

Data as of September 17th, 2012

Aim 1: Breast Cancer Cases with ANA data in possible RA cases previously included in BAA 20.

The phase 1 selection pool includes all breast cancers whom had ANA assay data from BAA 20.

Table 1. Original BAA 20 ANA Test Results

| ANA Assay Group | Total N | Breast Cancer Events |
|-----------------|---------|----------------------|
| 0 (Negative) | 8450 | 501 |
| 1 (Positive) | 509 | 28 |
| 2 (Positive) | 585 | 26 |
| 3 (Positive) | 411 | 20 |

From the original sample, exclusions were applied to reach the final set for matching.

Table 2. Aim 1.1 Exclusion Criteria

| Exclusion Criteria | ANA Group | |
|--|--------------|----------------|
| | Negative (0) | Positive (1-3) |
| Original Sample | 501 | 74 |
| Exclude all participants w/ missing hormone data | 500 | 74 |
| Exclude all participants w/ missing parity data | 499 | 74 |
| Exclude all participants w/ hx of breast cancer | 444 | 66 |
| Exclude all participants w/ inadequate serum volume (< 200 uL) | 429 | 64 |
| Exclude all participants w/ hx of any cancer (ANA Negative Only) | 399 | 64 |
| Exclude all participants w/ unknown ER/PR Assay (ANA Negative Only) | 328 | 64 |
| Subsets of Final Numbers (328 negative, 64 positive) | | |
| - Subset of those breast cancer cases that occur after a RA event / self-report RA at baseline | 291 | 52 |
| - Subset of Participants who also reported lupus at any time | 9 | 8 |
| - Subset of participants who reported RA on baseline only | 139 | 22 |

A total of 64 ANA positive and 328 ANA negative breast cancer participants were put into the matching process. 64 ANA positive cases were successfully matched with 1 ANA negative case each, matching on age (+/- 2 years) and time from WHI baseline to breast cancer event (+/- 1 year). Matching variables were selected based on 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). Matching was weighted to equate a difference of 1 year in age to a difference in 30 days in time from baseline to breast cancer event.

Specific matching summaries are given in the tables below. Each row summarizes the matching performance for a specific variable or overall summary. For example, the mean absolute difference in time from baseline to breast cancer between ANA positive and ANA negative cases is 60 days.

Table 3. Aim 1.1 Matching Results

| Matching Factor | Sum (weighted) of Absolute Differences | ANA Positive | ANA Negative |
|-----------------------|--|--------------|--------------|
| | <i>Mean (min, max)</i> | <i>Mean</i> | <i>Mean</i> |
| Overall | 93.0 (2.0, 318.0) | - | - |
| Age | 0.9 (0.0, 2.0) | 63.5 | 63.5 |
| Time to Breast Cancer | 65.8 (2.0, 264.0) | 2220.9 | 2227.9 |

Total Aim 1.1 Participants: 128

Aim 2: Match ANA+ Breast Cancer Cases to ANA+ and ANA- participants w/ no breast cancer

Table 4. Aim 1.2 Exclusion Criteria

| Exclusion Criteria | ANA Positive | | ANA Negative |
|--|---------------------|------------------------|------------------------|
| | Breast Cancer Cases | Breast Cancer Controls | Breast Cancer Controls |
| Original Sample | 74 | 1431 | 7949 |
| Exclude all participants w/ missing hormone data | 74 | 1428 | 7940 |
| Exclude all participants w/ missing parity data | 74 | 1415 | 7884 |
| Exclude all participants w/ hx of breast cancer | 66 | 1359 | 7594 |
| Exclude all participants w/ inadequate serum volume (< 200 uL) | 64 | 1317 | 7409 |
| Exclude all participants w/ hx of any cancer (controls only) | 64 | 1207 | 6796 |
| Exclude all participants w/ any cancer during follow-up (controls only) | 64 | 1102 | 6231 |
| Subsets of Final Numbers (64 cases, 1102 Positive controls, 6231 Negative controls) | | | |
| - Subset of Participants who also reported lupus at any time | 8 | 143 | 417 |
| - Subset of participants who reported RA on baseline only | 22 | 433 | 2448 |

A total of 64 ANA positive breast cancer cases and 1102 ANA positive breast cancer controls were put into the matching process. 64 ANA positive breast cancer cases were successfully matched with 64 ANA positive breast cancer controls, matching on ANA level (exact) and age (+/- 1 year). Matching for this

aim was done in a time forward manner to ensure that each control had at least as much control time as its matched case. For example, a case diagnosed with breast cancer two years after randomization would be matched with a control with at least two years of follow-up.

