3 (12.50)	0.090	20 (29.41)	24 (24.74)	0.504
	2–4+	100 (70.92)	21 (87.50)		48 (70.59)	73 (75.26)	
Disease volume [c]	High	90 (63.83)	18 (78.26)	0.176	50 (73.53)	58 (60.42)	0.081
	Low	51 (36.17)	5 (21.74)		18 (26.47)	38 (39.58)	

[a] Eastern Cooperative Oncology Group (ECOG) performance status, ranging from 0 to 5, with lower scores indicating better functionality.

[b] Number of anatomical locations (lymph nodes = 1, bone = 1, liver = 1, lung = 1, brain = 1)

[c] Disease volume is classified as high-volume disease based on CHAARTED criteria of visceral metastases or ≥ 4 bone lesions with ≥1 beyond axial skeleton

* The p-value is calculated by Chi-square test or Fisher's exact test, wherever appropriate.

[Ψ] "Below" defined as <0.1. "Above" defined as ≥0.1, with 0.1 being optimal cut.

[Ω] "Below" defined as <0.0142, "Above" defined as ≥ 0.0142, with 0.0142 being optimal cut

Table 2.

UVA for mOS in mHSPC Based on Baseline Lab Values.

Variable		N	Hazard Ratio (95% CI)‡	P-value*
Hgb Status (Normal: 12.9 – 16.1)	Abnormal	97	2.33 (1.18–4.62)	**0.015**
	Normal	68	-	-
Hgb at Optimal Cut (11.8)	Above	106	0.28 (0.15–0.51)	**<0.001**
	Below	59	-	-
Platelets Status (Normal: 150 – 400)	Abnormal	25	0.64 (0.25–1.63)	0.348
	Normal	140	-	-
Platelets at Optimal Cut (259)	Above	56	2.11 (1.17–3.82)	**0.013**
	Below	109	-	-
Neutrophils Status (Normal: 0.67 – 6.41)	Abnormal	18	1.33 (0.56–3.17)	0.513
	Normal	147	-	-
Neutrophils at Optimal Cut (3.08)	Above	102	1.04 (0.56–1.93)	0.897
	Below	63	-	-
Lymphocytes Status (Normal: 0.72 – 3.29)	Abnormal	26	1.05 (0.49–2.25)	0.910
	Normal	139	-	-
Lymphocytes at Optimal Cut (2.7)	Above	13	0.84 (0.29–2.44)	0.745
	Below	152	-	-
Monocytes Status (Normal: 0.14 – 0.71)	Abnormal	24	0.65 (0.26–1.66)	0.369
	Normal	141	-	-
Monocytes at Optimal Cut (0.53)	Above	57	1.25 (0.68–2.32)	0.472
	Below	108	-	-
Eosinophils Status (Normal: 0.05 – 0.29)	Abnormal	67	1.30 (0.72–2.36)	0.379
	Normal	98	-	-
Eosinophils at Optimal Cut (0.11)	Above	75	0.54 (0.29–1.02)	0.057
	Below	89	-	-
Basophils Status (Normal: 0 – 0.07)	Abnormal	29	3.20 (1.69–6.07)	**<0.001**
	Normal	136	-	-
Basophils at Optimal Cut (0.1)	Above	24	3.69 (1.91–7.12)	**<0.001**
	Below	141	-	-
NLR at Optimal Cut (1.67)	Above	121	0.94 (0.49–1.82)	0.864
	Below	44	-	-
NER at Optimal Cut (23)	Above	76	1.08 (0.55–2.10)	0.822
	Below	63	-	-
PLR at Optimal Cut (135.5)	Above	104	1.82 (0.93–3.55)	0.079
	Below	61	-	-
MLR at Optimal Cut (0.396)	Above	52	2.40 (1.31–4.39)	**0.005**
	Below	113	-	-

Variable		N	Hazard Ratio (95% CI)‡	P-value*
BLR at Optimal Cut (0.0142)	Above	97	1.35 (0.73–2.50)	0.338
	Below	68	-	-

* The p-value is calculated by Cox proportional hazard model; CI - 95% confidence interval.

Hgb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, NER = neutrophil-to-eosinophil ratio, PLR = platelet-to-lymphocyte ratio, MLR = monocyte-to-lymphocyte ratio, BLR = basophil-to-lymphocyte ratio

Table 3.

