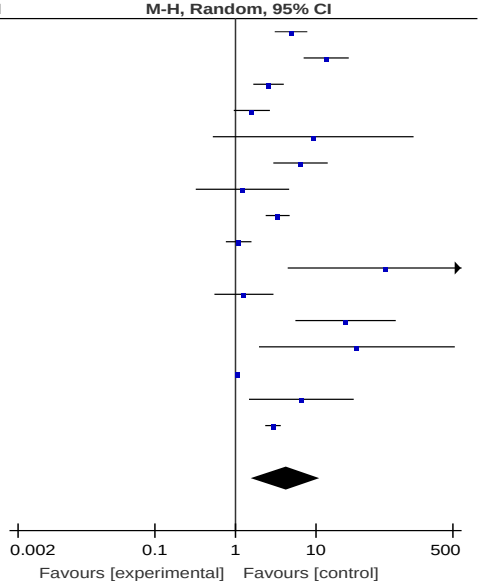
## Supplementary Material 1 Figures S1-S31 v.3.0

### Figure S1: Hypertension

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 104 | 247 | 20 | 233 | 6.9% | 4.91 [3.15, 7.65] |
| Coleman (GOG0213) | 135 | 330 | 10 | 327 | 6.8% | 13.38 [7.17, 24.96] |
| du Bois | 129 | 902 | 25 | 450 | 6.9% | 2.57 [1.70, 3.89] |
| Gore | 19 | 26 | 11 | 24 | 6.8% | 1.59 [0.97, 2.61] |
| Gotlieb | 5 | 30 | 0 | 25 | 4.4% | 9.23 [0.53, 159.14] |
| Herzog | 45 | 123 | 7 | 123 | 6.7% | 6.43 [3.02, 13.69] |
| Karlan | 7 | 105 | 3 | 55 | 6.2% | 1.22 [0.33, 4.54] |
| Kim (East Asian Study) | 117 | 179 | 34 | 174 | 6.9% | 3.35 [2.43, 4.61] |
| Ledermann (ICON6) | 38 | 95 | 42 | 115 | 6.9% | 1.10 [0.78, 1.55] |
| Liu | 34 | 44 | 0 | 46 | 4.5% | 72.07 [4.55, 1140.62] |
| Marth (TRINOVA-2) | 12 | 113 | 9 | 108 | 6.6% | 1.27 [0.56, 2.90] |
| Oza (ICON 7) | 46 | 745 | 2 | 753 | 6.1% | 23.25 [5.66, 95.42] |
| Pignata (MITO 11) | 16 | 37 | 0 | 36 | 4.4% | 32.13 [2.00, 516.29] |
| Pignata (MITO16B) | 197 | 201 | 186 | 200 | 7.0% | 1.05 [1.01, 1.10] |
| Pujade-Lauraine (AURELIA) | 13 | 179 | 2 | 181 | 6.0% | 6.57 [1.50, 28.71] |
| Vergote (AGO-OVAR16) | 275 | 477 | 91 | 461 | 7.0% | 2.92 [2.39, 3.57] |
| **Total (95% CI)** | | **3833** | | **3311** | **100.0%** | **4.26 [1.61, 11.26]** |
| Total events | 1192 | | 442 | | | |

Heterogeneity: Tau² = 3.53; Chi² = 1690.13, df = 15 (P < 0.00001); I² = 99%

Test for overall effect: Z = 2.92 (P = 0.003)

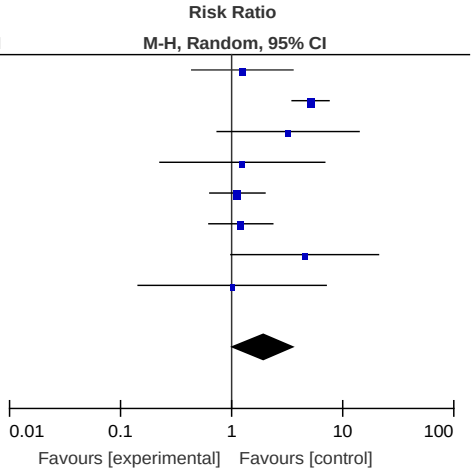


## Figure S2: Hemorrhagic events

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 7 | 83 | 6 | 89 | 13.1% | 1.25 [0.44, 3.57] |
| Coleman (GOG0213) | 140 | 330 | 27 | 327 | 18.3% | 5.14 [3.50, 7.53] |
| Gore | 7 | 26 | 2 | 24 | 10.0% | 3.23 [0.74, 14.06] |
| Gotlieb | 3 | 30 | 2 | 25 | 8.5% | 1.25 [0.23, 6.90] |
| Karlan | 28 | 105 | 13 | 55 | 17.0% | 1.13 [0.64, 2.00] |
| Ledermann (ICON6) | 15 | 95 | 15 | 115 | 16.3% | 1.21 [0.62, 2.35] |
| Oza (ICON 7) | 9 | 745 | 2 | 753 | 9.6% | 4.55 [0.99, 20.98] |
| Pujade-Lauraine (AURELIA) | 2 | 179 | 2 | 181 | 7.3% | 1.01 [0.14, 7.10] |
| **Total (95% CI)** | | **1593** | | **1569** | **100.0%** | **1.94 [1.00, 3.76]** |
| Total events | 211 | | 69 | | | |

Heterogeneity: Tau² = 0.59; Chi² = 30.27, df = 7 (P < 0.0001); I² = 77%

Test for overall effect: Z = 1.95 (P = 0.05)

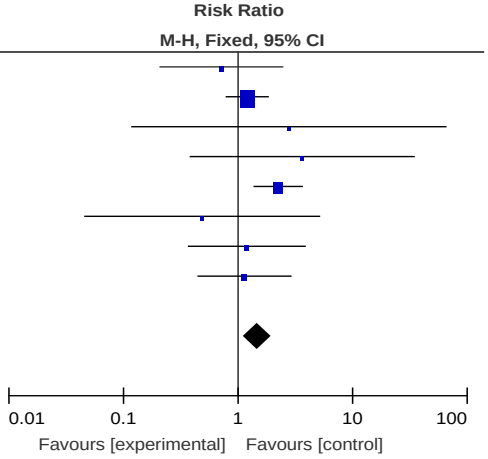



## Figure S3: Thrombosis or embolism

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 4 | 83 | 6 | 89 | 6.9% | 0.71 [0.21, 2.44] |
| du Bois | 70 | 902 | 29 | 450 | 46.2% | 1.20 [0.79, 1.83] |
| Gore | 1 | 26 | 0 | 24 | 0.6% | 2.78 [0.12, 65.08] |
| Ledermann (ICON6) | 3 | 95 | 1 | 115 | 1.1% | 3.63 [0.38, 34.35] |
| Oza (ICON 7) | 51 | 745 | 23 | 753 | 27.3% | 2.24 [1.38, 3.63] |
| Pignata (MITO 11) | 1 | 37 | 2 | 36 | 2.4% | 0.49 [0.05, 5.13] |
| Pignata (MITO16B) | 6 | 201 | 5 | 200 | 6.0% | 1.19 [0.37, 3.85] |
| Pujade-Lauraine (AURELIA) | 9 | 179 | 8 | 181 | 9.5% | 1.14 [0.45, 2.88] |
| **Total (95% CI)** | | **2268** | | **1848** | **100.0%** | **1.47 [1.12, 1.92]** |
| Total events | 145 | | 74 | | | |

Heterogeneity: Chi² = 7.17, df = 7 (P = 0.41); I² = 2%

Test for overall effect: Z = 2.75 (P = 0.006)

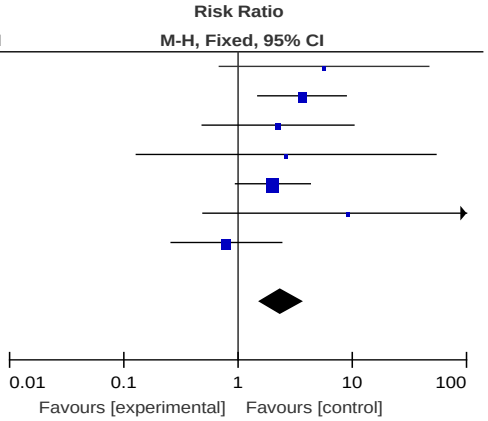


## Figure S4: Arterial thromboembolism

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 6 | 247 | 1 | 233 | 3.7% | 5.66 [0.69, 46.66] |
| Coleman (GOG0213) | 22 | 330 | 6 | 327 | 21.9% | 3.63 [1.49, 8.84] |
| du Bois | 9 | 902 | 2 | 450 | 9.7% | 2.25 [0.49, 10.35] |
| Karlan | 2 | 105 | 0 | 55 | 2.4% | 2.64 [0.13, 54.08] |
| Oza (ICON 7) | 20 | 745 | 10 | 753 | 36.2% | 2.02 [0.95, 4.29] |
| Pujade-Lauraine (AURELIA) | 4 | 179 | 0 | 181 | 1.8% | 9.10 [0.49, 167.79] |
| Tewari | 8 | 1215 | 5 | 601 | 24.3% | 0.79 [0.26, 2.41] |
| **Total (95% CI)** | | **3723** | | **2600** | **100.0%** | **2.38 [1.52, 3.70]** |
| Total events | 71 | | 24 | | | |

Heterogeneity: Chi² = 6.28, df = 6 (P = 0.39); I² = 4%

Test for overall effect: Z = 3.82 (P = 0.0001)




## Figure S5: Venous thromboembolism

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 11 | 247 | 6 | 233 | 11.7% | 1.73 [0.65, 4.60] |
| Coleman (GOG0213) | 0 | 330 | 0 | 327 | | Not estimable |
| du Bois | 33 | 902 | 22 | 450 | 21.5% | 0.75 [0.44, 1.27] |
| Gotlieb | 2 | 30 | 0 | 25 | 1.9% | 4.19 [0.21, 83.50] |
| Karlan | 7 | 105 | 6 | 55 | 10.8% | 0.61 [0.22, 1.73] |
| Oza (ICON 7) | 32 | 745 | 13 | 753 | 18.6% | 2.49 [1.32, 4.70] |
| Pujade-Lauraine (AURELIA) | 5 | 179 | 8 | 181 | 10.1% | 0.63 [0.21, 1.89] |
| Tewari | 78 | 1215 | 35 | 601 | 25.5% | 1.10 [0.75, 1.62] |
| **Total (95% CI)** | | **3753** | | **2625** | **100.0%** | **1.13 [0.74, 1.72]** |
| Total events | 168 | | 90 | | | |

Heterogeneity: Tau² = 0.14; Chi² = 12.19, df = 6 (P = 0.06); I² = 51%

Test for overall effect: Z = 0.58 (P = 0.56)

