Overall Survival Analysis of African American and Caucasian Patients Receiving Sipuleucel-T

Presented by: Stephen J. Freedland, MD

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Disclosures

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Racial Differences in Outcomes for Men With PC

- AA men present with aggressive PC[1-5]
  - Higher incidence
  - More advanced disease
  - More disease progression risk
  - More PC-related mortality
  - Unequal healthcare access

AA = African American; CAU = Caucasian; mCRPC = metastatic castration-resistant prostate cancer; OS = overall survival; PC = prostate cancer.

1. Siegel, et al. *CA Cancer J Clin*. 2017;67:7-30. 2. Ahaghotu, et al. *Clin Genitourin Cancer*. 2016;14:105-116. 3. SEER Database. Accessed: March 12, 2017. 4. Aizer, et al. *Cancer*. 2014;120:1532-1539. 5. Di Pietro, et al. *Int Neurourol J*. 2016;20:S112-119.

Race and Inflammation

- AA men more frequently have diseases linked with inflammation
  - Diabetes
  - Heart Disease
  - Hypertension
- AA men have greater inflammatory gene expression in their prostate tumors

AA = African American

Inflammation and Prostate Cancer

- Many studies show inflammation in early stage disease is linked with increased prostate cancer risk and progression
- Yet, we use immunotherapy as treatment for late stage disease

- Inflammation = bad and AA men have more inflammation:
  - Question: Does the greater inflammation in AA men explain the more aggressive prostate cancer
- Inflammation = good and AA men have more inflammation:
  - Question: Can we harness this greater inflammation to better treat prostate cancer in AA men?

AA = African American

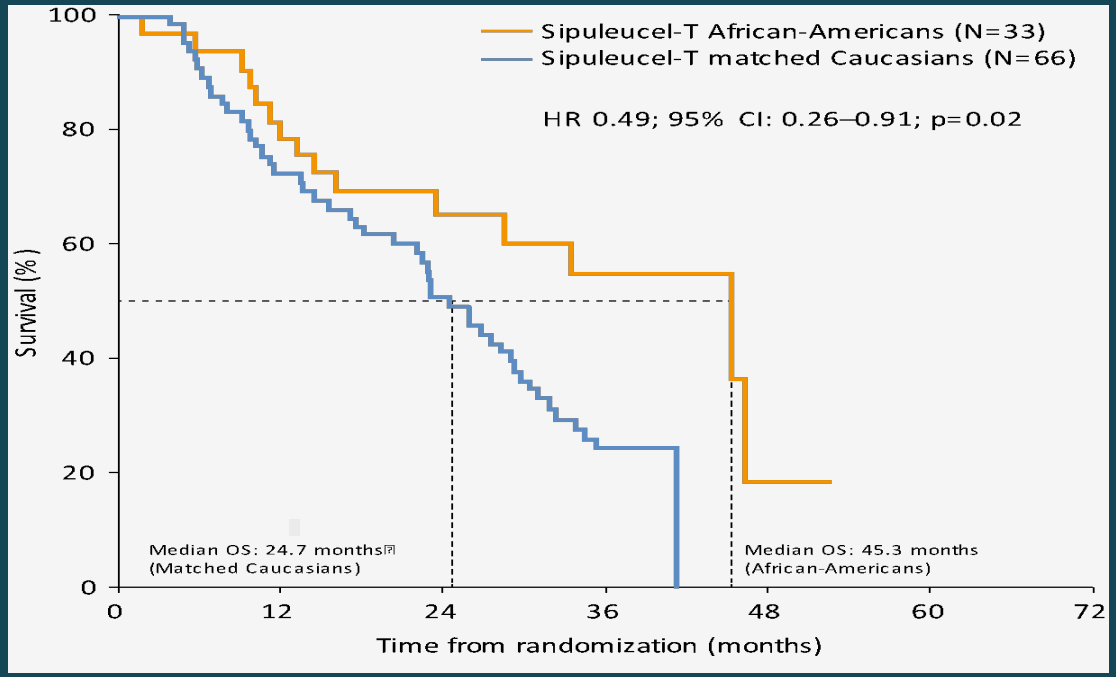
Methods of Data from Legacy mCRPC Trials

- Three, phase 3 trials of randomized patients with asymptomatic (D9901 and D9902A)[1] or asymptomatic/minimally symptomatic (IMPACT)[2] mCRPC were evaluated
- Based on Halabi-predicted survival, 66 sipuleucel-T-treated CAU men with mCRPC were matched with 33 sipuleucel-T-treated AA patients[3]

1. Higano CS, et al. Cancer 2009;115:3670–9.
2. Kantoff PW, et al. N Engl J Med 2010;363:411–22.
5. Halabi S, et al. J Clin Oncol 2014;671–7.

