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Effect of chemotherapy in metastatic prostate cancer according to race/ethnicity groups

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Abstract

Background: No North-American study tested the survival benefit of chemotherapy in de novo metastatic prostate cancer according to race/ethnicity. We addressed this void.

Methods: We identified de novo metastatic prostate cancer patients within the Surveillance, Epidemiology, and End Results database (2014–2015). Separate and specific Kaplan–Meier plots and Cox regression models tested for overall survival differences between chemotherapy-exposed versus chemotherapy-naïve patients in four race/ethnicity groups: Caucasian versus African-American versus Hispanic/Latino

vs Asian. Race/ethnicity specific propensity score matching was applied. Here, additional landmark analysis was performed.

Results: Of 4232 de novo metastatic prostate cancer patients, 2690 (63.3%) were Caucasian versus 783 (18.5%) African-American versus 504 (11.8%) Hispanic/Latino versus 257 (6.1%) Asian. Chemotherapy rates were: 21.3% versus 20.8% versus 21.0% versus 20.2% for Caucasians versus African-Americans versus Hispanic/Latinos versus Asians, respectively. At 30 months of follow-up, overall survival rates between chemotherapy-exposed versus chemotherapy-naïve patients were 61.5 versus 53.2% (multivariable hazard ratio [mHR]: 0.76, 95 confidence interval [CI]: 0.63–0.92, $p = 0.004$) in Caucasians, 55.2 versus 51.6% (mHR: 0.76, 95 CI: 0.54–1.07, $p = 0.11$) in African-Americans, 62.8 versus 57.0% (mHR: 1.11, 95 CI: 0.73–1.71, $p = 0.61$) in Hispanic/Latinos and 77.7 versus 65.0% (mHR: 0.31, 95 CI: 0.11–0.89, $p = 0.03$) in Asians. Virtually the same findings were recorded after propensity score matching within each race/ethnicity group.

Conclusions: Caucasian and Asian de novo metastatic prostate cancer patients exhibit the greatest overall survival benefit from chemotherapy exposure. Conversely, no overall survival benefit from chemotherapy exposure could be identified in either African-Americans or Hispanic/Latinos. Further studies are clearly needed to address these race/ethnicity specific disparities.

KEYWORDS

chemotherapy, metastatic prostate cancer, race/ethnicity disparities

1 | INTRODUCTION

Survival in metastatic prostate cancer (mPCa), irrespectively of promising new systemic therapies, remains low.[1–6] To the best of our knowledge, no large scale, sufficiently-powered, North-American study examined the effect of race/ethnicity on overall survival benefit from chemotherapy in de novo mPCa.[2,7–11] The effect of race/ethnicity was examined in few post hoc analyses of prospective randomized trials.[12] However, no prospective randomized trials examining the effect of systemic therapies on overall survival in de novo mPCa, relied on preplanned race/ethnicity stratification schemes.[13–15] Moreover, the proportions of race/ethnicity groups other than Caucasian, were small, and so were the actual numbers of included patients from race/ethnicity groups other than Caucasians.[12] Taken together, it is unknown, whether North-American race/ethnicity groups other than Caucasians, benefit of systemic chemotherapy. We addressed these knowledge gaps in the current analysis. Specifically, we hypothesized that chemotherapy in de novo mPCa is associated with similar benefits across all race/ethnicity groups. We tested this hypothesis relying on the Surveillance, Epidemiology, and End Results (SEER) database (2014–2015).

2 | MATERIALS AND METHODS

2.1 | Study population

The current SEER database samples 34.6% of the US population and approximates it in demographic composition and cancer incidence.[16] Within the SEER database (2014–2015), we identified patients ≥18 years old with de novo metastatic, histologically confirmed adenocarcinoma of the prostate, diagnosed at biopsy (International Classification of Disease for Oncology [ICD-O-3] code 8140 site code C61.9) between 2014 and 2015. Patients with unknown cM-stage, cases identified at autopsy or through death certificates, unknown histology or non-primary prostate cancers were excluded. The study focused on the four most prevalent race/ethnicity groups (Caucasian, African-American, Hispanic/Latino, Asian). These selection criteria resulted in a cohort of eligible 4234 de novo mPCa patients.

2.2 | Statistical analyses

The statistical analyses consisted of four steps. First, we addressed overall survival in separate and distinct analyses that addressed four