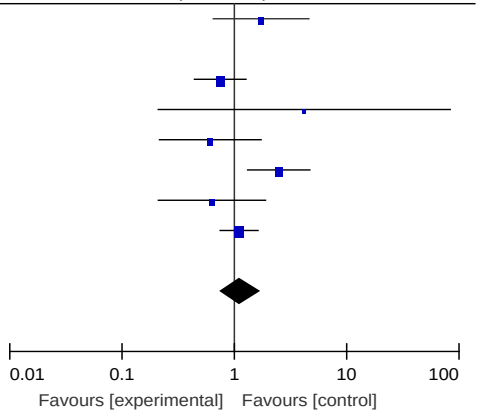


**Figure S6: Proteinuria**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 27 | 247 | 2 | 233 | 8.8% | 12.73 [3.06, 52.96] |
| Coleman (GOG0213) | 56 | 330 | 3 | 327 | 9.6% | 18.50 [5.85, 58.50] |
| Gotlieb | 18 | 30 | 16 | 25 | 11.4% | 0.94 [0.62, 1.42] |
| Karlan | 7 | 105 | 2 | 55 | 8.4% | 1.83 [0.39, 8.53] |
| Kim (East Asian Study) | 26 | 179 | 4 | 174 | 10.0% | 6.32 [2.25, 17.73] |
| Ledermann (ICON6) | 16 | 95 | 11 | 115 | 10.8% | 1.76 [0.86, 3.61] |
| Liu | 5 | 44 | 0 | 46 | 5.0% | 11.49 [0.65, 201.83] |
| Pignata (MITO16B) | 82 | 201 | 7 | 200 | 10.7% | 11.66 [5.53, 24.59] |
| Pujade-Lauraine (AURELIA) | 3 | 179 | 0 | 181 | 4.8% | 7.08 [0.37, 136.04] |
| Tewari | 16 | 1215 | 4 | 601 | 9.8% | 1.98 [0.66, 5.89] |
| Vergote (AGO-OVAR16) | 40 | 477 | 8 | 461 | 10.7% | 4.83 [2.29, 10.21] |
| **Total (95% CI)** | | **3102** | | **2418** | **100.0%** | **4.52 [1.93, 10.55]** |
| Total events | 296 | | 57 | | | |

Heterogeneity: Tau² = 1.60; Chi² = 83.41, df = 10 (P < 0.00001); I² = 88%
Test for overall effect: Z = 3.48 (P = 0.0005)

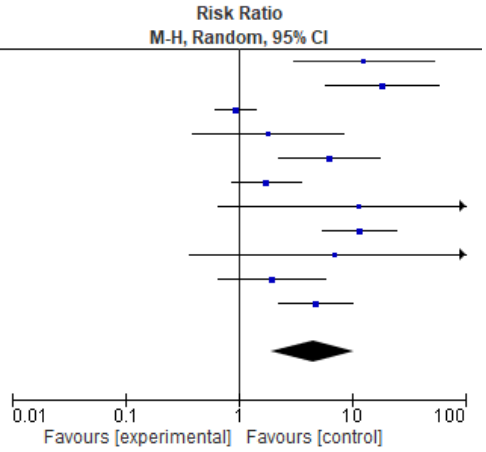



**Figure S7: Reversible posterior leukoencephalopathy syndrome**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Coleman (GOG0213) | 0 | 330 | 0 | 327 | | Not estimable |
| Pujade-Lauraine (AURELIA) | 1 | 179 | 0 | 181 | 27.1% | 3.03 [0.12, 73.97] |
| Tewari | 1 | 1215 | 1 | 601 | 72.9% | 0.49 [0.03, 7.89] |
| **Total (95% CI)** | | **1724** | | **1109** | **100.0%** | **1.18 [0.18, 7.94]** |
| Total events | 2 | | 1 | | | |

Heterogeneity: Chi² = 0.71, df = 1 (P = 0.40); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.86)

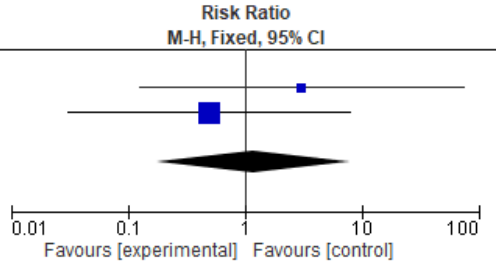


**Figure S8: Gastrointestinal perforations**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 2 | 247 | 1 | 233 | 11.3% | 1.89 [0.17, 20.67] |
| Coleman (GOG0213) | 6 | 330 | 1 | 327 | 11.1% | 5.95 [0.72, 49.11] |
| Gore | 1 | 26 | 0 | 24 | 5.7% | 2.78 [0.12, 65.08] |
| Gotlieb | 3 | 30 | 1 | 25 | 12.0% | 2.50 [0.28, 22.56] |
| Karlan | 0 | 105 | 1 | 55 | 21.6% | 0.18 [0.01, 4.25] |
| Oza (ICON 7) | 10 | 745 | 3 | 753 | 32.8% | 3.37 [0.93, 12.19] |
| Pujade-Lauraine (AURELIA) | 3 | 179 | 0 | 181 | 5.5% | 7.08 [0.37, 136.04] |
| **Total (95% CI)** | | **1662** | | **1598** | **100.0%** | **2.86 [1.36, 6.04]** |
| Total events | 25 | | 7 | | | |

Heterogeneity: Chi² = 3.96, df = 6 (P = 0.68); I² = 0%
Test for overall effect: Z = 2.76 (P = 0.006)

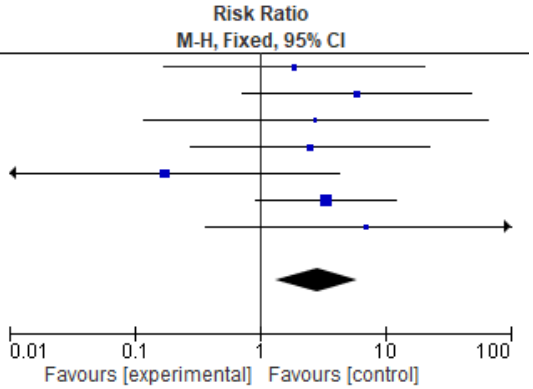



**Figure S9: Infection**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 31 | 83 | 31 | 89 | 20.8% | 1.07 [0.72, 1.60] |
| Coleman (GOG0213) | 126 | 330 | 89 | 327 | 62.3% | 1.40 [1.12, 1.76] |
| Gore | 6 | 26 | 4 | 24 | 2.9% | 1.38 [0.44, 4.32] |
| Pignata (MITO 11) | 5 | 37 | 3 | 36 | 2.1% | 1.62 [0.42, 6.29] |
| Richardson | 15 | 50 | 17 | 50 | 11.8% | 0.88 [0.50, 1.57] |
| **Total (95% CI)** | | **526** | | **526** | **100.0%** | **1.28 [1.07, 1.53]** |
| Total events | 183 | | 144 | | | |

Heterogeneity: Chi² = 3.15, df = 4 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.65 (P = 0.008)

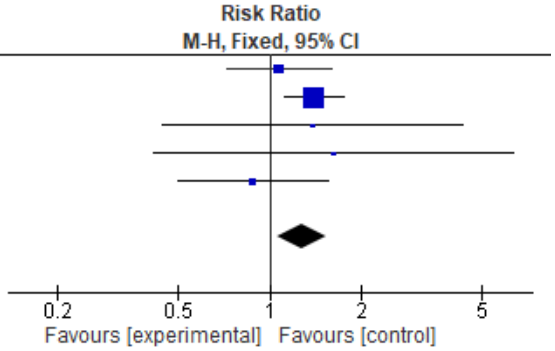


**Figure S10: Pyrexia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Gore | 3 | 26 | 3 | 24 | 2.8% | 0.92 [0.21, 4.14] |
| Herzog | 13 | 123 | 10 | 123 | 9.1% | 1.30 [0.59, 2.85] |
| Marth (TRINOVA-2) | 20 | 113 | 18 | 108 | 16.7% | 1.06 [0.59, 1.90] |
| Pignata (MITO16B) | 23 | 201 | 16 | 200 | 14.5% | 1.43 [0.78, 2.63] |
| Vergote (TRINOVA-3) | 72 | 675 | 47 | 336 | 56.9% | 0.76 [0.54, 1.08] |
| **Total (95% CI)** | | **1138** | | **791** | **100.0%** | **0.96 [0.75, 1.23]** |
| Total events | 131 | | 94 | | | |

Heterogeneity: Chi² = 4.08, df = 4 (P = 0.40); I² = 2%
Test for overall effect: Z = 0.30 (P = 0.76)

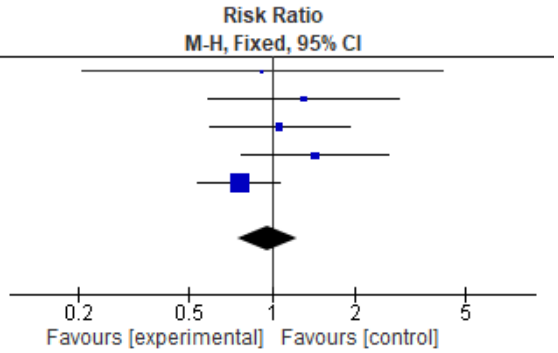



**Figure S11: Wound related issues**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 2 | 247 | 0 | 233 | 2.0% | 4.72 [0.23, 97.75] |
| Coleman (GOG0213) | 10 | 330 | 2 | 327 | 7.7% | 4.95 [1.09, 22.44] |
| Karlan | 2 | 105 | 0 | 55 | 2.5% | 2.64 [0.13, 54.08] |
| Pujade-Lauraine (AURELIA) | 0 | 179 | 0 | 181 | | Not estimable |
| Tewari | 40 | 1215 | 17 | 601 | 87.7% | 1.16 [0.67, 2.04] |
| **Total (95% CI)** | | **2076** | | **1397** | **100.0%** | **1.57 [0.96, 2.56]** |
| Total events | 54 | | 19 | | | |

Heterogeneity: Chi² = 3.94, df = 3 (P = 0.27); I² = 24%
Test for overall effect: Z = 1.78 (P = 0.07)

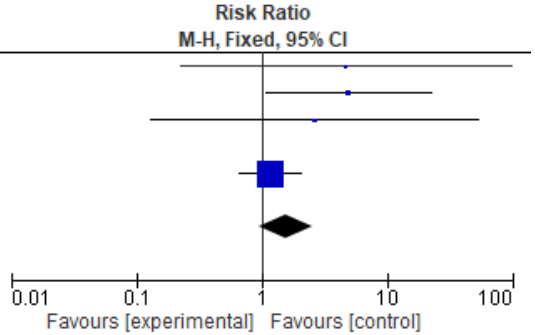



**Figure S12: Ascites**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Marth (TRINOVA-2) | 33 | 113 | 10 | 108 | 9.7% | 3.15 [1.64, 6.08] |
| Monk (TRINOVA-1) | 101 | 461 | 57 | 452 | 54.7% | 1.74 [1.29, 2.34] |
| Vergote (TRINOVA-3) | 127 | 675 | 28 | 336 | 35.5% | 2.26 [1.53, 3.33] |
| **Total (95% CI)** | | **1249** | | **896** | **100.0%** | **2.06 [1.65, 2.57]** |
| Total events | 261 | | 95 | | | |