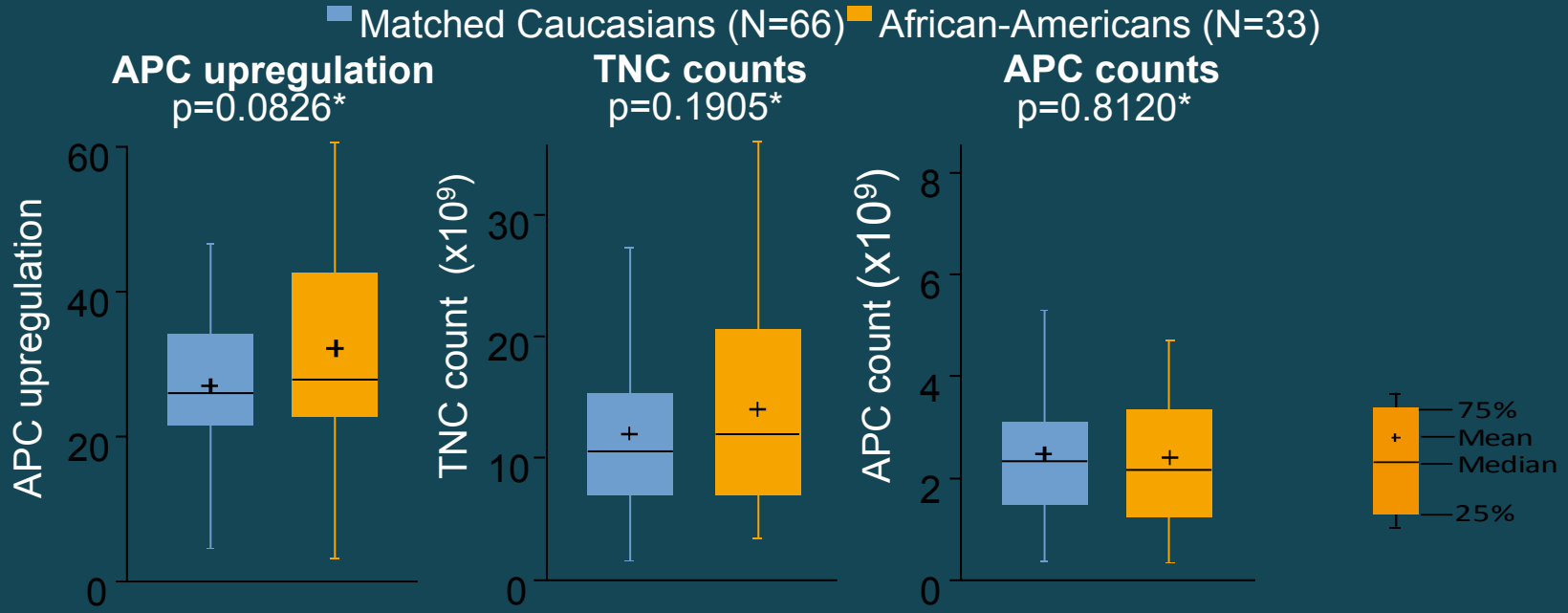
AA = African American; CAU = Caucasian; mCRPC = metastatic castration-resistant prostate cancer

Prolonged Survival of African-American Patients Treated with Sipuleucel-T vs Matched Caucasian Patients



HR and 95% CI obtained using Cox proportional hazards regression

Cumulative Sipuleucel-T Product Parameters for African-American Patients vs Matched Caucasian Patients



*An analysis of variance model

APC = antigen-presenting cell; TNC = total nucleated cell

The PROCEED Registry: Real-World Sipuleucel-T Use

- PROCEED (NCT01306890) enrolled >1900 real-world mCRPC patients receiving sipuleucel-T (2011-2013)
- 12% AA patients enrolled
  - Allows prospective outcomes assessments AA vs CAU patients
- Analysis
  - CAU and AA patients (2:1) matched by baseline PSA[1]
  - OS
  - Quartile PSA subsets
  - Multivariate analysis for independent factors associated with OS

AA = African American; CAU = Caucasian; mCRPC = metastatic castration-resistant prostate cancer; OS = overall survival; PSA = prostate-specific antigen.