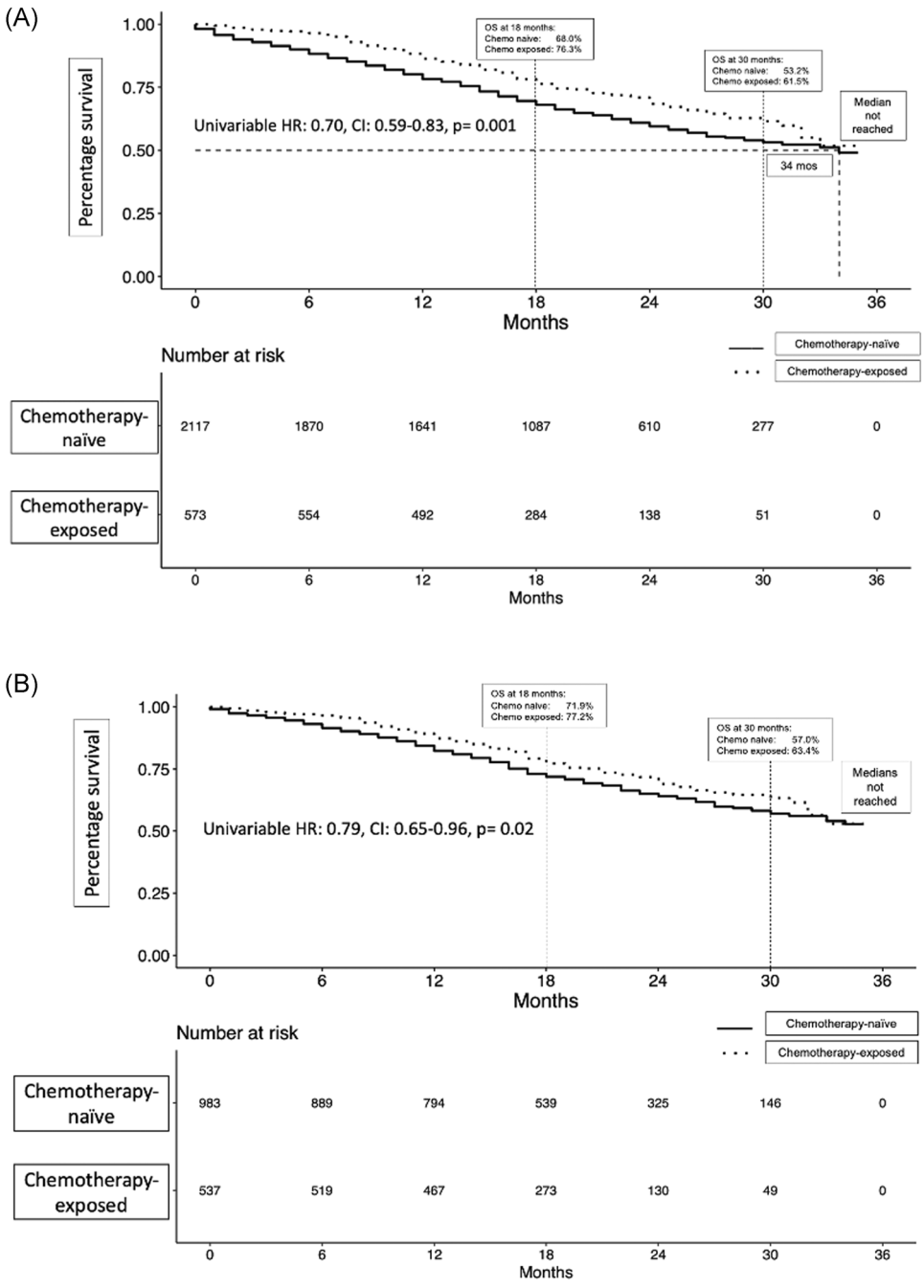

FIGURE 1 Kaplan–Meier plots illustrating overall survival in 2690 Caucasian de novo metastatic prostate cancer patients (A) before propensity score matching and (B) in 1520 patients after propensity score matching, stratified by chemotherapy status

race/ethnicity groups: Caucasian, African-American, Hispanic/Latino, Asian. Within each race/ethnicity group-specific analysis, we relied on Kaplan–Meier plots and Cox regression models to test for overall survival differences according to chemotherapy status. Covariates consisted of age at diagnosis, PSA groups (<20, 20–90, >90 ng/ml), Gleason Grade group (GGG) at biopsy (≤IV, V, unknown), clinical M-stage (cM1a/b, cM1c) and local treatment (yes, no) for each race/ethnicity group separately.

Second within each race/ethnicity group, we separately relied on propensity score matching to address potential differences between chemotherapy-exposed versus chemotherapy-naïve patients. Propensity score matching variables consisted of age (per year interval), PSA (≤97, >97 ng/ml), GGG (≤IV, V, unknown), cT-stage (≤cT2, cT3/4, cTx), cN-stage (cN0, cN1, cNx), cM-stage (cM1a/b, cM1c, cM1unspecific) and local treatment (yes, no, unknown). Due to sample size limitations in Asian patients, propensity score matching variables consisted of age (per year

TABLE 1 Descriptive characteristics of 4234 metastatic prostate cancer patients between 2014 and 2015 stratified by race/ethnicity groups and chemotherapy exposure status