UVA for Progression Free Survival (PFS) in mHSPC Based on Baseline Lab Values.

Variable		N	Hazard Ratio (95% CI)‡	P-value*
Hgb Status (Normal: 12.9 – 16.1)	Abnormal	97	1.77 (1.15–2.71)	**0.010**
	Normal	68	-	-
Hgb at Optimal Cut (11.8)	Above	106	0.34 (0.23–0.51)	**<0.001**
	Below	59	-	-
Platelets Status (Normal: 150 – 400)	Abnormal	25	0.78 (0.43–1.40)	0.408
	Normal	140	-	-
Platelets at Optimal Cut (259)	Above	56	2.05 (1.36–3.08)	**<0.001**
	Below	109	-	-
Neutrophils Status (Normal: 0.67 – 6.41)	Abnormal	18	1.29 (0.70–2.36)	0.417
	Normal	147	-	-
Neutrophils at Optimal Cut (3.08)	Above	102	0.81 (0.54–1.22)	0.312
	Below	63	-	-
Lymphocytes Status (Normal: 0.72 – 3.29)	Abnormal	26	1.04 (0.62–1.76)	0.878
	Normal	139	-	-
Lymphocytes at Optimal Cut (2.7)	Above	13	2.07 (1.10–3.90)	**0.023**
	Below	152	-	-
Monocytes Status (Normal: 0.14 – 0.71)	Abnormal	24	0.87 (0.50–1.51)	0.617
	Normal	141	-	-
Monocytes at Optimal Cut (0.53)	Above	57	0.89 (0.57–1.37)	0.587
	Below	108	-	-
Eosinophils Status (Normal: 0.05 – 0.29)	Abnormal	67	1.39 (0.93–2.08)	0.109
	Normal	98	-	-
Eosinophils at Optimal Cut (0.11)	Above	75	0.58 (0.38–0.88)	**0.011**
	Below	89	-	-
Basophils Status (Normal: 0 – 0.07)	Abnormal	29	1.97 (1.20–3.25)	**0.007**
	Normal	136	-	-
Basophils at Optimal Cut (0.1)	Above	24	2.39 (1.42–4.01)	**0.001**
	Below	141	-	-
NLR at Optimal Cut (1.67)	Above	121	0.72 (0.47–1.12)	0.149
	Below	44	-	-
NER at Optimal Cut (23)	Above	76	1.35 (0.85–2.13)	0.199
	Below	63	-	-
PLR at Optimal Cut (135.5)	Above	104	1.55 (1.00–2.40)	**0.049**
	Below	61	-	-
MLR at Optimal Cut (0.396)	Above	52	1.52 (1.00–2.33)	0.052
	Below	113	-	-

Variable		N	Hazard Ratio (95% CI)‡	P-value*
BLR at Optimal Cut (0.0142)	Above	97	0.76 (0.51–1.14)	0.187
	Below	68	-	-

*The p-value is calculated by Cox proportional hazard model; CI - 95% confidence interval.

Hgb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, NER = neutrophil-to-eosinophil ratio, PLR = platelet-tolymphocyte ratio, MLR = monocyte-to-lymphocyte ratio, BLR = basophil-to-lymphocyte ratio

Table 4.

UVA and MVA of CO Associated with Baseline Basophils and BLR in mHSPC.

	UVA				MVA†			
	OS		PFS		OS		PFS	
	HR (CI‡)	p-value	HR (CI‡)	p-value	HR (CI‡)	p-value	HR (CI‡)	p-value
Basophils ≥ 0.1 (Above) vs. <0.1 (Below optimal cut)	3.69 (1.91–7.12)	**<0.001**	2.39 (1.42–4.01)	**0.001**	3.51 (1.65–7.43)	**0.001**	1.88 (1.05–3.38)	**0.034**
BLR ≥ 0.0142 (Above) vs. < 0.0142 (Below optimal cut)	1.35 (0.73–2.50)	0.338	0.76 (0.51–1.14)	0.187	2.11 (1.09–4.10)	**0.028**	0.87 (0.55–1.35)	0.526

†The MVA was built in Cox proportional hazard model by controlling for drug, race, age at diagnosis, disease volume, ECOG, and Gleason.

‡95% confidence interval

BLR = basophil-to-lymphocyte ratio