Appendix A

Search Strategy

((((((cancer[Title/Abstract]) OR tumor[Title/Abstract]) OR carcinoma[Title/Abstract]) OR neoplasm[Title/Abstract])) AND ((breast[Title/Abstract]) OR mammary[Title/Abstract]))) AND ((bevacizumab[Title/Abstract]) OR avastin[Title/Abstract])) AND ((neoadjuvant[Title/Abstract]) OR preoperative[Title/Abstract])) AND ((randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract])).

Note: We used same search strategy in all three databases.
### Appendix B

#### AEs included into meta-analysis

| AE1-Hypertension | study         | Bev size | Bev event | Control size | Control event | Pts rate |
|------------------|---------------|----------|-----------|--------------|---------------|----------|
| Hypertension     | TBCRC 002     | 50       | 4         | 25           | 0             |          |
| Hypertension     | NSABP B40     | 595      | 65        | 596          | 5             |          |
| Arterial hypertension | GaperQuinto   | 951      | 25        | 965          | 4             |          |
| Hypertension     | SWOG S0800    | 95       | 7         | 110          | 3             |          |
| Hypertension     | CALGB 40603   | 216      | 24        | 217          | 2             |          |
| Hypertension     | ARTemis       | 384      | 8         | 391          | 6             |          |
| Hypertension     | AVATAXHER     | 47       | 0         | 25           | 1             |          |
| Total            |               | 2338     | 133       | 2329         | 21            | 4667     | 3.3%    |

#### AE2-Hand foot syndrome

| Hand-foot sydrome | study         | Bev size | Bev event | Control size | Control event | Pts rate |
|-------------------|---------------|----------|-----------|--------------|---------------|----------|
| Hand-foot sydrome | NSABP B-40    | 595      | 65        | 596          | 42            |          |
| Hand-foot sydrome | GaperQuinto   | 951      | 52        | 965          | 33            |          |
| Hand-foot sydrome | SWOG S0800    | 95       | 1         | 110          | 2             |          |
| Peripheral neuropathy | CALGB 40603 | 216   | 10        | 217          | 9             |          |
| Peripheral neuropathy | ARTemis     | 384      | 6         | 391          | 4             |          |
| Peripheral sensory neuropathy | AVATAXHER | 47      | 0         | 25           | 0             |          |
| Total             |               | 2288     | 134       | 2304         | 90            | 4592     | 4.9%    |

#### AE3-Fatigue

| Fatigue | study         | Bev size | Bev event | Control size | Control event | Pts rate |
|---------|---------------|----------|-----------|--------------|---------------|----------|
| Fatigue | TBCRC 002     | 50       | 1         | 25           | 0             |          |
| Fatigue | NSABP B-40    | 595      | 65        | 596          | 59            |          |
| Fatigue | CALGB 40603   | 216      | 25        | 217          | 22            |          |
| Fatigue | ARTemis       | 384      | 39        | 391          | 32            |          |
| Asthenia | AVATAXHER    | 47       | 3         | 25           | 0             |          |
| Total   |               | 1292     | 133       | 1254         | 113           | 2546     | 9.7%    |

#### AE4-Diarrhea

| Diarrhea | study         | Bev size | Bev event | Control size | Control event | Pts rate |
|----------|---------------|----------|-----------|--------------|---------------|----------|
| Diarrhea | NSABP B-40    | 595      | 30        | 596          | 47            |          |
| Diarrhea | SWOG S0800    | 95       | 3         | 110          | 2             |          |
| Diarrhea | CALGB 40603   | 216      | 6         | 217          | 2             |          |
| Diarrhoea | ARTemis      | 384      | 16        | 391          | 20            |          |
| Diarrhoea | AVATAXHER   | 47       | 0         | 25           | 0             |          |
| AE5 - Nausea |         |         |         |         |         |         |
|--------------+---------+---------+---------+---------+---------+---------|
| Total        | 1337    | 55      | 1339    | 71      | 2676    | 4.7%    |
| Nausea       | NSABP B-40 | 595     | 30      | 596     | 29      |         |
|              | SWOG    | 95      | 6       | 110     | 9       |         |
|              | S0800   | 216     | 13      | 217     | 7       |         |
|              | CALGB   | 384     | 13      | 391     | 17      |         |
|              | 40603   | 47      | 0       | 25      | 0       |         |
| Total        | 1337    | 62      | 1339    | 62      | 2676    | 4.6%    |

| AE6 - Vomiting |         |         |         |         |         |         |
|----------------+---------+---------+---------+---------+---------+---------|
| Total          | 1292    | 38      | 1254    | 46      | 2546    | 3.3%    |
| Nausea/Vomiting| TBCRC 002 | 50      | 0       | 25      | 0       |         |
| Vomiting       | NSABP B-40 | 595     | 18      | 596     | 35      |         |
|                | CALGB   | 216     | 6       | 217     | 4       |         |
|                | ARTEMIS | 384     | 14      | 391     | 7       |         |
|                | AVATAXHR| 47      | 0       | 25      | 0       |         |

| AE7 - Thromboembolic events |         |         |         |         |         |         |
|-----------------------------+---------+---------+---------+---------+---------+---------|
| Total                       | 1907    | 51      | 1913    | 39      | 3820    | 2.4%    |
| Hemorrhagic and thrombotic event | TBCRC 002 | 50      | 3       | 25      | 0       |         |
| Thrombosis, thrombus, or embolism | NSABP B-40 | 595     | 11      | 596     | 17      |         |
| Thromboembolic events     | GaperQuinto | 951     | 26      | 965     | 18      |         |
| Thromboembolic events (SAE) | SWOG S0800 | 95      | 1       | 110     | 2       |         |
| Thromboembolic events     | CALGB   | 216     | 10      | 217     | 2       |         |