	Caucasian (*n* = 2690)			African-American (*n* = 783)			Hispanic/Latino (*n* = 504)			Asian (*n* = 257)		
	CT-naïve *n* = 2117 (78.7%)	CT-exposed *n* = 573 (21.3%)	*p* value	CT-naïve *n* = 620 (79.2%)	CT-exposed *n* = 163 (20.8%)	*p* value	CT-naïve *n* = 398 (79.0%)	CT-exposed *n* = 106 (21.0%)	*p* value	CT-naïve *n* = 205 (79.8%)	CT-exposed *n* = 52 (20.2%)	*p* value
Age in years median (IQR)	72 (65–80)	64 (59–71)	<0.001	65 (60–74)	61 (56–68)	<0.001	68 (61–77)	61 (55–68)	<0.001	70 (64–78)	64 (57–70)	<0.001
PSA-groups in ng/ml *n* (%)			0.3			0.025			0.4			0.2
low (<20)	507 (24%)	130 (23%)		92 (15%)	15 (9.2%)		73 (18%)	14 (13%)		46 (22%)	6 (12%)	
intermediate (20–90)	587 (28%)	146 (25%)		133 (21%)	26 (16%)		112 (28%)	28 (26%)		55 (27%)	17 (33%)	
high (>90)	1023 (48%)	297 (52%)		395 (64%)	122 (75%)		213 (54%)	64 (60%)		104 (51%)	29 (56%)	
GGG Biopsy *n* (%)			<0.001			0.12			0.2			0.6
I	26 (1.2%)	7 (1.2%)		16 (2.6%)	0 (0%)		6 (1.5%)	1 (0.9%)		3 (1.5%)	0 (0%)	
II	94 (4.4%)	8 (1.4%)		25 (4.0%)	5 (3.1%)		18 (4.5%)	1 (0.9%)		9 (4.4%)	1 (1.9%)	
III	163 (7.7%)	39 (6.8%)		41 (6.6%)	5 (3.1%)		36 (9.0%)	5 (4.7%)		16 (7.8%)	1 (1.9%)	
IV	400 (19%)	95 (17%)		108 (17%)	29 (18%)		82 (21%)	18 (17%)		45 (22%)	11 (21%)	
V	934 (44%)	313 (55%)		273 (44%)	80 (49%)		154 (39%)	45 (42%)		93 (45%)	29 (56%)	
Unknown	500 (24%)	111 (19%)		157 (25%)	44 (27%)		102 (26%)	36 (34%)		39 (19%)	10 (19%)	
cT-stage *n* (%)			0.2			>0.9			0.2			0.8
cT1	569 (27%)	159 (28%)		193 (31%)	49 (30%)		127 (32%)	24 (23%)		58 (28%)	14 (27%)	
cT2	631 (30%)	173 (30%)		156 (25%)	40 (25%)		101 (25%)	32 (30%)		48 (23%)	14 (27%)	
cT3	247 (12%)	69 (12%)		52 (8.4%)	13 (8.0%)		43 (11%)	10 (9.4%)		16 (7.8%)	6 (12%)	
cT4	257 (12%)	84 (15%)		96 (15%)	27 (17%)		36 (9.0%)	15 (14%)		34 (17%)	6 (12%)	
cTx	413 (20%)	88 (15%)		123 (20%)	34 (21%)		91 (23%)	25 (24%)		49 (24%)	12 (23%)	
cN-stage *n* (%)			<0.001			0.013			0.040			0.4
cN0	1,136 (54%)	259 (45%)		338 (55%)	75 (46%)		203 (51%)	40 (38%)		105 (51%)	24 (46%)	
cN1	655 (31%)	258 (45%)		202 (33%)	73 (45%)		130 (33%)	47 (44%)		63 (31%)	21 (40%)	
cNx	326 (15%)	56 (9.8%)		80 (13%)	15 (9.2%)		65 (16%)	19 (18%)		37 (18%)	7 (13%)	
cM-stage *n* (%)			0.004			0.11			0.2			0.6
M1a	170 (8.0%)	27 (4.7%)		47 (7.6%)	13 (8.0%)		39 (9.8%)	5 (4.7%)		13 (6.3%)	3 (5.8%)	
M1b	1617 (76%)	434 (76%)		443 (71%)	109 (67%)		283 (71%)	75 (71%)		156 (76%)	36 (69%)	

(Continues)

TABLE 1 (Continued)

	Caucasian (*n* = 2690)			African-American (*n* = 783)			Hispanic/Latino (*n* = 504)			Asian (*n* = 257)		
	CT-naïve *n* = 2117 (78.7%)	CT-exposed *n* = 573 (21.3%)	*p* value	CT-naïve *n* = 620 (79.2%)	CT-exposed *n* = 163 (20.8%)	*p* value	CT-naïve *n* = 398 (79.0%)	CT-exposed *n* = 106 (21.0%)	*p* value	CT-naïve *n* = 205 (79.8%)	CT-exposed *n* = 52 (20.2%)	*p* value
M1c	283 (13%)	102 (18%)		107 (17%)	39 (24%)		67 (17%)	25 (24%)		33 (16%)	12 (23%)	
M1x	47 (2.2%)	10 (1.7%)		23 (3.7%)	2 (1.2%)		9 (2.3%)	1 (0.9%)		3 (1.5%)	1 (1.9%)	
Local treatment *n* (%)			0.4			0.6			0.4			0.5
None	1502 (71%)	417 (73%)		449 (72%)	112 (69%)		284 (71%)	77 (73%)		150 (73%)	44 (85%)	
RP	62 (2.9%)	10 (1.7%)		11 (1.8%)	1 (0.6%)		11 (2.8%)	0 (0%)		4 (2.0%)	0 (0%)	
RT	415 (20%)	114 (20%)		118 (19%)	37 (23%)		85 (21%)	22 (21%)		37 (18%)	5 (9.6%)	
RP + RT	93 (4.4%)	24 (4.2%)		26 (4.2%)	9 (5.5%)		10 (2.5%)	3 (2.8%)		9 (4.4%)	2 (3.8%)	
Unkown	45 (2.1%)	8 (1.4%)		16 (2.6%)	4 (2.5%)		8 (2.0%)	4 (3.8%)		5 (2.4%)	1 (1.9%)	

Note: All values are median (IQR) or frequencies (percentage).