Heterogeneity: Chi² = 3.09, df = 2 (P = 0.21); I² = 35%
Test for overall effect: Z = 6.37 (P < 0.00001)

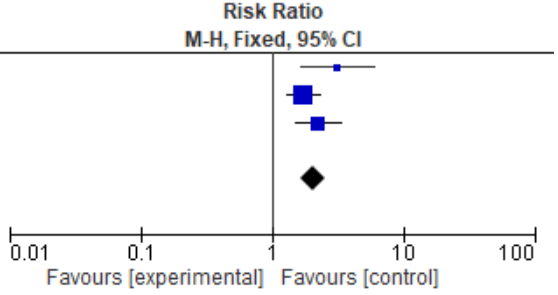


**Figure S13: Neutropenia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 52 | 247 | 51 | 233 | 5.6% | 0.96 [0.68, 1.35] |
| Chekerov (TRIAS) | 52 | 83 | 56 | 89 | 6.7% | 1.00 [0.79, 1.25] |
| Coleman (GOG0213) | 40 | 330 | 26 | 327 | 4.5% | 1.52 [0.95, 2.44] |
| du Bois | 498 | 902 | 226 | 450 | 7.6% | 1.10 [0.99, 1.23] |
| Gore | 11 | 26 | 12 | 24 | 3.5% | 0.85 [0.46, 1.54] |
| Herzog | 3 | 123 | 2 | 123 | 0.7% | 1.50 [0.26, 8.82] |
| Kim (East Asian Study) | 86 | 179 | 26 | 174 | 5.2% | 3.22 [2.19, 4.73] |
| Ledermann (ICON6) | 28 | 95 | 55 | 115 | 5.4% | 0.62 [0.43, 0.89] |
| Liu | 4 | 44 | 5 | 46 | 1.2% | 0.84 [0.24, 2.91] |
| Marth (TRINOVA-2) | 15 | 113 | 22 | 108 | 3.5% | 0.65 [0.36, 1.19] |
| Monk (TRINOVA-1) | 104 | 461 | 129 | 452 | 6.7% | 0.79 [0.63, 0.99] |
| Oza (ICON 7) | 123 | 745 | 114 | 753 | 6.6% | 1.09 [0.86, 1.38] |
| Pignata (MITO 11) | 28 | 37 | 11 | 36 | 4.0% | 2.48 [1.46, 4.19] |
| Pignata (MITO16B) | 147 | 201 | 130 | 200 | 7.5% | 1.13 [0.99, 1.28] |
| Pujade-Lauraine (AURELIA) | 29 | 179 | 31 | 181 | 4.5% | 0.95 [0.60, 1.50] |
| Richardson | 41 | 50 | 23 | 50 | 5.7% | 1.78 [1.29, 2.47] |
| Tewari | 770 | 1215 | 347 | 601 | 7.7% | 1.10 [1.01, 1.19] |
| Vergote (AGO-OVAR16) | 151 | 477 | 36 | 461 | 5.6% | 4.05 [2.88, 5.70] |
| Vergote (TRINOVA-3) | 526 | 675 | 282 | 336 | 7.8% | 0.93 [0.87, 0.99] |
| **Total (95% CI)** | | **6182** | | **4759** | **100.0%** | **1.20 [1.03, 1.40]** |
| Total events | 2708 | | 1584 | | | |

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 165.51$, $df = 18$ ($P < 0.00001$); $I^2 = 89\%$

Test for overall effect: $Z = 2.40$ ($P = 0.02$)

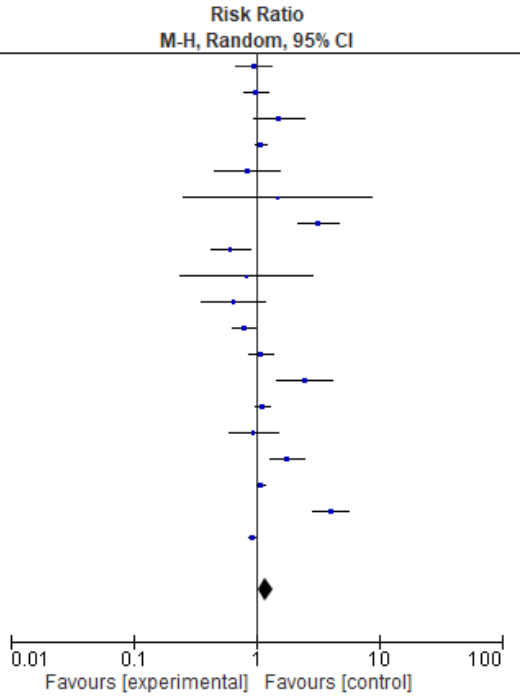


**Figure S14: Anemia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 66 | 83 | 79 | 89 | 17.4% | 0.90 [0.79, 1.02] |
| Gore | 10 | 26 | 19 | 24 | 5.3% | 0.49 [0.29, 0.82] |
| Ledermann (BIBF 1120) | 0 | 43 | 0 | 40 | | Not estimable |
| Liu | 7 | 44 | 8 | 46 | 2.1% | 0.91 [0.36, 2.31] |
| Marth (TRINOVA-2) | 11 | 113 | 15 | 108 | 3.1% | 0.70 [0.34, 1.46] |
| Monk (TRINOVA-1) | 50 | 461 | 94 | 452 | 10.1% | 0.52 [0.38, 0.72] |
| Pignata (MITO 11) | 25 | 37 | 22 | 36 | 9.3% | 1.11 [0.78, 1.56] |
| Pignata (MITO16B) | 134 | 201 | 137 | 200 | 17.3% | 0.97 [0.85, 1.11] |
| Pujade-Lauraine (AURELIA) | 3 | 179 | 4 | 181 | 0.9% | 0.76 [0.17, 3.34] |
| Richardson | 46 | 50 | 46 | 50 | 18.1% | 1.00 [0.89, 1.12] |
| Vergote (TRINOVA-3) | 261 | 675 | 146 | 336 | 16.5% | 0.89 [0.76, 1.04] |
| **Total (95% CI)** | | **1912** | | **1562** | **100.0%** | **0.86 [0.75, 0.99]** |
| Total events | 613 | | 570 | | | |

Heterogeneity: Tau² = 0.03; Chi² = 28.27, df = 9 (P = 0.0009); I² = 68%
Test for overall effect: Z = 2.13 (P = 0.03)

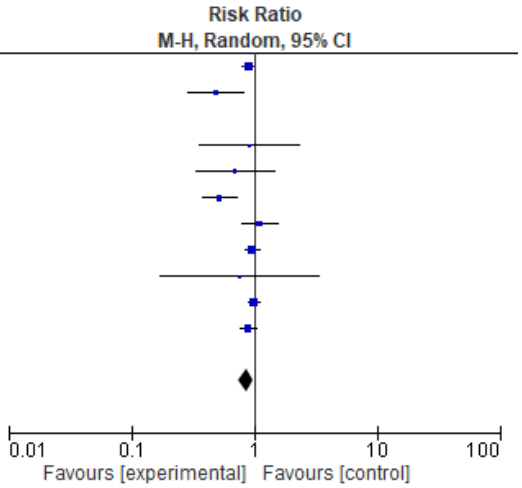



**Figure S15: Leucopenia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 66 | 83 | 79 | 89 | 17.4% | 0.90 [0.79, 1.02] |
| Gore | 10 | 26 | 19 | 24 | 5.3% | 0.49 [0.29, 0.82] |
| Ledermann (BIBF 1120) | 0 | 43 | 0 | 40 | | Not estimable |
| Liu | 7 | 44 | 8 | 46 | 2.1% | 0.91 [0.36, 2.31] |
| Marth (TRINOVA-2) | 11 | 113 | 15 | 108 | 3.1% | 0.70 [0.34, 1.46] |
| Monk (TRINOVA-1) | 50 | 461 | 94 | 452 | 10.1% | 0.52 [0.38, 0.72] |
| Pignata (MITO 11) | 25 | 37 | 22 | 36 | 9.3% | 1.11 [0.78, 1.56] |
| Pignata (MITO16B) | 134 | 201 | 137 | 200 | 17.3% | 0.97 [0.85, 1.11] |
| Pujade-Lauraine (AURELIA) | 3 | 179 | 4 | 181 | 0.9% | 0.76 [0.17, 3.34] |
| Richardson | 46 | 50 | 46 | 50 | 18.1% | 1.00 [0.89, 1.12] |
| Vergote (TRINOVA-3) | 261 | 675 | 146 | 336 | 16.5% | 0.89 [0.76, 1.04] |
| **Total (95% CI)** | | **1912** | | **1562** | **100.0%** | **0.86 [0.75, 0.99]** |
| Total events | 613 | | 570 | | | |

Heterogeneity: Tau² = 0.03; Chi² = 28.27, df = 9 (P = 0.0009); I² = 68%
Test for overall effect: Z = 2.13 (P = 0.03)