| AE8 - Neutropenia        |         |         |         |         |         |         |
|--------------------------+---------+---------+---------+---------+---------+---------|
| Total                    | 2131    | 1170    | 2143    | 1110    | 4274    | 53.3%   |
| Neutropenia              | NSABP B-40 | 595     | 137     | 596     | 131     |         |
| Neutropenia              | GaperQuinto | 936     | 763     | 939     | 747     |         |
| Neutropenia              | CALGB   | 216     | 102     | 217     | 86      |         |
| Neutropenia              | ARTEMIS | 384     | 168     | 391     | 146     |         |

| AE9 - Febrile neutropenia |         |         |         |         |         |         |
|---------------------------+---------+---------+---------+---------+---------+---------|
| Total                     | 2131    | 1170    | 2143    | 1110    | 4274    | 53.3%   |
| Febrile neutropenia       | NSABP B-40 | 595     | 65      | 596     | 41      |         |
| Febrile neutropenia, any grade | GaperQuinto | 951     | 130     | 965     | 69      |         |
| Febrile neutropenia       | CALGB   | 216     | 36      | 217     | 20      |         |
| Febrile neutropenia       | AVATAXHR| 47      | 3       | 25      | 1       |         |
|                      | Total  | 1809 | 234  | 1803 | 131  | 3612 | 10.1% |
|----------------------|--------|------|------|------|------|------|-------|
| **AE10-Mucositis**   |        |      |      |      |      |      |       |
| Mucositis            |        |      |      |      |      |      |       |
| NSABP B-40           | 595    | 29   | 596  | 6    |      |      |       |
| GaperQuinto          | 951    | 157  | 965  | 26   |      |      |       |
| CALGB 40603          | 216    | 4    | 217  | 3    |      |      |       |
| Total                | 1762   | 190  | 1778 | 35   | 3540 | 6.4% |       |
| **AE11-Headache**    |        |      |      |      |      |      |       |
| Headache             |        |      |      |      |      |      |       |
| TBCRC 002            | 50     | 0    | 25   | 0    |      |      |       |
| NSABP B-40           | 595    | 29   | 596  | 5    |      |      |       |
| AVATAHER             | 47     | 1    | 25   | 0    |      |      |       |
| Total                | 692    | 30   | 646  | 5    | 1338 | 2.6% |       |
| **AE12-Dyspnea**     |        |      |      |      |      |      |       |
| Dyspnea              |        |      |      |      |      |      |       |
| TBCRC 002            | 50     | 0    | 25   | 0    |      |      |       |
| NSABP B-40           | 595    | 11   | 596  | 5    |      |      |       |
| SWOG S0800           | 95     | 3    | 110  | 1    |      |      |       |
| Total                | 740    | 14   | 731  | 6    | 1471 | 1.5% |       |
| **Surgical complication, any grade** | | | | |
| wound healing complications | | | | | | | |
| TORI B-02            | 30     | 10   | 32   | 2    |      |      |       |
| NSABP B-40           | 560    | 141  | 562  | 106  |      |      |       |
| GaperQuinto          | 394    | 58   | 349  | 38   |      |      |       |
| Total                | 984    | 209  | 943  | 146  | 1927 | 18.4%|       |
Figure S1. Efficacy of Bev Adding to NAT. (a) Pooled OR for bpCR. (b) Pooled HR for ORR. (C) Pooled HR for BCS.
**Figure S2.** Subgroup Analysis. Comparing pCR between different subgroups.

| Study                | K  | pCR_CR with 95% CI | P-value |
|----------------------|----|--------------------|---------|
| Planned Bev dose     |    |                    |         |
| 60 mg/kg             | 3  | 1.62 [1.21, 2.18]  | 0.001   |
| 90/105 mg/kg         | 3  | 1.28 [1.03, 1.59]  | 0.023   |
| 120 mg/kg            | 3  | 1.29 [1.03, 1.60]  | 0.024   |
| Test of group differences: Q(2) = 1.92, p = 0.38 |
| HER2 status          |    |                    |         |
| HER2-                | 8  | 1.34 [1.16, 1.53]  | 0.000   |
| HER2+                | 1  | 2.46 [0.84, 7.28]  | 0.102   |
| Test of group differences: Q(1) = 1.21, p = 0.27 |
| HR status            |    |                    |         |
| HR-                  | 1  | 1.30 [0.95, 1.82]  | 0.094   |
| HR+                  | 1  | 6.65 [3.5, 125.65] | 0.206   |
| Both                 | 7  | 1.34 [1.16, 1.55]  | 0.000   |
| Test of group differences: Q(2) = 1.18, p = 0.56 |
| Overall              |    |                    |         |
| Heterogeneity: $I^2 = 0.00\%$, $H^2 = 0.97$ |
| Test of $Q(8) = 7.78$, p = 0.45 |

![Graph showing subgroup analysis results](image-url)
Figure S3. Funnel plot with pseudo 95% confidence limits
|                  | Num | group                      | B(slope) | SE     |
|------------------|-----|----------------------------|----------|--------|
| pCR~DFS          | 6   | all                        | 0.0878   | 46.8789|
| pCR~DFS          | 5   | Bev pre-surgery only       | 0.1096   | 1.1187 |
| pCR~OS           | 5   | all                        | 0.0703   | 4.1188 |
| pCR~OS           | 4   | Bev pre-surgery only       | 0.1053   | 2.5227 |
| DFS~OS           | 5   | all                        | 1.5947   | 1.0134 |

Legend and footnotes: Num= Number of included studies; SE= Standard error.