Abbreviations: CT, chemotherapy; GGG, Gleason Group Grade; IQR, interquartile range; RP, radical prostatectomy; RT, radiotherapy.

interval), PSA (≤97, >97 ng/ml), GGG (≤IV, V, unknown), cT-stage (≤cT2, cT3/4, cTx), cM-stage (cM1a/b, cM1c, cM1unspecific) and local treatment (yes, no, unknown). Each chemotherapy exposed patient was matched with one chemotherapy naïve patient within each race group. The exception consisted of Caucasians, in which one chemotherapy-exposed patient was matched with two chemotherapy-naïve patients.

Third, after propensity score matching, all Kaplan–Meier plots and Cox regression models were separately refitted within the four separate and distinct race/ethnicity groups: Caucasian, African-American, Hispanic/Latino, Asian. The same covariates as above were used.

Finally, survival analyses were repeated in propensity score matched cohorts after landmark analysis (3 months) was applied.

3 | RESULTS

3.1 | Descriptive characteristics

Between 2014 and 2015, we identified 4234 de novo mPCa patients. Of those, 2690 (63.3%) were Caucasian, 783 (18.5%) were African-American, 504 (11.8%) were Hispanic/Latino and 257 (6.1%) were Asian. Chemotherapy rates were: 21.3% (*n* = 573), 20.8% (*n* = 163), 21.0% (*n* = 106), 20.2% (*n* = 52) for the four race/ethnicity groups: Caucasian, African-American, Hispanic/Latinos and Asian.

In general, chemotherapy-exposed patients differed from their chemotherapy-naïve counterparts with respect to younger age: Caucasian (64 vs. 72 years, $p < 0.001$), African-American (61 vs. 65 years, $p < 0.001$), Hispanic/Latino (61 vs. 68 years, $p < 0.001$), Asian (64 vs. 70 years, $p < 0.001$) (Figure 1). Similarly, chemotherapy-exposed Caucasians, African-Americans and Hispanic/Latinos also harbored higher proportions of clinical N1-stage (45% vs. 31%, $p < 0.001$; 45% vs. 33%, $p = 0.013$; 44% vs. 33%, $p = 0.040$) compared to their chemotherapy-naïve counterparts. Race/ethnicity specific differences were also identified. For example, chemotherapy-exposed Caucasians harbored higher proportions of GGG V (55% vs. 44%, $p < 0.001$) and higher proportions of cM1c-stage (18% vs. 13%, $p = 0.004$) compared to their chemotherapy-naïve counterparts. Furthermore, higher proportions of PSA >90 ng/ml only applied to chemotherapy-exposed African-American (75% vs. 64%, $p = 0.025$), compared to their chemotherapy-naïve counterparts. Finally, unlike other race/ethnicity groups, no significant differences were recorded among chemotherapy-exposed and chemotherapy-naïve Asian patients (Table 1).

3.2 | Overall survival in Caucasian race/ethnicity

Unmatched analyses compared 573 chemotherapy-exposed versus 2117 chemotherapy-naïve Caucasian patients. At 30 months of follow-up, overall survival rates were 61.5 versus 53.2%, favoring chemotherapy-exposed patients (Figure 1A), translating into a multivariable hazard ratio of 0.76 (confidence interval [CI]: 0.63–0.92, $p = 0.004$). Propensity score matched analyses resulted in 537 chemotherapy-exposed versus 983 chemotherapy-naïve patients. No

statistically significant differences remained between two cohorts. At 30 months of follow-up, overall survival rates were 63.4 versus 57.0%, favoring chemotherapy-exposed patients (Figure 1B), translating into a multivariable hazard ratio of 0.77 (CI: 0.62–0.93, $p = 0.008$) (Table 2). The above results remained unchanged in propensity score matched cohorts following landmark analyses (multivariable hazard ratio: 0.80; CI: 0.65–0.98; $p = 0.03$).

3.3 | Overall survival in African-American race/ethnicity

Unmatched analyses compared 163 chemotherapy-exposed versus 620 chemotherapy-naïve African-American patients. At 30 months of follow-up, overall survival rates were 55.2 versus 51.6%, favoring chemotherapy-exposed patients (Figure 2A), translating into a multivariable hazard ratio of 0.76 (CI: 0.54–1.07, $p = 0.11$). Propensity score matched analyses resulted in 150 chemotherapy-exposed versus 150 chemotherapy-naïve patients. No statistically significant differences remained between the two cohorts. At 30 months of follow-up, overall survival rates were 56.3 versus 51.9%, favoring chemotherapy-exposed patients (Figure 2B), translating into a multivariable hazard ratio of 0.83 (CI: 0.55–1.26, $p = 0.37$) (Table 2).

3.4 | Overall survival in Hispanic/Latino race/ethnicity

Unmatched analyses compared 106 chemotherapy-exposed versus 398 chemotherapy-naïve Hispanic/Latino patients. At 30 months of follow-up, overall survival rates were 62.8 versus 57.0%, favoring chemotherapy-exposed patients (Figure 3A), translating into a multivariable hazard ratio of 1.11 (CI: 0.73–1.71, $p = 0.61$). Propensity score matched analyses resulted in 97 chemotherapy-exposed versus 97 chemotherapy-naïve patients. No statistically significant differences remained between the two cohorts. At 30 months of follow-up, overall survival rates were 62.7 versus 56.1%, favoring chemotherapy-exposed patients (Figure 3B), translating into a multivariable hazard ratio of 0.79 (CI: 0.48–1.32, $p = 0.37$) (Table 2).