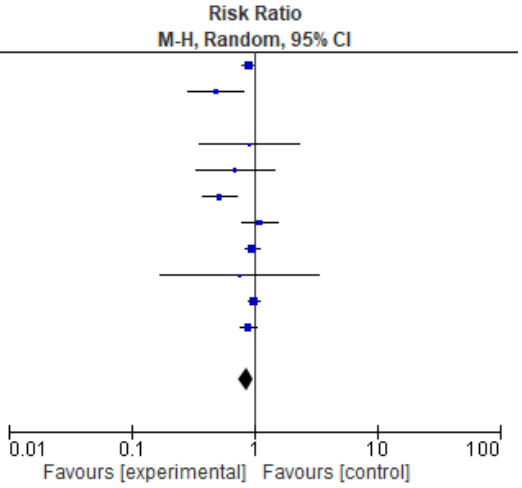


**Figure S16: Thrombocytopenia**

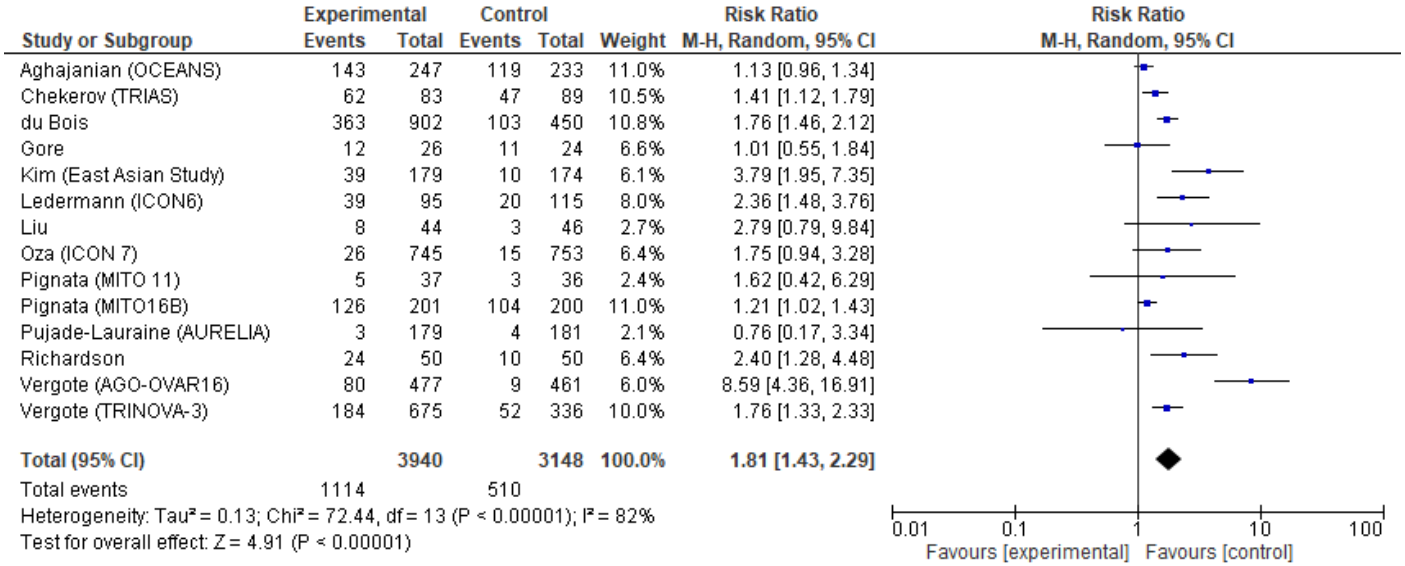


**Figure S17: Nausea**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 179 | 247 | 153 | 233 | 10.8% | 1.10 [0.98, 1.24] |
| Chekerov (TRIAS) | 51 | 83 | 50 | 89 | 8.8% | 1.09 [0.85, 1.40] |
| du Bois | 586 | 902 | 236 | 450 | 11.0% | 1.24 [1.12, 1.37] |
| Gotlieb | 9 | 30 | 7 | 25 | 2.6% | 1.07 [0.47, 2.46] |
| Herzog | 33 | 123 | 26 | 123 | 5.8% | 1.27 [0.81, 1.99] |
| Karlan | 58 | 105 | 17 | 55 | 6.1% | 1.79 [1.16, 2.75] |
| Kim (East Asian Study) | 37 | 179 | 17 | 174 | 4.8% | 2.12 [1.24, 3.61] |
| Liu | 34 | 44 | 32 | 46 | 8.9% | 1.11 [0.87, 1.43] |
| Marth (TRINOVA-2) | 67 | 113 | 62 | 108 | 9.3% | 1.03 [0.83, 1.29] |
| Pignata (MITO 11) | 14 | 37 | 13 | 36 | 4.2% | 1.05 [0.58, 1.91] |
| Pignata (MITO16B) | 110 | 201 | 96 | 200 | 9.8% | 1.14 [0.94, 1.38] |
| Richardson | 34 | 50 | 30 | 50 | 8.1% | 1.13 [0.84, 1.52] |
| Vergote (TRINOVA-3) | 408 | 675 | 88 | 336 | 9.8% | 2.31 [1.91, 2.79] |
| **Total (95% CI)** | | **2789** | | **1925** | **100.0%** | **1.28 [1.10, 1.49]** |
| Total events | 1620 | | 827 | | | |

Heterogeneity: Tau² = 0.05; Chi² = 62.82, df = 12 (P < 0.00001); I² = 81%

Test for overall effect: Z = 3.17 (P = 0.002)

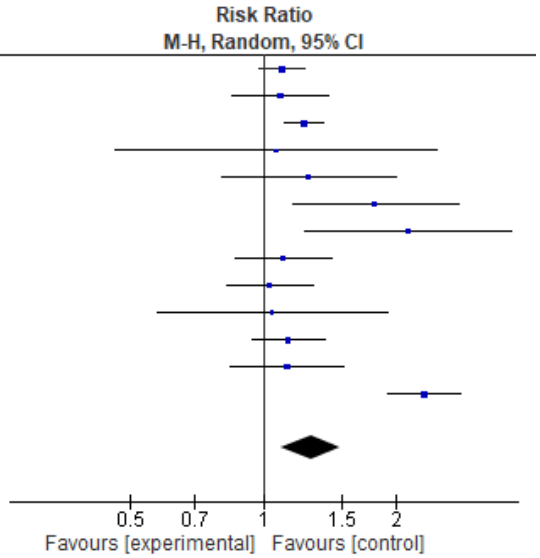


**Figure S18: Vomiting**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 33 | 83 | 36 | 89 | 10.4% | 0.98 [0.68, 1.42] |
| du Bois | 406 | 902 | 126 | 450 | 16.8% | 1.61 [1.36, 1.90] |
| Gotlieb | 16 | 30 | 13 | 25 | 7.3% | 1.03 [0.62, 1.70] |
| Herzog | 21 | 123 | 17 | 123 | 5.9% | 1.24 [0.69, 2.23] |
| Karlan | 28 | 105 | 9 | 55 | 4.8% | 1.63 [0.83, 3.21] |
| Kim (East Asian Study) | 13 | 179 | 7 | 174 | 3.1% | 1.81 [0.74, 4.42] |
| Liu | 9 | 44 | 8 | 46 | 3.3% | 1.18 [0.50, 2.77] |
| Marth (TRINOVA-2) | 51 | 113 | 36 | 108 | 11.3% | 1.35 [0.97, 1.89] |
| Pignata (MITO 11) | 11 | 37 | 6 | 36 | 3.1% | 1.78 [0.74, 4.31] |
| Pignata (MITO16B) | 44 | 201 | 42 | 200 | 10.2% | 1.04 [0.72, 1.52] |
| Pujade-Lauraine (AURELIA) | 2 | 179 | 9 | 181 | 1.2% | 0.22 [0.05, 1.03] |
| Richardson | 21 | 50 | 13 | 50 | 6.2% | 1.62 [0.91, 2.86] |
| Vergote (TRINOVA-3) | 247 | 675 | 119 | 336 | 16.5% | 1.03 [0.87, 1.23] |
| **Total (95% CI)** | | **2721** | | **1873** | **100.0%** | **1.24 [1.04, 1.47]** |
| Total events | 902 | | 441 | | | |

Heterogeneity: Tau² = 0.04; Chi² = 24.41, df = 12 (P = 0.02); I² = 51%
Test for overall effect: Z = 2.45 (P = 0.01)

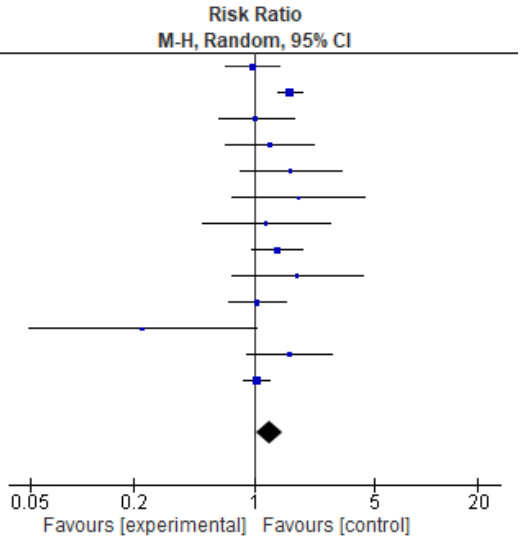



**Figure S19: Anorexia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Gotlieb | 7 | 30 | 7 | 25 | 13.2% | 0.83 [0.34, 2.06] |
| Herzog | 20 | 123 | 5 | 123 | 12.8% | 4.00 [1.55, 10.32] |
| Liu | 13 | 44 | 4 | 46 | 12.0% | 3.40 [1.20, 9.63] |
| Marth (TRINOVA-2) | 27 | 113 | 23 | 108 | 16.7% | 1.12 [0.69, 1.83] |
| Pignata (MITO 11) | 9 | 37 | 5 | 36 | 12.4% | 1.75 [0.65, 4.72] |
| Pignata (MITO16B) | 21 | 201 | 9 | 200 | 14.5% | 2.32 [1.09, 4.94] |
| Vergote (TRINOVA-3) | 187 | 675 | 146 | 336 | 18.5% | 0.64 [0.54, 0.76] |
| **Total (95% CI)** | | **1223** | | **874** | **100.0%** | **1.53 [0.84, 2.78]** |
| Total events | 284 | | 199 | | | |

Heterogeneity: Tau² = 0.49; Chi² = 38.98, df = 6 (P < 0.00001); I² = 85%
Test for overall effect: Z = 1.40 (P = 0.16)

