Race-Related Germline Polymorphisms in Key Androgen Transport Genes Among Black (B) and White (W) Men with Metastatic Castrate Resistant Prostate Cancer (mCRPC) Treated with Abiraterone Acetate plus Prednisone: Single Nucleotide Polymorphism Analyses from the Abi Race Trial

Megan A McNamara[1], Susan Halabi[1], Elisabeth I. Heath[2], A. Oliver Sartor[3], Guru Sonpavde[4], William R. Berry[5], Patrick Healy[1], Carolyn Winters[1], Colleen Riggan[1], Monika Anand[1], Julie Kephart[1], Matthew I. Milowsky[6], Mark T. Fleming[7], Tian Zhang[1], [8]Rhonda L. Bitting, Michael R Harrison[1], Jennifer A. Freedman[1], [9]Deborah Bruner, Andrew J. Armstrong[1], Daniel J. George[1].

[1]Duke Cancer Institute, Duke University, Durham, NC; [2]Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, MI; [3]Tulane Medical School, New Orleans, LA; [4]Dana-Farber Cancer Institute, Boston, MA; [5]Duke University School of Medicine, Raleigh, NC; [6]UNC School of Medicine, Chapel Hill, NC; [7]Virginia Oncology Associates, US Oncology Research, Norfolk, VA; [8]Wake Forest University Health Sciences, Winston Salem, NC; [9]Winship Cancer Institute at Emory University, Atlanta, GA

Background: Black (B) men have higher incidence, aggressiveness, and mortality from prostate cancer (PC) than men of other racial groups, even after accounting for differences in social and behavioral determinants of health. Germline polymorphisms in androgen metabolism genes, some of which vary in relative allelic frequency by ancestry, have prognostic value in regards to the time to development of castrate resistant prostate cancer (CRPC). The solute carrier organic anion (SLCO) genes are involved in steroid hormone transport across plasma membranes, potentially regulating the intracellular concentrations of androgen precursors that may account for relatively high intracellular androgen levels in CRPC. Single nucleotide polymorphisms (SNPs) in *SLCO2B1* and *SLCO1B3* have been correlated with a significantly *shorter* time to CRPC. Additionally, since abiraterone has a steroid backbone in its structure, *SLCO2B1* may regulate the efficacy of abiraterone.

Methods: We conducted a prospective, multicenter, parallel group study of abiraterone acetate (AA) plus prednisone (P) in 50 B and 50 white (W) men with mCRPC, self-identified by race (Abi Race (NCT01940276). All patients received AA 1000 mg/D and P 10 mg/D (AAP) until disease progression or adverse events (AE). The primary objective was radiographic progression-free survival (rPFS); key secondary endpoints include PSA kinetics and safety. Exploratory analyses include SNP, metabolomics and hormonal differences by race.

Results: Median rPFS for B and W pts was 16.8 months (mo) in each. PSA PFS varied by race; median PSA PFS for B and W pts were 16.6 and 11.5 mo. For *SLCO2B1* SNP rs12422149, 91.9% (n=34/37) of W pts were genotype BB and 8.1% (n=3/37) were AB, while 69.8% (n=30/43) of B pts were genotype BB, 27.9% (n=12/43) were AB, and 2.3% (n=1/43) were AA. The racial distribution of *SLCO1B3* SNP rs4149117 was 64.9% (n=24/37) BB, 32.4% (n=12/37) AB, and 2.7% (n=1/37) AA among W pts, compared to 20.9% (n=9/43) BB, 51.2% (n=22/43) AB, and 27.9% (n=12/43) AA among B pts.

Conclusions: We found that self-reported B with mCRPC were much more likely to have one or more A alleles in *SLCO2B1* SNP rs12422149 than W men. Similarly, 28% of B men were found to have the AA genotype in *SLCO1B3* SNP rs4149117, compared to < 5% of W, suggesting that ancestry correlates with genetic differences in these key androgen transport genes. Confirmation of these findings is planned in the similarly structured PANTHER study of AA plus apalutamide (NCT03098836). We will also use the combined Abi Race and PANTHER cohorts to perform an analysis of these SNPs, and others that are known to vary in minor allele frequency by ancestry and have previously been shown to associate with response to ADT, in order to determine if these SNPs also associate with response to second generation androgen-directed therapies.