Table 5. Aim 1.2 (ANA positive breast cancer controls) Matching Results

| Matching Factor | Sum (weighted) of Absolute Differences | ANA Positive | ANA Negative |
|-----------------|--|--------------|--------------|
| | <i>Mean (min, max)</i> | <i>Mean</i> | <i>Mean</i> |
| Overall | 0.0 (0.0, 0.0) | - | - |
| Age | 0.0 (0.0, 0.0) | 63.5 | 63.5 |
| ANA Level | 0.0 (0.0, 0.0) | % | % |
| 1 | | 35.9 | 35.9 |
| 2 | | 34.4 | 34.4 |
| 3 | | 29.7 | 29.7 |

The average control time was 6.1 years for cases and 13.0 years for controls.

A total of 64 ANA positive breast cancer cases and 6231 ANA negative breast cancer controls were put into the matching process. 64 ANA positive breast cancer cases were successfully matched with 64 ANA negative breast cancer controls, matching on age (+/- 1 year). Matching for this aim was done in a time forward manner to ensure that each control had at least as much control time as its matched case. For example, a case diagnosed with breast cancer two years after randomization would be matched with a control with at least two years of follow-up.

Table 5. Aim 1.2 (ANA negative breast cancer controls) Matching Results

| Matching Factor | Sum (weighted) of Absolute Differences | ANA Positive | ANA Negative |
|-----------------|--|--------------|--------------|
| | <i>Mean (min, max)</i> | <i>Mean</i> | <i>Mean</i> |
| Overall | 0.0 (0.0, 0.0) | - | - |
| Age | 0.0 (0.0, 0.0) | 63.5 | 63.5 |

The average control time was 6.1 years for cases and 13.1 years for controls.

Total Aim 1.2 Participants: 192 (128 new)

Aim 2: Breast cancer cases and controls with lupus not included in BAA 20 sample.

The phase 1 selection pool includes all breast cancers whom had ANA assay data from BAA 20.

Table 6. Non-BAA 20 Sample Lupus Participants

| Lupus Participants | Total N | Breast Cancer Events |
|--------------------------------------|---------|----------------------|
| No Lupus | 139760 | 9610 |
| Lupus at both baseline and follow-up | 109 | 4 |
| Lupus at baseline only | 483 | 32 |
| Lupus as follow-up only | 1699 | 127 |

From the original sample, exclusions were applied to reach the final set for matching.

Table 7. Aim 2.1 Exclusion Criteria

| Exclusion Criteria | Lupus Participants | |
|---|---------------------|------------------------|
| | Breast Cancer Cases | Breast Cancer Controls |
| Original Sample | 163 | 2291 |
| Exclude all participants w/ missing hormone data | 163 | 2291 |
| Exclude all participants w/ missing parity data | 161 | 2280 |
| Exclude all participants w/ hx of breast cancer | 149 | 2202 |
| Exclude all participants w/ inadequate serum volume (< 350 uL) | 144 | 2140 |
| Exclude all participants w/ any hx of cancer | 131 | 1987 |
| Exclude all participants w/ any follow-up cancer (controls only) | 131 | 1815 |
| Exclude all participants w/ breast cancer prior to lupus (cases only) | 82 | 1815 |
| Subsets of Final Numbers (82 cases, 1815 controls) | | |
| - Subset of Participants who also reported RA at any time | 9 | 206 |

From the 82 eligible cases, a random sample of 50 cases was selected for matching. A total of 50 SLE breast cancer cases and 1815 SLE breast cancer controls were put into the matching process. 50 cases were successfully matched with 50 controls, matching on age (+/- 1 year). Matching for this aim was done in a time forward manner to ensure that each control had at least as much control time as its matched case. For example, a case diagnosed with breast cancer two years after randomization would be matched with a control with at least two years of follow-up.

Table 8. Aim 2.1 Matching Results

| Matching Factor | Sum (weighted) of Absolute Differences | ANA Positive | ANA Negative |
|-----------------|--|--------------|--------------|
| | <i>Mean (min, max)</i> | <i>Mean</i> | <i>Mean</i> |
| Overall | 0.0 (0.0, 0.0) | - | - |
| Age | 0.0 (0.0, 0.0) | 62.4 | 62.4 |

The average control time was 8.3 years for cases and 14.2 years for controls.

Total Aim 2.1 Participants: 100 (100 new)

Total Participants in all aims: 356