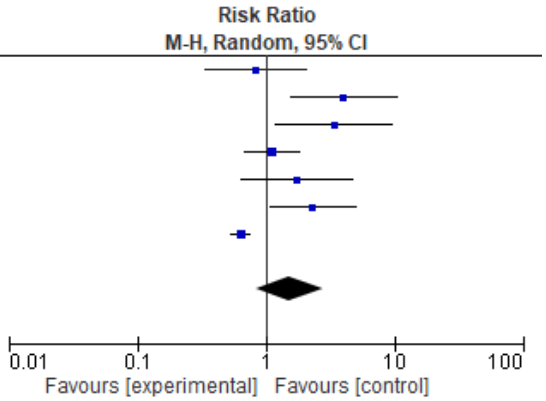


**Figure S20: Diarrhea**

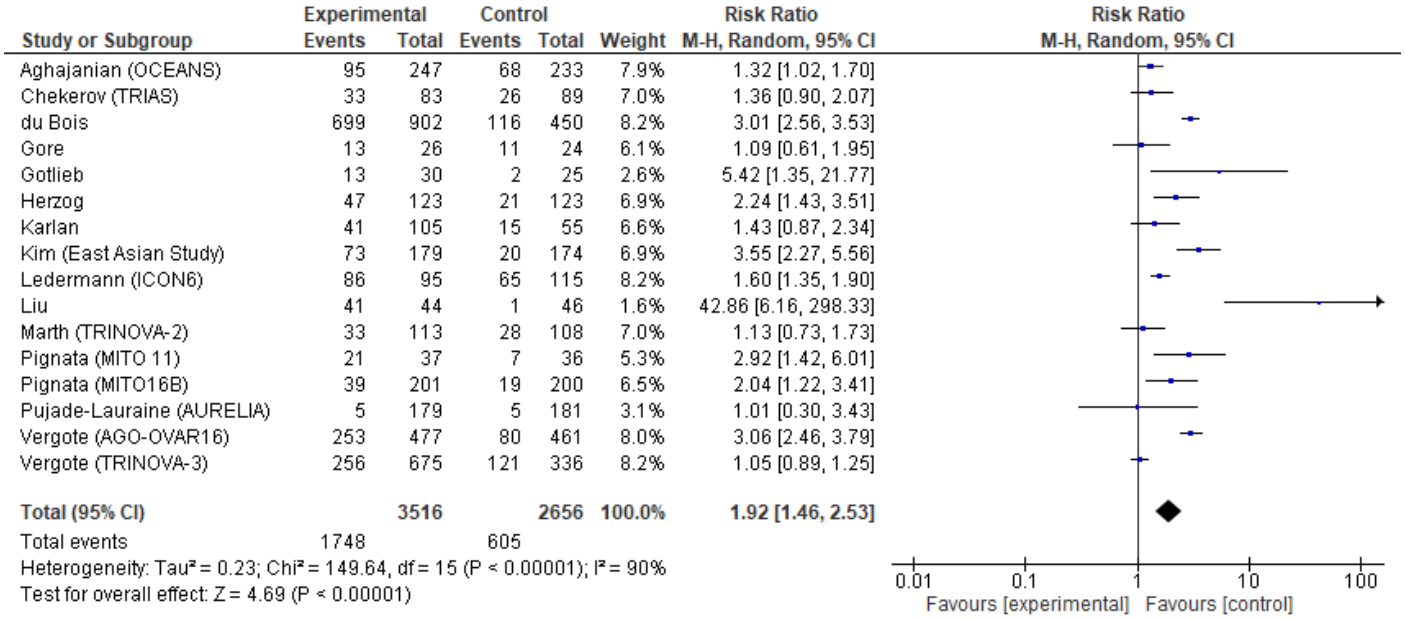


**Figure S21: Constipation**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 31 | 83 | 30 | 89 | 8.1% | 1.11 [0.74, 1.66] |
| Gore | 1 | 24 | 0 | 26 | 0.1% | 3.24 [0.14, 75.91] |
| Herzog | 24 | 123 | 18 | 123 | 5.0% | 1.33 [0.76, 2.33] |
| Karlan | 34 | 105 | 9 | 55 | 3.3% | 1.98 [1.02, 3.82] |
| Liu | 8 | 44 | 2 | 46 | 0.5% | 4.18 [0.94, 18.62] |
| Marth (TRINOVA-2) | 39 | 113 | 35 | 108 | 10.0% | 1.06 [0.73, 1.55] |
| Pignata (MITO 11) | 11 | 37 | 12 | 36 | 3.4% | 0.89 [0.45, 1.76] |
| Pignata (MITO16B) | 64 | 201 | 57 | 200 | 16.0% | 1.12 [0.83, 1.51] |
| Vergote (TRINOVA-3) | 277 | 675 | 143 | 336 | 53.4% | 0.96 [0.83, 1.12] |
| **Total (95% CI)** | | **1405** | | **1019** | **100.0%** | **1.08 [0.96, 1.21]** |
| Total events | 489 | | 306 | | | |

Heterogeneity: Chi² = 9.90, df = 8 (P = 0.27); I² = 19%
Test for overall effect: Z = 1.31 (P = 0.19)

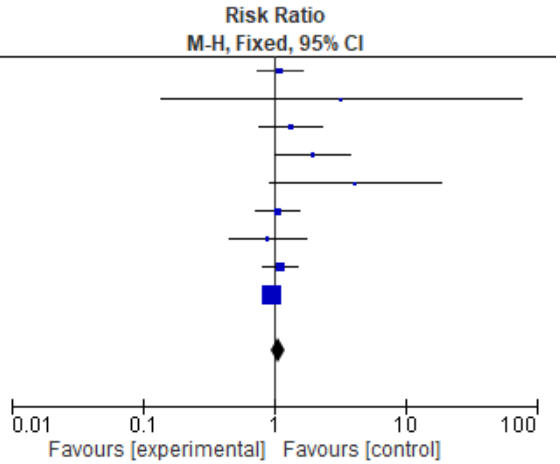



**Figure S22: Fatigue**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 31 | 83 | 30 | 89 | 8.1% | 1.11 [0.74, 1.66] |
| Gore | 1 | 24 | 0 | 26 | 0.1% | 3.24 [0.14, 75.91] |
| Herzog | 24 | 123 | 18 | 123 | 5.0% | 1.33 [0.76, 2.33] |
| Karlan | 34 | 105 | 9 | 55 | 3.3% | 1.98 [1.02, 3.82] |
| Liu | 8 | 44 | 2 | 46 | 0.5% | 4.18 [0.94, 18.62] |
| Marth (TRINOVA-2) | 39 | 113 | 35 | 108 | 10.0% | 1.06 [0.73, 1.55] |
| Pignata (MITO 11) | 11 | 37 | 12 | 36 | 3.4% | 0.89 [0.45, 1.76] |
| Pignata (MITO16B) | 64 | 201 | 57 | 200 | 16.0% | 1.12 [0.83, 1.51] |
| Vergote (TRINOVA-3) | 277 | 675 | 143 | 336 | 53.4% | 0.96 [0.83, 1.12] |
| **Total (95% CI)** | | **1405** | | **1019** | **100.0%** | **1.08 [0.96, 1.21]** |
| Total events | 489 | | 306 | | | |

Heterogeneity: Chi² = 9.90, df = 8 (P = 0.27); I² = 19%
Test for overall effect: Z = 1.31 (P = 0.19)

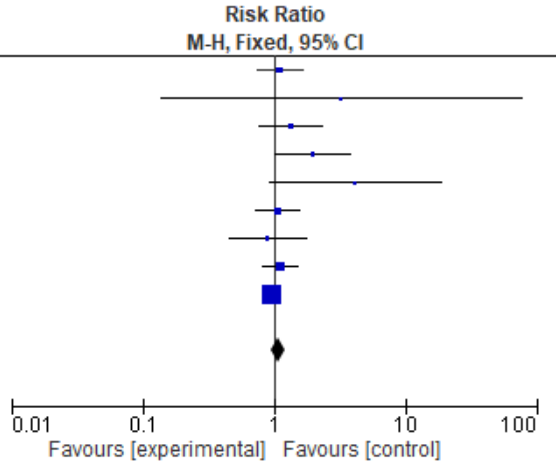


**Figure S23: Dyspnea**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 74 | 247 | 56 | 233 | 22.0% | 1.25 [0.93, 1.68] |
| Chekerov (TRIAS) | 22 | 83 | 17 | 89 | 6.3% | 1.39 [0.79, 2.42] |
| du Bois | 116 | 902 | 57 | 450 | 29.0% | 1.02 [0.76, 1.37] |
| Gore | 3 | 26 | 3 | 24 | 1.2% | 0.92 [0.21, 4.14] |
| Gotlieb | 13 | 30 | 7 | 25 | 2.9% | 1.55 [0.73, 3.28] |
| Karlan | 33 | 105 | 12 | 55 | 6.0% | 1.44 [0.81, 2.56] |
| Liu | 1 | 44 | 0 | 46 | 0.2% | 3.13 [0.13, 74.93] |
| Marth (TRINOVA-2) | 24 | 113 | 18 | 108 | 7.0% | 1.27 [0.73, 2.21] |
| Pignata (MITO16B) | 8 | 201 | 5 | 200 | 1.9% | 1.59 [0.53, 4.78] |
| Pujade-Lauraine (AURELIA) | 3 | 179 | 8 | 181 | 3.0% | 0.38 [0.10, 1.41] |
| Vergote (TRINOVA-3) | 125 | 675 | 40 | 336 | 20.4% | 1.56 [1.12, 2.17] |
| **Total (95% CI)** | | **2605** | | **1747** | **100.0%** | **1.25 [1.08, 1.45]** |
| Total events | 422 | | 223 | | | |

Heterogeneity: Chi² = 8.10, df = 10 (P = 0.62); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)

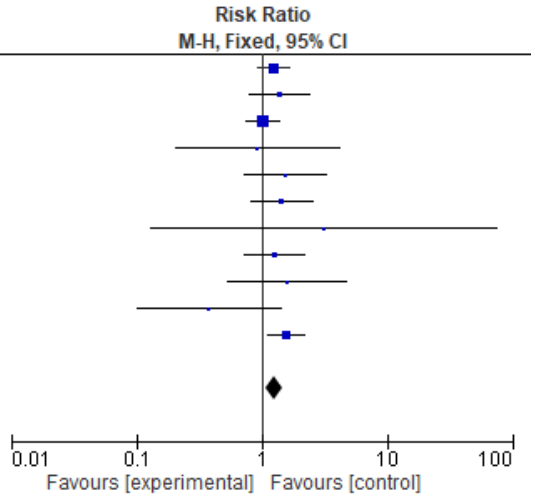



**Figure S24: Alopecia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 46 | 83 | 47 | 89 | 13.0% | 1.05 [0.80, 1.38] |
| Gore | 14 | 26 | 12 | 24 | 3.6% | 1.08 [0.63, 1.84] |
| Herzog | 13 | 123 | 6 | 123 | 1.7% | 2.17 [0.85, 5.52] |
| Karlan | 46 | 105 | 20 | 55 | 7.5% | 1.20 [0.80, 1.82] |
| Marth (TRINOVA-2) | 21 | 113 | 12 | 108 | 3.5% | 1.67 [0.87, 3.23] |
| Pignata (MITO 11) | 7 | 37 | 7 | 36 | 2.0% | 0.97 [0.38, 2.50] |
| Vergote (TRINOVA-3) | 363 | 675 | 179 | 336 | 68.6% | 1.01 [0.89, 1.14] |
| **Total (95% CI)** | | **1162** | | **771** | **100.0%** | **1.07 [0.97, 1.19]** |
| Total events | 510 | | 283 | | | |

Heterogeneity: Chi² = 5.27, df = 6 (P = 0.51); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)

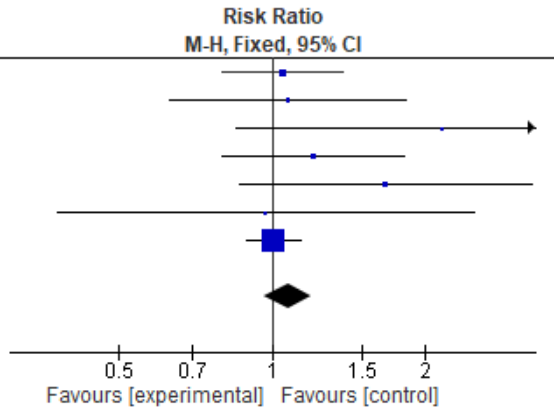


**Figure S25: Rash**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Coleman (GOG0213) | 295 | 330 | 278 | 327 | 27.5% | 1.05 [0.99, 1.12] |
| Gore | 7 | 26 | 6 | 24 | 14.7% | 1.08 [0.42, 2.75] |
| Gotlieb | 3 | 30 | 1 | 25 | 4.7% | 2.50 [0.28, 22.56] |
| Herzog | 62 | 123 | 17 | 123 | 22.5% | 3.65 [2.27, 5.86] |
| Marth (TRINOVA-2) | 2 | 113 | 2 | 108 | 5.8% | 0.96 [0.14, 6.67] |
| Pignata (MITO 11) | 0 | 37 | 0 | 36 | | Not estimable |
| Vergote (TRINOVA-3) | 76 | 675 | 49 | 336 | 24.8% | 0.77 [0.55, 1.08] |
| **Total (95% CI)** | | **1334** | | **979** | **100.0%** | **1.34 [0.79, 2.27]** |
| Total events | 445 | | 353 | | | |

