

September 5, 2012

## **WHI AS346: Serum 25-hydroxyvitamin D levels and risk of developing melanoma**

Study population: Observational Study (OS)

### **Case sample:**

As of April 6, 2012, there are 814 confirmed melanoma cancers among OS participants, 545 of which were previously selected for the PAGE study (where exclusion criteria included baseline history of melanoma cancer, insufficient DNA sample, unknown race, and refused supplemental consent or genetic testing). In an effort to include as many case-control pairs from PAGE as possible, PAGE cases were considered first. 37 of the 545 PAGE case-control pairs had a case and/or control with insufficient serum or a control that had since been diagnosed with melanoma cancer (n=2). These case-control pairs were excluded, leaving 508 PAGE case-control pairs.

Of the 269 non-PAGE melanoma cases, 2 were previously selected as PAGE controls and 4 had insufficient serum available. Additionally, 46 reported history of melanoma at baseline and 5 were of unknown race. After excluding these 57 cases, there are 212 additional melanoma cases remaining. For a total of 212 + 508 PAGE cases = 720 cases.

AS346 is approved for 700 cases plus an additional 21 (3%) in case of insufficient specimen at the lab stage. We will use all 720 cases, newly matching the 212 non-PAGE cases.

### **Number of Controls to be selected:**

508 controls have been previously selected for the PAGE study (where exclusion criteria included baseline history of any cancer (including non-melanoma skin cancer), any incident cancer (excluding non-melanoma skin cancer), insufficient DNA sample, unknown race, and refused supplemental consent or genetic testing). There are 212 controls to be newly selected.

Control selection was done in a time-forward manner, selecting one control for each case from the risk set at the time of the case's event. The matching algorithm was allowed to select the closest match based on a criteria to minimize an overall distance measure (Bergstralh EJ, Kosanke JL. Computerized matching of cases to controls. Technical Report #56, Department of Health Sciences Research, Mayo Clinic, Rochester MN. April 1995). Each matching factor was given the same weight.

### **Eligible Controls:**

Eligible controls are all OS participants without any cancer at baseline (including non-melanoma skin cancer), no incident cancer (excluding non-melanoma skin cancer) during follow-up as of April 6, 2012, not previously selected as a PAGE case, not one of the PAGE controls already selected for this study, sufficient serum available at baseline, and known race.

Exclusions (not mutually exclusive):

- a) History of any cancer (including non-melanoma skin cancer) or unknown cancer history at baseline (n=18,503)
- b) Incident cancer during follow-up as of April 6, 2012 (n=14,058)
- c) Previously selected as a PAGE case (n=545)

- d) PAGE control included in this study (n=508)
- e) Insufficient sample at baseline (< 200 µl) (n=2,147)
- f) Unknown ethnicity (n=1,324)

**Number of eligible controls = 61,959**

**Case-control matching (1:1):**

Matching criteria:

- a) Age at screening (+/-1 year)
- b) WHI randomization date (+/-365 days)
- c) Ethnicity (exact match)

**Matching results/summary:**

Using full matching criteria for the 212 cases:

210 cases matched exactly  
2 cases with no match

**Final number of matched cases = 210 new matches + 508 PAGE matches = 718**

**AS346: Age and ethnicity distributions of matched cases and controls**

	PAGE participant				Non-PAGE participant				Total			
	Case		Control		Case		Control		Case		Control	
	N	%	N	%	N	%	N	%	N	%	N	%
Age at screening, y												
<i>Mean (SD)</i>	508	63.2 (6.9)	508	63.2 (6.8)	212	63.1 (7.2)	210	63.2 (7.3)	720	63.2 (7.0)	718	63.2 (7.0)
50-59	158	31.1	157	30.9	72	34.0	72	34.0	230	31.9	229	31.9
60-69	253	49.8	255	50.2	99	46.7	97	46.2	352	48.9	352	49.0
70-79	97	19.1	96	18.9	41	19.3	41	19.5	138	19.2	137	19.1
Ethnicity												
White	502	98.8	502	98.8	210	99.1	208	99.0	712	98.9	710	98.9
Black	2	0.4	2	0.4	0	0.0	0	0.0	2	0.3	2	0.3
Hispanic	3	0.6	3	0.6	2	0.9	2	1.0	5	0.7	5	0.7
Asian/Pacific Islander	1	0.2	1	0.2	0	0.0	0	0.0	1	0.1	1	0.1