3.5 | Overall survival in Asian race/ethnicity

Unmatched analyses compared 52 chemotherapy-exposed versus 205 chemotherapy-naïve Asian patients. At 30 months of follow-up, overall survival rates were 77.7 versus 65.0%, favoring chemotherapy-exposed patients (Figure 4A), translating into a multivariable hazard ratio of 0.31 (CI: 0.11–0.89, $p = 0.03$). Propensity score matched analyses resulted in 40 chemotherapy-exposed vs 40 chemotherapy-naïve patients. No statistically significant differences remained between the two cohorts. At 30 months of follow-up, overall survival rates were 79.8 versus 55.0%, favoring chemotherapy-exposed patients (Figure 4B), translating into a multivariable hazard ratio of 0.20 (CI: 0.06–0.71, $p = 0.01$) (Table 2). The above results remained unchanged in propensity score matched cohorts following landmark analyses (multivariable hazard ratio: 0.20; CI: 0.06–0.72; $p = 0.01$).

4 | DISCUSSION

We hypothesized that chemotherapy in mPCa is associated with similar benefits across all race/ethnicity groups. We tested this hypothesis within the SEER database between 2014 and 2015. We made several noteworthy findings.

TABLE 2 Race/ethnicity group specific uni- and multivariable Cox regression models predicting overall mortality in metastatic prostate cancer patients according to chemotherapy exposure before and after propensity score matching

	Univariable			Multivariable		
	Hazard ratio	95 CI	*p* value	Hazard ratio	95 CI	*p* value
Caucasian						
Unmatched data	0.70	0.59–0.83	0.001	0.76	0.63–0.92	0.004
PSM data	0.79	0.65–0.96	0.02	0.77	0.62–0.93	0.008
African-American						
Unmatched data	0.79	0.57–1.08	0.14	0.76	0.54–1.07	0.11
PSM data	0.80	0.53–1.20	0.29	0.83	0.55–1.26	0.37
HIspanic/Latino						
Unmatched data	0.93	0.62–1.38	0.70	1.11	0.73–1.71	0.61
PSM data	0.80	0.48–1.31	0.37	0.79	0.48–1.32	0.37
Asian						
Unmatched data	0.34	0.14–0.85	0.02	0.31	0.11–0.89	0.03
PSM data	0.21	0.06–0.72	0.01	0.20	0.06–0.71	0.01

Note: Cox regression models were adjusted for age, PSA, Gleason grade group, cM-stage and local treatment. Hazard Ratios indicate effect of chemotherapy exposure on overall mortality.

Abbreviations: CI, confidence interval; PSM, propensity-score matching.