Heterogeneity: Tau² = 0.26; Chi² = 34.10, df = 5 (P < 0.00001); I² = 85%
Test for overall effect: Z = 1.09 (P = 0.28)

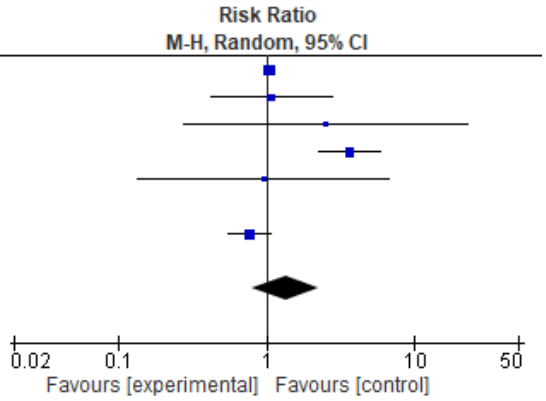



**Figure S26: Hypomagnesemia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Gore | 3 | 26 | 1 | 24 | 12.2% | 2.77 [0.31, 24.85] |
| Marth (TRINOVA-2) | 11 | 113 | 3 | 108 | 27.2% | 3.50 [1.00, 12.22] |
| Vergote (TRINOVA-3) | 97 | 675 | 44 | 336 | 60.6% | 1.10 [0.79, 1.53] |
| **Total (95% CI)** | | **814** | | **468** | **100.0%** | **1.69 [0.72, 3.93]** |
| Total events | 111 | | 48 | | | |

Heterogeneity: Tau² = 0.28; Chi² = 3.70, df = 2 (P = 0.16); I² = 46%
Test for overall effect: Z = 1.21 (P = 0.23)

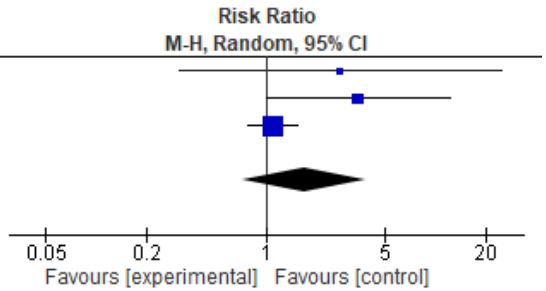


**Figure S27: Hypokalemia**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 6 | 83 | 2 | 89 | 2.6% | 3.22 [0.67, 15.49] |
| Karlan | 19 | 105 | 3 | 55 | 5.4% | 3.32 [1.03, 10.72] |
| Marth (TRINOVA-2) | 24 | 113 | 11 | 108 | 15.4% | 2.09 [1.07, 4.05] |
| Vergote (TRINOVA-3) | 146 | 675 | 42 | 336 | 76.6% | 1.73 [1.26, 2.38] |
| **Total (95% CI)** | | **976** | | **588** | **100.0%** | **1.91 [1.45, 2.51]** |
| Total events | 195 | | 58 | | | |

Heterogeneity: Chi² = 1.71, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 4.64 (P < 0.00001)

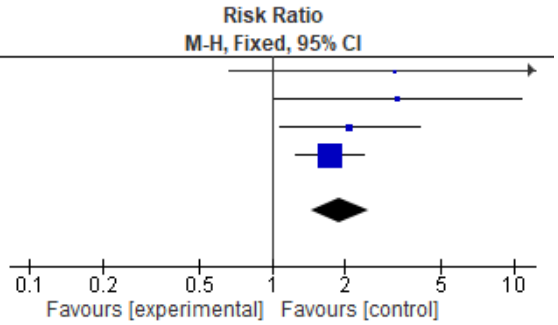



**Figure S28: Pain**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 62 | 83 | 59 | 89 | 15.6% | 1.13 [0.93, 1.37] |
| Coleman (GOG0213) | 272 | 330 | 241 | 327 | 66.4% | 1.12 [1.03, 1.21] |
| Gore | 15 | 26 | 15 | 24 | 4.3% | 0.92 [0.59, 1.45] |
| Pignata (MITO 11) | 10 | 37 | 6 | 36 | 1.7% | 1.62 [0.66, 4.00] |
| Vergote (TRINOVA-3) | 72 | 675 | 33 | 336 | 12.1% | 1.09 [0.73, 1.61] |
| **Total (95% CI)** | | **1151** | | **812** | **100.0%** | **1.12 [1.03, 1.21]** |
| Total events | 431 | | 354 | | | |

Heterogeneity: Chi² = 1.37, df = 4 (P = 0.85); I² = 0%
Test for overall effect: Z = 2.63 (P = 0.009)

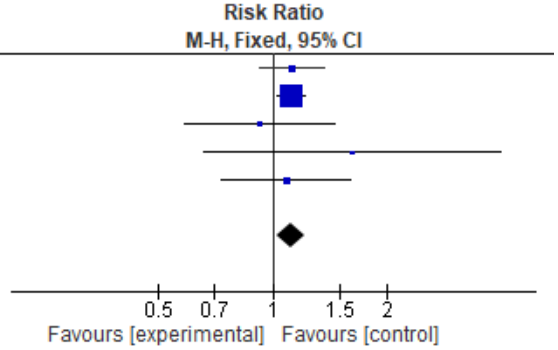


**Figure S29: Headache**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 120 | 247 | 70 | 233 | 16.3% | 1.62 [1.28, 2.04] |
| Gore | 9 | 26 | 7 | 24 | 6.3% | 1.19 [0.52, 2.69] |
| Gotlieb | 7 | 30 | 1 | 25 | 1.4% | 5.83 [0.77, 44.28] |
| Herzog | 28 | 123 | 19 | 123 | 10.4% | 1.47 [0.87, 2.49] |
| Karlan | 28 | 105 | 7 | 55 | 6.9% | 2.10 [0.98, 4.49] |
| Kim (East Asian Study) | 34 | 179 | 17 | 174 | 10.1% | 1.94 [1.13, 3.35] |
| Liu | 20 | 44 | 4 | 46 | 4.8% | 5.23 [1.94, 14.08] |
| Marth (TRINOVA-2) | 15 | 113 | 16 | 108 | 8.3% | 0.90 [0.47, 1.72] |
| Pignata (MITO16B) | 26 | 201 | 4 | 200 | 4.5% | 6.47 [2.30, 18.19] |
| Vergote (AGO-OVAR16) | 136 | 477 | 70 | 461 | 15.8% | 1.88 [1.45, 2.43] |
| Vergote (TRINOVA-3) | 125 | 675 | 55 | 336 | 15.2% | 1.13 [0.85, 1.51] |
| **Total (95% CI)** | | **2220** | | **1785** | **100.0%** | **1.73 [1.34, 2.22]** |
| Total events | 548 | | 270 | | | |

Heterogeneity: Tau² = 0.09; Chi² = 25.93, df = 10 (P = 0.004); I² = 61%
Test for overall effect: Z = 4.25 (P < 0.0001)

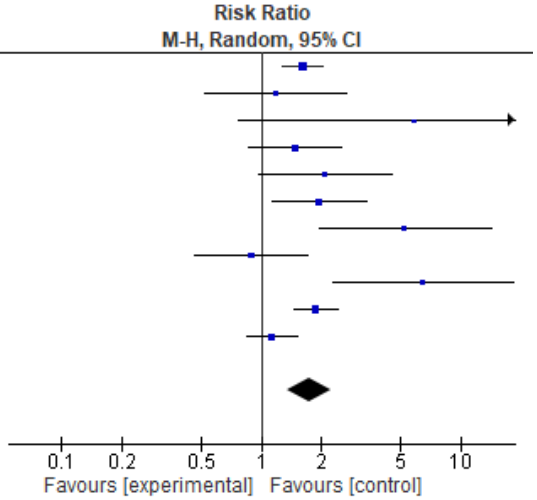



**Figure S30: Abdominal pain**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chekerov (TRIAS) | 30 | 83 | 31 | 89 | 6.3% | 1.04 [0.69, 1.55] |
| Gotlieb | 7 | 30 | 5 | 25 | 1.1% | 1.17 [0.42, 3.23] |
| Herzog | 22 | 123 | 21 | 123 | 4.4% | 1.05 [0.61, 1.80] |
| Karlan | 34 | 105 | 18 | 55 | 5.0% | 0.99 [0.62, 1.58] |
| Kim (East Asian Study) | 22 | 179 | 20 | 174 | 4.3% | 1.07 [0.61, 1.89] |
| Liu | 9 | 44 | 3 | 46 | 0.6% | 3.14 [0.91, 10.83] |
| Marth (TRINOVA-2) | 35 | 113 | 41 | 108 | 8.8% | 0.82 [0.57, 1.18] |
| Pignata (MITO16B) | 23 | 201 | 16 | 200 | 3.4% | 1.43 [0.78, 2.63] |
| Pujade-Lauraine (AURELIA) | 5 | 179 | 10 | 181 | 2.1% | 0.51 [0.18, 1.45] |
| Vergote (AGO-OVAR16) | 169 | 477 | 142 | 461 | 30.3% | 1.15 [0.96, 1.38] |
| Vergote (TRINOVA-3) | 241 | 675 | 121 | 336 | 33.9% | 0.99 [0.83, 1.18] |
| **Total (95% CI)** | | **2209** | | **1798** | **100.0%** | **1.05 [0.95, 1.17]** |
| Total events | 597 | | 428 | | | |

Heterogeneity: Chi² = 9.15, df = 10 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

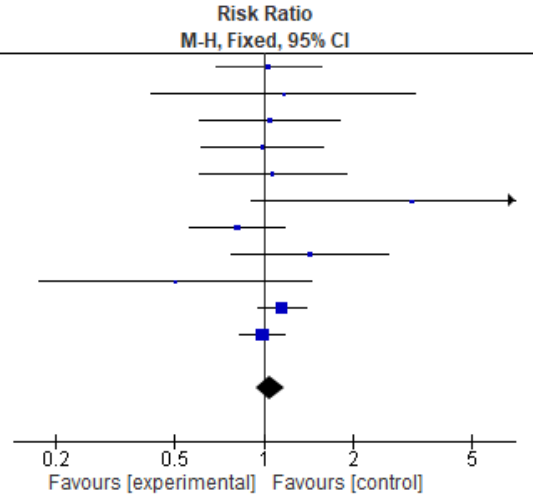
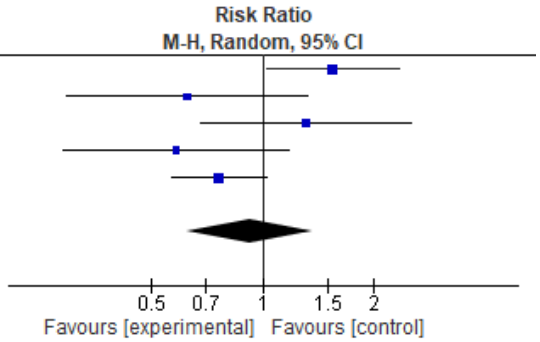