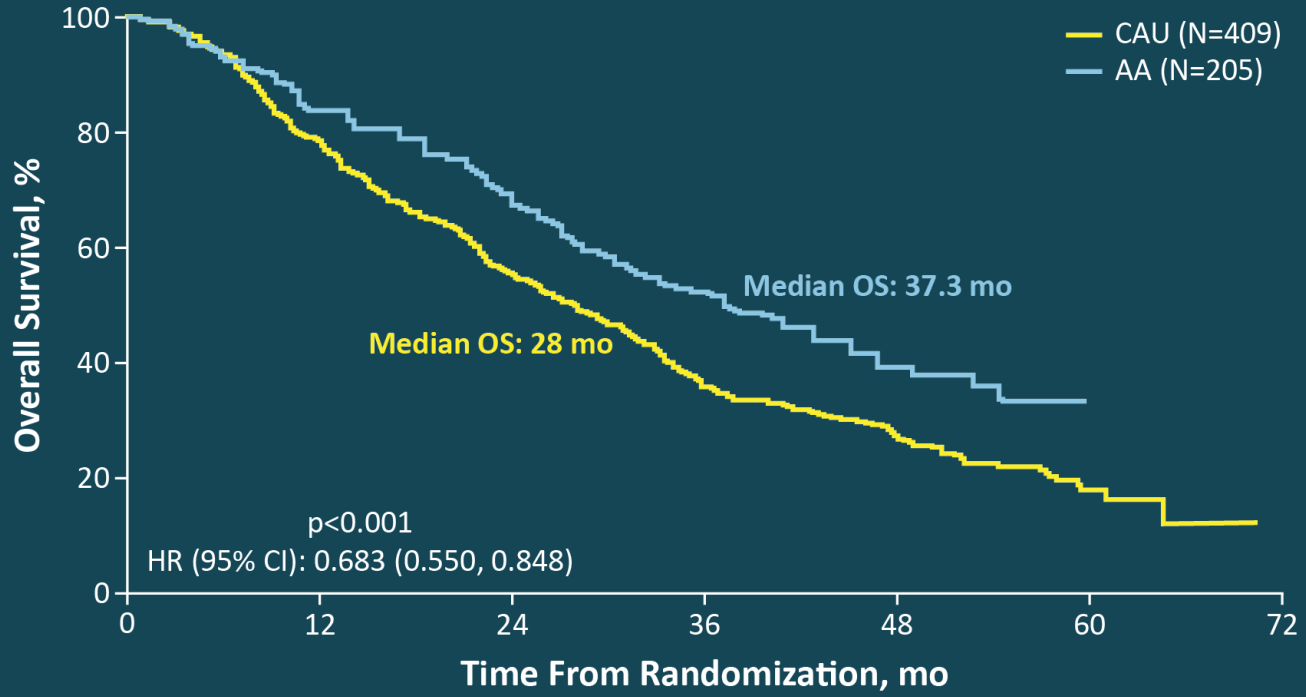
1. Schellhammer, et al. *Urology*. 2013;81:1297-1302.

Baseline Characteristics in a Matched Subset of PROCEED Patients

	Caucasian (n=420)	African American (n=210)	p-value*
Median age, y (range)	72 (48-93)	71 (42-94)	0.27
ECOG PS, n (%) **0** **1**	 300 (71) 107 (25)	 132 (63) 71 (34)	**0.01**
Worst Gleason sum, n (%) **≤7** **≥8**	 186 (44) 207 (49)	 89 (42) 97 (46)	0.45
Median PSA, ng/mL (IQR)	27.1 (7.2-68.3)	26.5 (8.0-69.4)	0.71
Median hemoglobin, g/dL (IQR)	13.0 (12.1-13.8)	12.1 (11.1-13.0)	**<0.001**
Median alkaline phosphatase, U/L (IQR)	81 (64-115)	87 (68-111)	0.14
Median LDH, U/L (IQR)	186 (155-211)	191 (170-233)	0.13
Prior local therapy, n (%)	326 (80)	149 (73)	**0.02**
Prior chemotherapy, n (%)	83 (20)	21 (10)	**<0.001**

ECOG PS = Eastern Cooperative Oncology Group performance score; IQR = interquartile range; LDH = lactate dehydrogenase; PSA = prostate-specific antigen.
*Wilcoxon rank sum test for continuous data and Trend test for categorical data.