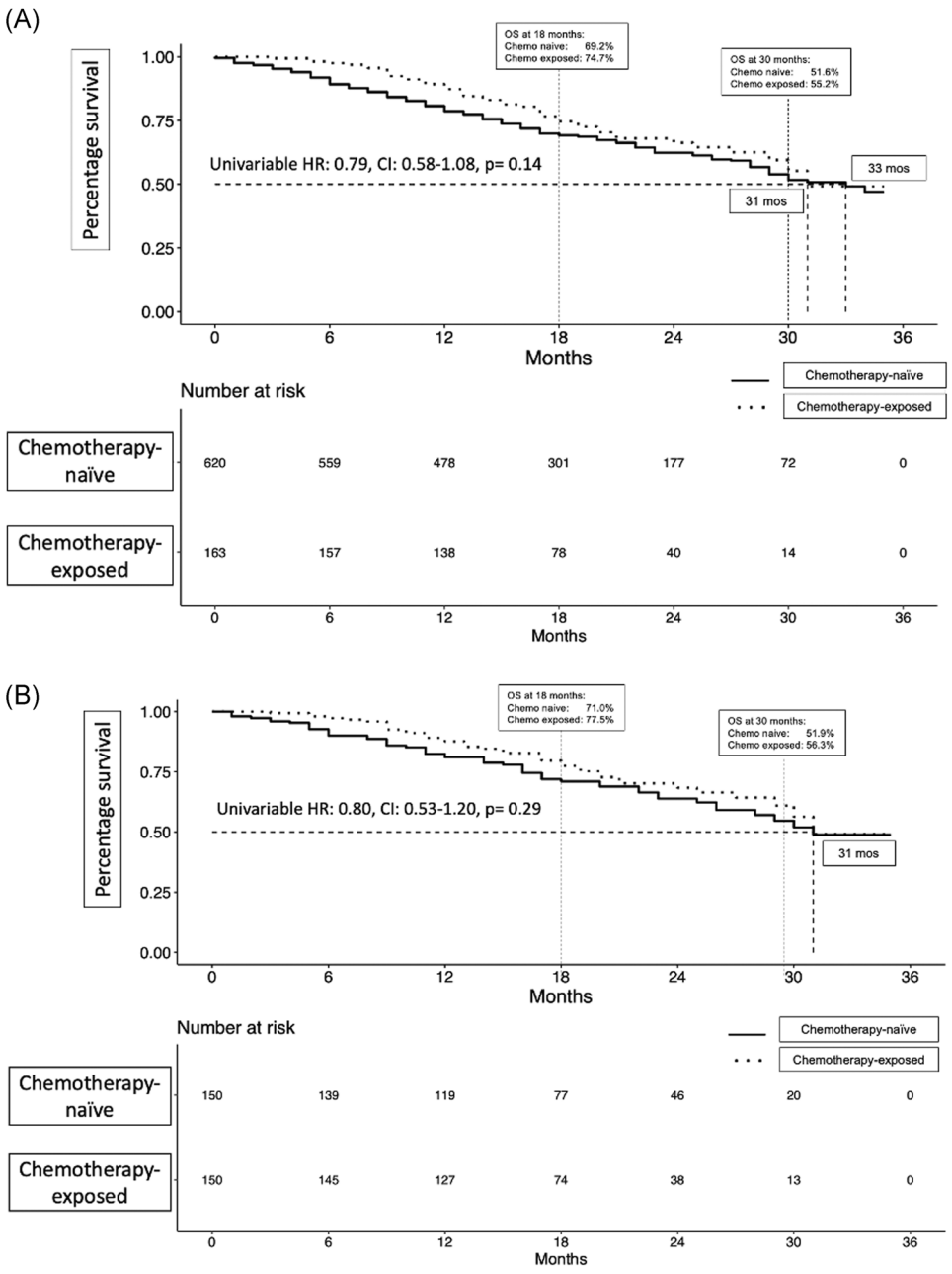

FIGURE 2 Kaplan–Meier plots illustrating overall survival in 783 African-American de novo metastatic prostate cancer patients (A) before propensity score matching and (B) in 300 patients after propensity score matching, stratified by chemotherapy status

First, the proportions and absolute numbers of patients identified within race/ethnicity groups other than Caucasian are small in prostate cancer and even smaller in numbers in mPCa.[17–20] The current analysis validates the difficulty in analyses addressing race/ethnicity specific differences. In mPCa, these difficulties related to small numbers of observations in African-American (n = 738), Hispanic/Latino (n = 257) and Asian (n = 257) patients relative to a large contingent of Caucasians (n = 2690). We relied on the second largest North-American, epidemiological database (SEER).[16] Relative to SEER, only one similar observational database, namely the National Cancer Database (NCDB), can provide larger absolute numbers. The same sample size limitations, that apply to race/ethnicity groups other than Caucasian, were operational in all mPCa trials, where very small proportions and very small absolute numbers of race/ethnicity groups other than Caucasian were included.[13,14,21] For example post hoc analyses of one of the largest phase 3 trials addressing systemic therapy in mPCa (CHAARTED) only enrolled 78 African-American, 38 Hispanic and 8 Asian patients.[12] These numbers were clearly