**Figure S31: Back pain**

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Aghajanian (OCEANS) | 51 | 247 | 31 | 233 | 24.2% | 1.55 [1.03, 2.34] |
| Herzog | 10 | 123 | 16 | 123 | 15.0% | 0.63 [0.30, 1.32] |
| Karlan | 25 | 105 | 10 | 55 | 17.1% | 1.31 [0.68, 2.53] |
| Marth (TRINOVA-2) | 11 | 113 | 18 | 108 | 16.1% | 0.58 [0.29, 1.18] |
| Vergote (TRINOVA-3) | 92 | 675 | 60 | 336 | 27.6% | 0.76 [0.57, 1.03] |
| **Total (95% CI)** | | **1263** | | **855** | **100.0%** | **0.92 [0.62, 1.37]** |
| Total events | 189 | | 135 | | | |

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 11.53$, $df = 4$ ($P = 0.02$); $I^2 = 65\%$

Test for overall effect: $Z = 0.39$ ($P = 0.70$)



**Supplementary Material 2 Prisma Checklist**

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number or statement of absence of registration. | 1,3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 2 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 3 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3.4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4 |

| | | | |
|---|---|---|---|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4,5 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 4,5 |



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 4, Figure 2 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 5 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 4 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Table 2. and Table 3. |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Figure 2 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 4,5 Figures 3-7 Supplementary material 1 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 4,5 Figures 3-7 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 6 Figure 2 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 6 Supplementary |

| | | | |
|---|---|---|---|
| | | | material 3 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 23-24 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 23 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 7,20-22 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 24 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

**Supplementary Material 3 Graphical representation of statistical analysis**

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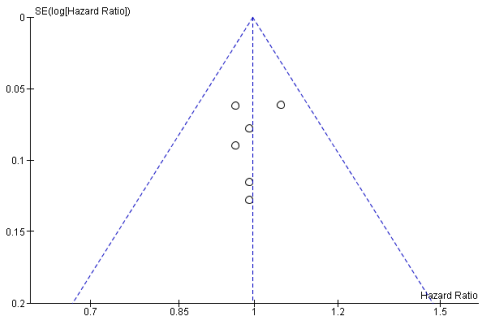


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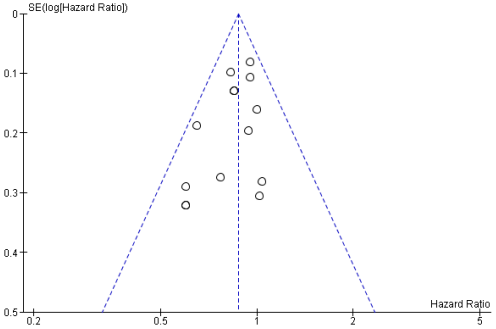


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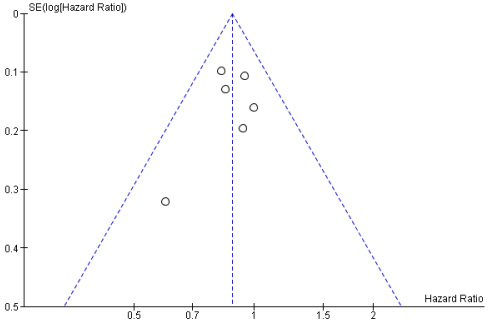


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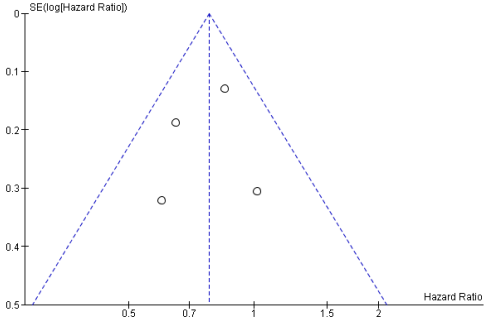


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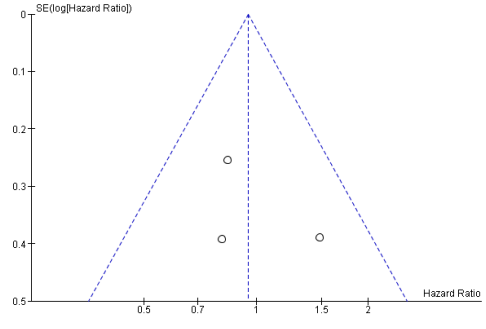


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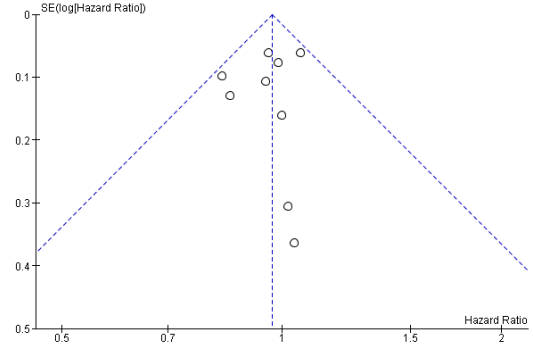

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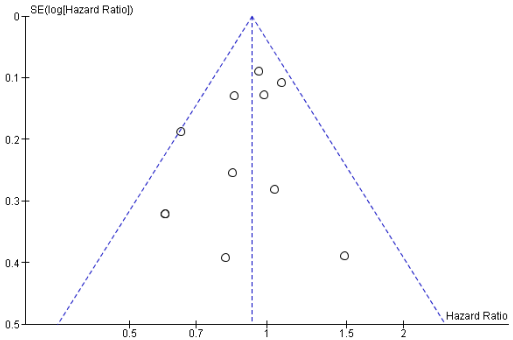


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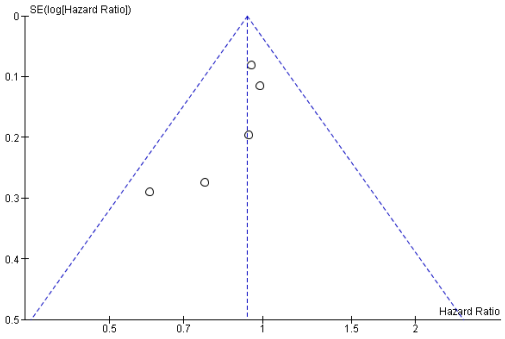
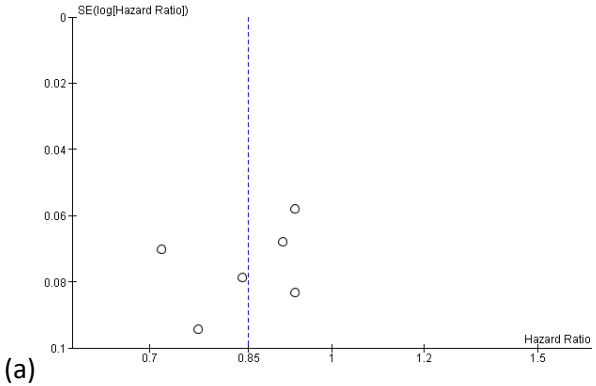



Figure S32 – Sensitivity analysis (OS): (a)first-line; (b)recurrent disease; (c)P-S R; (d) P-R R; (e)maintenance; (f)VEGF inhibitors; (g)VEGF-R inhibitors; (h)angiopoietin inhibitors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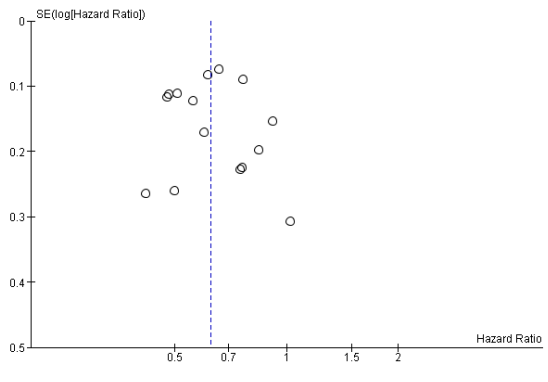
0.06
0.08
0.1
Hazard Ratio
0.7
0.85
1
1.2
1.5

(a)


SE(log[Hazard Ratio])
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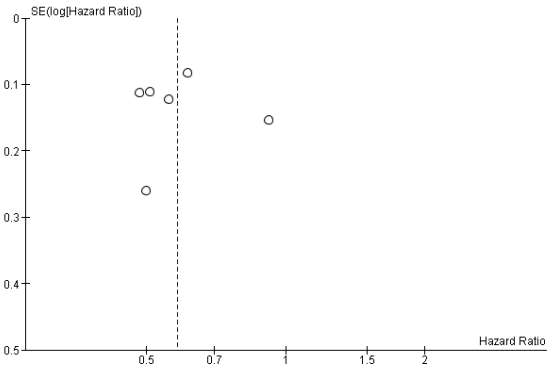
0.1
0.2
0.3
0.4
0.5
Hazard Ratio
0.5
0.7
1
1.5
2

(b)


SE(log[Hazard Ratio])
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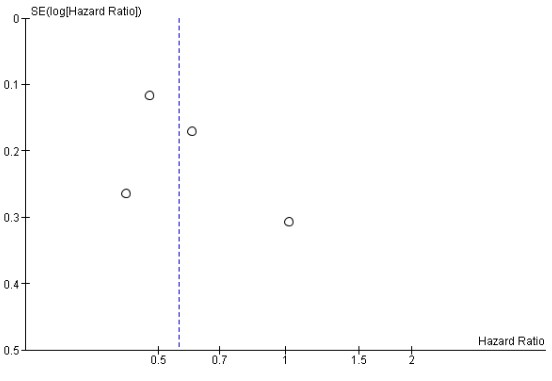
0.2
0.3
0.4
0.5
Hazard Ratio
0.5
0.7
1
1.5
2

(c)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Hazard Ratio
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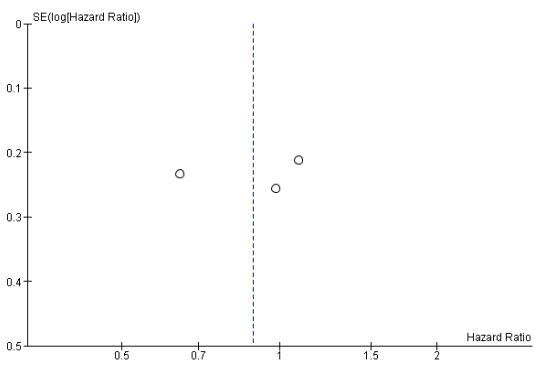
0.7
1
1.5
2

(d)