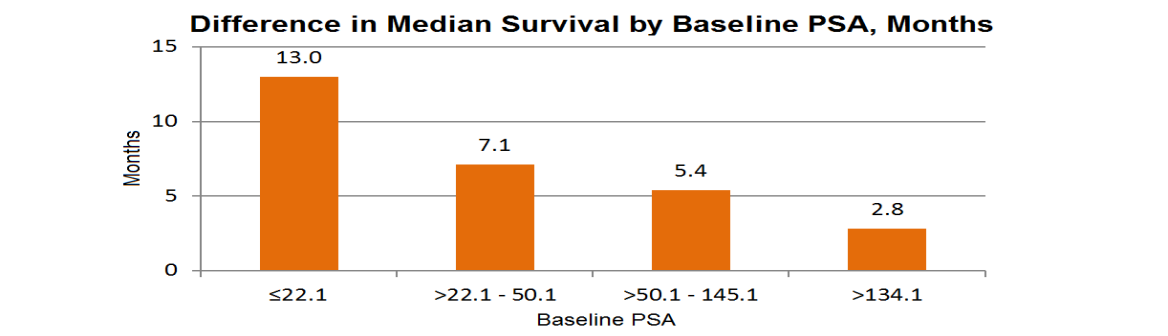
OS in a PSA-matched Subset of PROCEED Patients



- Estimated median follow-up: 57.2 months in CAUs and 45.0 months in AAs

AA = African American; CAU = Caucasian; CI = confidence interval; HR = hazard ratio; OS = overall survival; PSA = prostate-specific antigen.

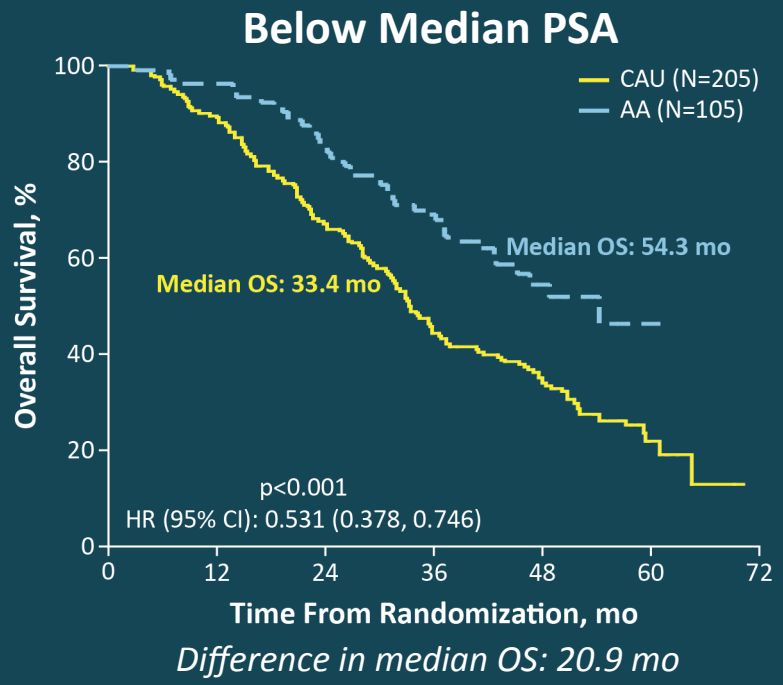
Sipuleucel-T Survival Benefit by PSA Quartile – IMPACT Trial