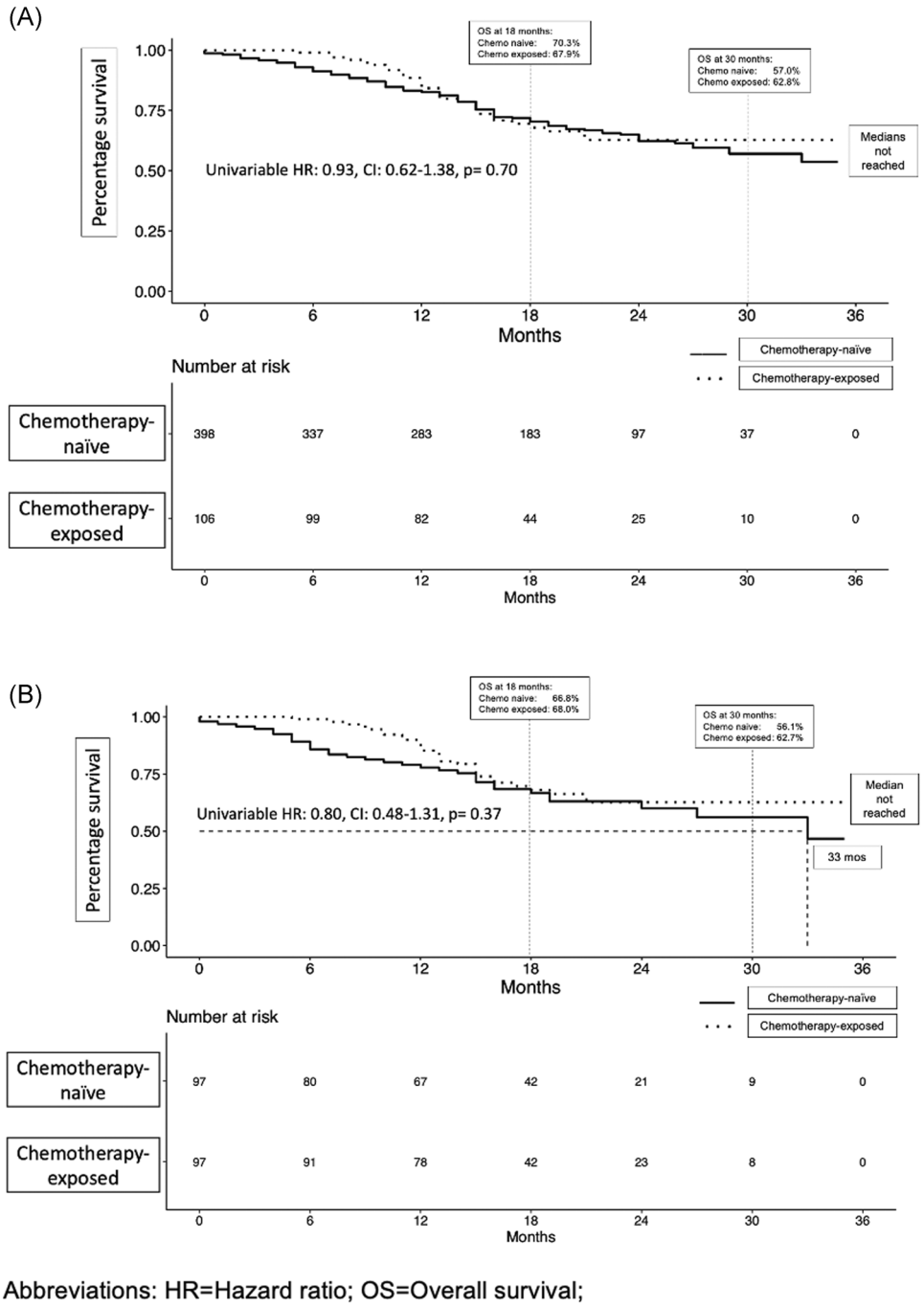

FIGURE 3 Kaplan–Meier plots illustrating overall survival in 504 Hispanic de novo metastatic prostate cancer patients (A) before propensity score matching and (B) in 194 patients after propensity score matching, stratified by chemotherapy status

insufficient to prospectively plan a stratification scheme that would allow specific race/ethnicity group analyses.[22] In consequence, few completed and reported phase 3 trials provided post hoc race/ethnicity stratified analyses.[12] Several others did not even include race/ethnicity in post hoc analyses.

Taken together, these observations emphasize important data gaps related to race/ethnicity when systemic chemotherapy for mPCa is considered.

Second, we relied on four race/ethnicity group specific analyses testing the effect of chemotherapy on overall survival in (1) Caucasian, (2) African-American, (3) Hispanic/Latino and (4) Asian mPCa patients. Within three race/ethnicity groups (Caucasian, African-American, Hispanic/Latino) we observed a more aggressive prostate cancer phenotype in chemotherapy-exposed patients than in their chemotherapy-naïve counterparts. Based on these race/ethnicity prostate cancer phenotype differences, our analyses relied on

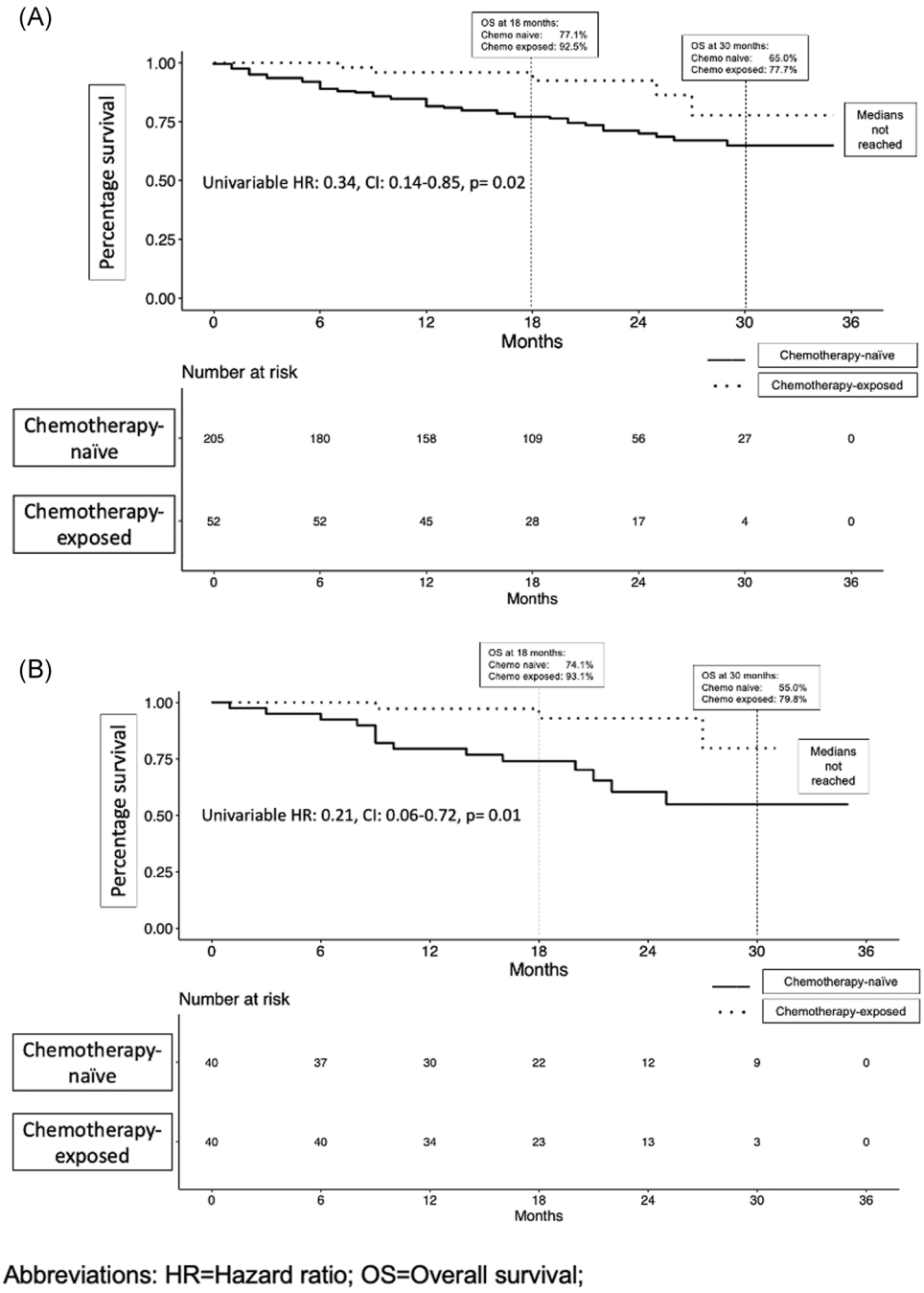

FIGURE 4 Kaplan–Meier plot illustrating overall survival in 257 Asian de novo metastatic prostate cancer patients (A) before propensity score matching and (B) in 80 patients after propensity score matching, stratified by chemotherapy status

propensity score matched data to maximally reduce the differences in age and prostate cancer characteristics between chemotherapy-exposed versus chemotherapy-naïve prostate cancer patients, within each specific race/ethnicity group.