SE(log[Hazard Ratio])
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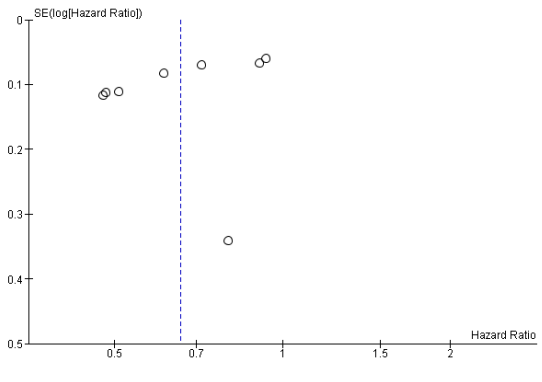
0.5
Hazard Ratio
0.5
0.7
1
1.5
2

(e)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Hazard Ratio
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2

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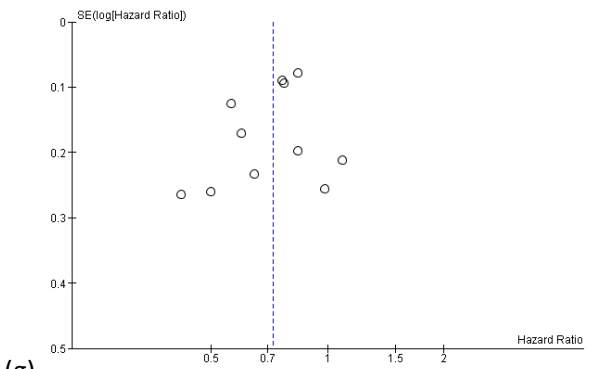


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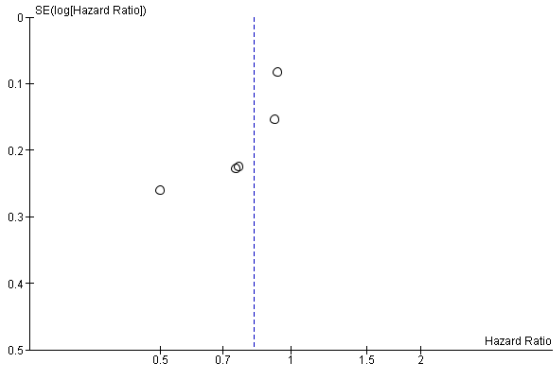
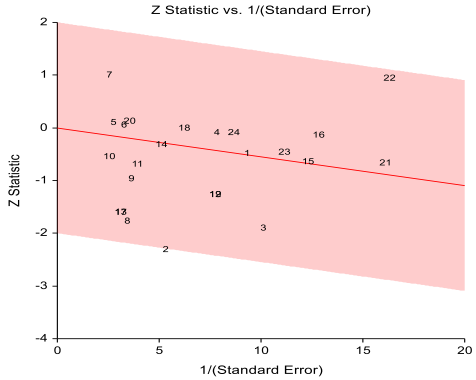



(h)

Figure S33 – Sensitivity analysis (PFS): (a)first-line; (b)recurrent disease; (c)P-S R; (d) P-R R; (e)maintenance; (f)VEGF inhibitors; (g)VEGF-R inhibitors; (h)angiopoietin inhibitors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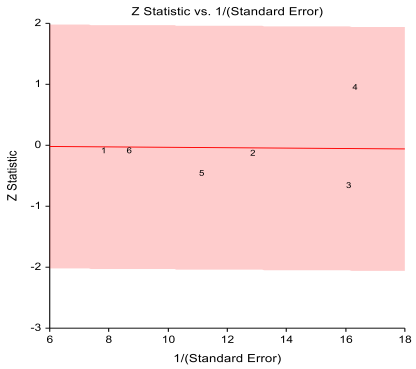
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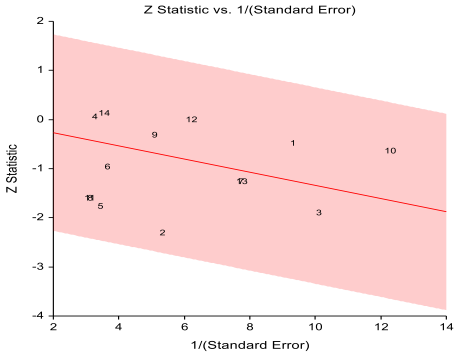
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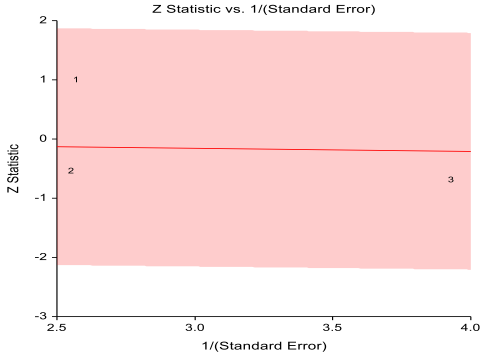
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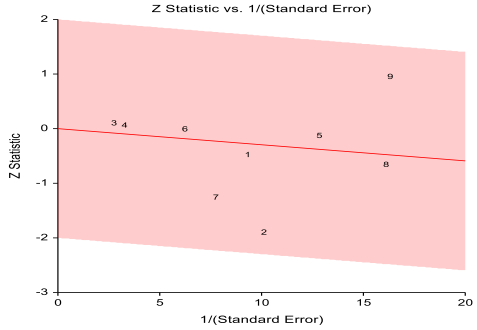
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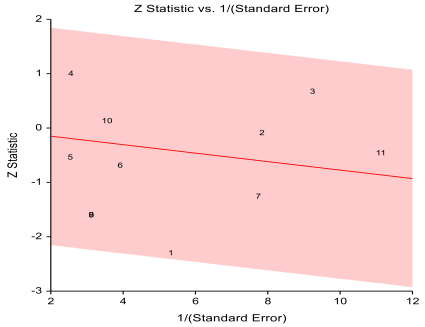
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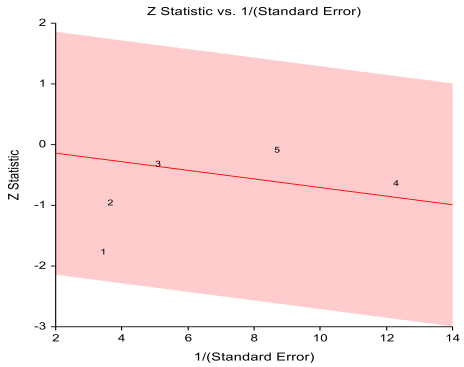
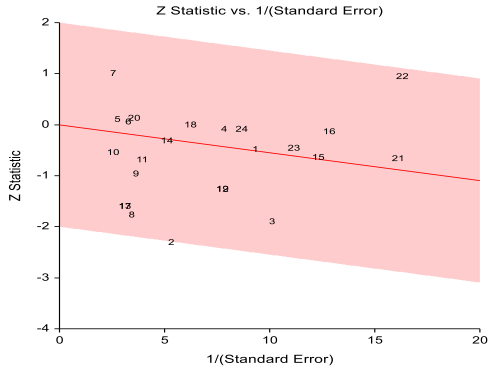



(g)

Figure S34 – Radial plots (OS): (a)pooled OS; (b)first-line; (c)recurrent disease; (d)maintenance; (e)VEGF inhibitors; (f)VEGF-R inhibitors; (g)angiopoietin inhibitors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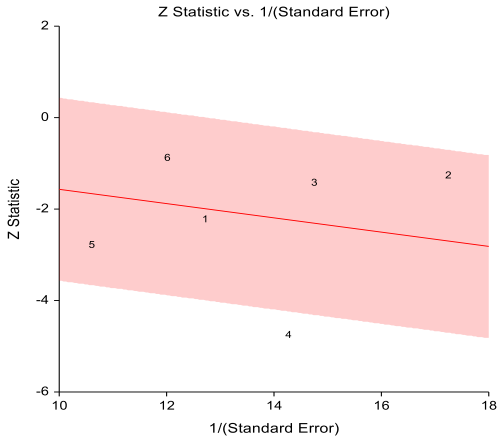
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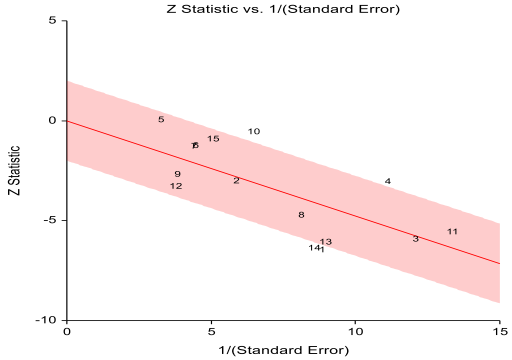
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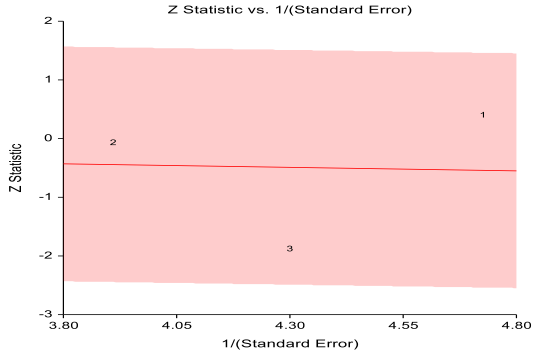
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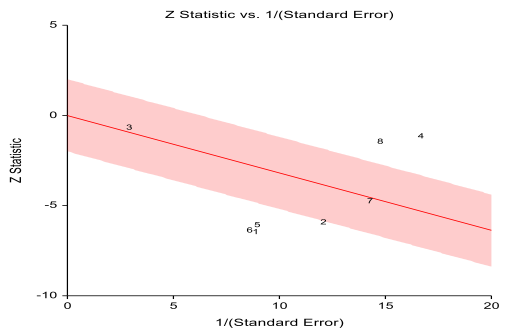
(e)

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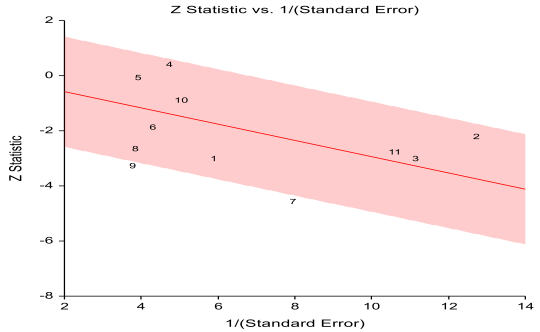


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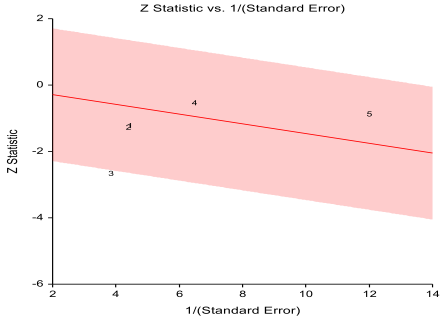


Figure S35 – Radial plots (PFS): (a)pooled PFS; (b)first-line; (c)recurrent disease; (d)maintenance; (e)VEGF inhibitors; (f)VEGF-R inhibitors; (g)angiopoietin inhibitors