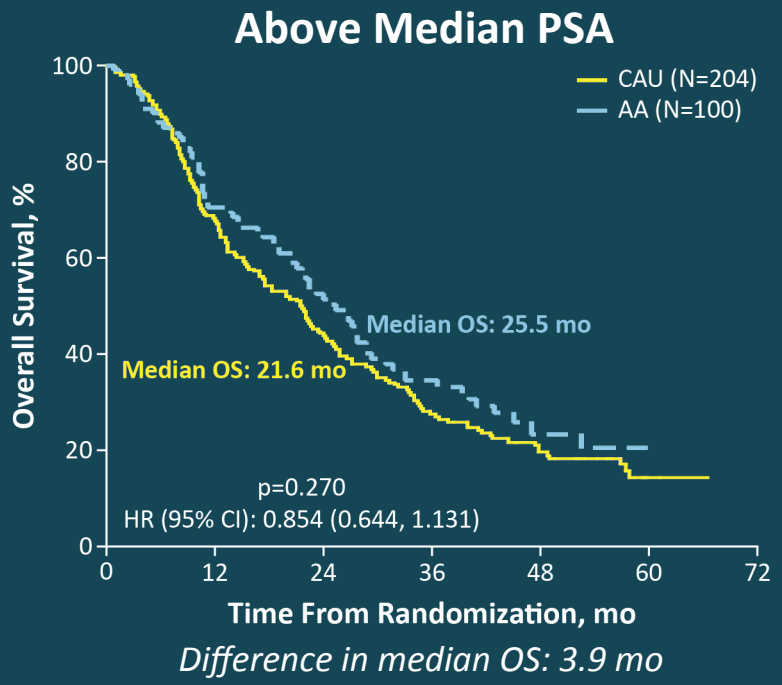
Overall Survival by Quartiles	Baseline PSA, ng/mL			
	≤22.1 (n=128)	>22.1-50.1 (n=128)	>501.-134.1 (n=128)	>134.1 (n=128)
Median OS, months				
Sipuleucel-T	41.3	27.1	20.4	18.4
Control	28.3	20.1	15.0	15.6
Difference, months	**13.0**	**7.1**	**5.4**	**2.8**
Hazard ratio	0.521	0.685	0.819	0.853
(95% CI	(0.309-0.879)	0.431-1.088)	0.532-1.262)	0.554-1.315)

Schellhammer, et al. *Urology*, 2013;81(6):1297-1302

Overall Survival in CAUs and AAs by Median PSA



Difference in median OS: 20.9 mo



Difference in median OS: 3.9 mo

- Median PSA: 26.8 ng/mL

AA = African American; CAU = Caucasian; CI = confidence interval; HR = hazard ratio; OS = overall survival; PSA = prostate-specific antigen.

Overall Survival in CAUs and AAs by PSA Quartiles

Overall Survival by PSA Quartiles	Baseline PSA, ng/mL			
	Q1 < 7.5	Q2 7.5-26.8	Q3 26.81-68.49	Q4 ≥68.5
Median OS, mo				
AA	54.3	46.7	28.7	20.5
CAU	37.4	31.9	22.0	18.3
Difference, mo	**16.9**	**14.8**	**6.7**	**2.2**
HR	0.442	0.602	0.800	0.913
(95% CI)	(0.260, 0.753)	(0.386, 0.939)	(0.537, 1.194)	(0.614, 1.360)
p-value	**0.003**	**0.025**	**0.275**	**0.655**

AA = African American; CAU = Caucasian; CI = confidence interval; HR = hazard ratio; OS = overall survival; PSA = prostate-specific antigen.

Independent Baseline Predictors of OS: Multivariate Analysis*

Covariate	Hazard Ratio (95% CI)	p-value
Prior chemotherapy (yes vs no)	1.46 (1.12, 1.90)	0.005
Age, y (>median vs ≤median)	1.45 (1.16, 1.80)	0.001
Alkaline phosphatase, U/L (>median vs ≤median)	1.64 (1.31, 2.05)	<0.001
Ethnicity (CAUs vs AAs)	1.58 (1.23, 2.04)	<0.001
Hemoglobin, g/dL (>median vs ≤median)	0.64 (0.51, 0.80)	<0.001
PSA, ng/mL (>median vs ≤median)	1.62 (1.29, 2.03)	<0.001

*Variables examined in multivariate analysis: age, ethnicity, ECOG performance score, prior chemotherapy, prior radiation, weight, PSA, alkaline phosphatase, hemoglobin, liver metastases, and practice setting.

AA = African American; CAU = Caucasian; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; OS = overall survival; PSA = prostate-specific antigen.

Conclusions

- Historically, AA PC patients fare worse in real world[1] and trials[2]
- These data strongly support an added OS benefit for sipuleucel-T treatment in AA patients
- AA race independently associated with better OS post–sipuleucel-T
- These findings contrast with historical poor outcomes for AA patients
  - A unique population for sipuleucel-T and other immunotherapies?
- Future research
  - Benefits of immunotherapies for AA men in other cancers
  - Immune response differences by race

AA = African American; OS = overall survival; PC = prostate cancer

1. Siegel, et al. *CA Cancer J Clin*. 2017;67:7-30. 2. Thompson, et al. *J Natl Cancer Inst*. 2001;93:219-225.

Acknowledgments

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