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Conflict of Interest:

Megan A McNamara

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Susan Halabi

Consulting or Advisory Role - Bayer; Eisai; Tokai Pharmaceuticals

Travel, Accommodations, Expenses - Bayer

Elisabeth I. Heath

Honoraria - Bayer; Dendreon; Sanofi

Consulting or Advisory Role - Agensys

Speakers' Bureau - Sanofi

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A. Oliver Sartor

Consulting or Advisory Role - Advanced Accelerator Applications; AstraZeneca; Bavarian Nordic; Bayer; Bellicum Pharmaceuticals; Bristol-Myers Squibb; Celgene; Constellation Pharmaceuticals; Dendreon; EMD Serono; Endocyte; Johnson & Johnson; Oncogenex; Pfizer; Sanofi

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Guru Sonpavde

Honoraria - UpToDate

Consulting or Advisory Role - Agensys; Amgen; Argos Therapeutics; AstraZeneca; Bayer; Bristol-Myers Squibb; Eisai; Exelixis; Genentech; Janssen; Merck; Novartis; Pfizer; Sanofi

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Other Relationship - AstraZeneca; Boehringer Ingelheim

William R. Berry

Speakers' Bureau - Bayer; Dendreon; Sanofi

Research Funding - Medivation

Patrick Healy

No Relationships to Disclose

Carolyn Winters

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Colleen Riggan

No Relationships to Disclose

Monika Anand

No Relationships to Disclose

Julie Kephart

No Relationships to Disclose

Matthew I. Milowsky

Research Funding - Acerta Pharma (Inst); Agensys (Inst); Bristol-Myers Squibb (Inst); Incyte (Inst); Merck (Inst); Pfizer (Inst); Roche/Genentech (Inst)

Travel, Accommodations, Expenses - Roche/Genentech

Mark T. Fleming

Employment - Virginia Oncology Associates

Speakers' Bureau - Genentech; Medivation/Astellas

Travel, Accommodations, Expenses - Genentech; Medivation/Astellas

Tian Zhang

Leadership - Capio BioSciences (I)

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Consulting or Advisory Role - AstraZeneca; Bayer; Exelixis; G1 Therapeutics; Genentech/Roche; Janssen; Sanofi

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Rhonda L. Bitting

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Michael R Harrison

Consulting or Advisory Role - Bayer; Exelixis; Genentech; Sanofi

Speakers' Bureau - Genentech

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Jennifer A. Freedman

No Relationships to Disclose

Deborah Bruner

No Relationships to Disclose

Andrew J. Armstrong

Honoraria - Dendreon; Janssen Oncology; Sanofi

Consulting or Advisory Role - Bayer; Dendreon; Janssen Biotech; Medivation; Novartis; Pfizer; Sanofi

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Patents, Royalties, Other Intellectual Property - Circulating tumor cell novel capture technology (Inst)

Travel, Accommodations, Expenses - Bayer; Dendreon; Janssen Biotech; Medivation; Sanofi

Daniel J. George

Honoraria - Axess Oncology; Bayer; BIOPHARM; Dendreon; Medivation; Novartis; Sanofi

Consulting or Advisory Role - Acceleron Pharma; Astellas Pharma; Bayer; Bristol-Myers Squibb; Celgene; Dendreon; Exelixis; Genentech; GlaxoSmithKline; Innocrin Pharma; Janssen; Medivation; Merck Sharp & Dohme; Myovant Sciences; Novartis; Pfizer; Sanofi

Speakers' Bureau - Bayer; Exelixis; Sanofi

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Travel, Accommodations, Expenses - Bayer; Exelixis; Genentech/Roche; Medivation; Merck; Pfizer