Third, in both unmatched, as well propensity score matched analyses, we recorded statistically significantly lower overall mortality in Caucasians, who represent the largest race/ethnicity group. It is also noteworthy, that statistically significantly lower overall mortality was also recorded in Asians, who represent the smallest race/ethnicity group. These observations indicate two important facts. Chemotherapy-exposure is associated with a potential survival benefit in Caucasian and Asian patients with or without adjustment for patient and tumor characteristics differences. Specifically, the magnitude of overall mortality reduction was even stronger in matched Asian cohorts. Additionally, it is of utmost importance to note, that lower overall mortality, that was recorded in chemotherapy-exposed patients, was documented in equally important degree in the numerically smallest, Asian race/ethnicity group. In consequence, despite most important sample size and power limitations that apply to Asian race/ethnicity group, the effect of chemotherapy and lower

overall mortality rates in chemotherapy-exposed patients could be documented with high degree of statistically significance, in both matched and unmatched analyses. These observations regarding Asian mPCa patients are in agreement with previous reports.[23–25] It is of utmost importance to note, that the effect of chemotherapy was not associated with lower overall mortality in African-Americans (second largest race/ethnicity group), as well as in Hispanic/Latinos (third largest race/ethnicity group).

Taken together, our results indicate, that the recorded lack of overall survival benefit associated with chemotherapy administration in African-American and Hispanic/Latino patients cannot be solely attributed to sample size or power consideration, since a strong overall survival benefit was recorded in a much smaller patient subgroup (Asian). Clinical implications of the above findings clearly indicate that prospective analyses addressing chemotherapy benefit in African-American and Hispanic/Latino patients are urgently needed. In absence of such data in the foreseeable future, additional retrospective epidemiological analyses mirroring the current study should be carried out. The NCDB represents an ideal data pool to carry out such analysis with the intent of validating or refusing our analysis.

Several limitations applied to our study. First, the rate of chemotherapy exposure is low in the current study. It is nonetheless very similar to the rate observed in other large-scale population-based studies.[18,26] Moreover, the nature of administered chemotherapy and adherence is unknown with respect to its type, number of lines, overall duration as well as, individual efficacy of used regimens. Moreover, SEER does not provide information regarding concomitant medication such as antiandrogen deprivation therapy. This limitation is shared with other population-based data examining chemotherapy effects and should be interpretated accordingly.[26–28] Second, the retrospective nature of the study introduces a number of selection biases, that distinguish chemotherapy exposed patients from others. Differences in patient and clinicopathological features that were not captured by SEER may have influenced the current findings. Moreover, as reported, chemotherapy-exposed patients tended to harbor more aggressive prostate cancer phenotypes. To address these biases multivariable analyses were complemented by propensity score matching, to more completely and strictly address these differences. Third, patient numbers, especially for Asians were low. Finally, a number of established predictors of survival (lactate dehydrogenase, hemoglobin) for mPCa patients were unavailable in both the current as well as other population-based studies that include the NCDB.[29,30]

5 | CONCLUSIONS

De novo mPCa Caucasian and Asian race/ethnicity patients exhibit higher overall survival, when exposed to chemotherapy. Conversely, these observations could not be made for African-American and Hispanic/Latino patients. Since we observed significant improved overall survival in the largest and smallest race/ethnicity subgroup, lack of improved overall survival in the second and third subgroup is unlikely related to sample size limitations.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Benedikt Hoeh: conceptualization, formal analysis, writing—original draft. **Christoph Würnschimmel**: methodology, formal analysis. **Rocco Simone Flammia**: visualization, formal analysis. **Benedikt Horlemann**: validation, visualization. **Gabriele Sorce**: methodology, validation. **Francesco Chierigo**: methodology. **Zhe Tian**: methodology, software. **Fred Saad**: project administration, writing—review and editing. **Markus Graefen**: supervision, project administration. **Michele Gallucci**: project administration. **Alberto Briganti**: writing—review and editing. **Carlo Terrone**: writing—review and editing. **Shahrokh F. Shariat**: writing—review and editing. **Derya Tilki**: supervision, visualization, formal analysis. **Luis A. Kluth**: supervision, writing—review and editing. **Philipp Mandel**: supervision, writing—review and editing. **Felix K.H. Chun**: conceptualization, project administration. **Pierre I. Karakiewicz**: conceptualization, project administration, formal analysis, writing—original draft.

ETHICS STATEMENT

All analyses and their reporting followed the SEER reporting guidelines. Due to the anonymously coded design of the SEER database, study-specific Institutional Review Board ethics approval was not required.

DATA AVAILABILITY STATEMENT

All data generated for this analysis were from the SEER database. The code for the analyses will be made available upon request.

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