Supplementary Figure 1 Forest plot of the comparison of complete response rates (CR, A), partial response rates (PR, B) stable disease rates (SD, C) and progressive disease rates (PD, D) between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 2. Forest plot of the comparison of all-grade hand-foot syndrome between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 3. Forest plot of the comparison of all-grade hypertension between Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 4. Forest plot of the comparison of all-grade albuminuria between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 5. Forest plot of the comparison of all-grade hemoglobin reduction between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 6. Forest plot of the comparison of all-grade nausea and vomiting between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 7. Forest plot of the comparison of all-grade diarrhea between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

Supplementary Figure 8. Forest plot of the comparison of all-grade thrombocytopenia between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

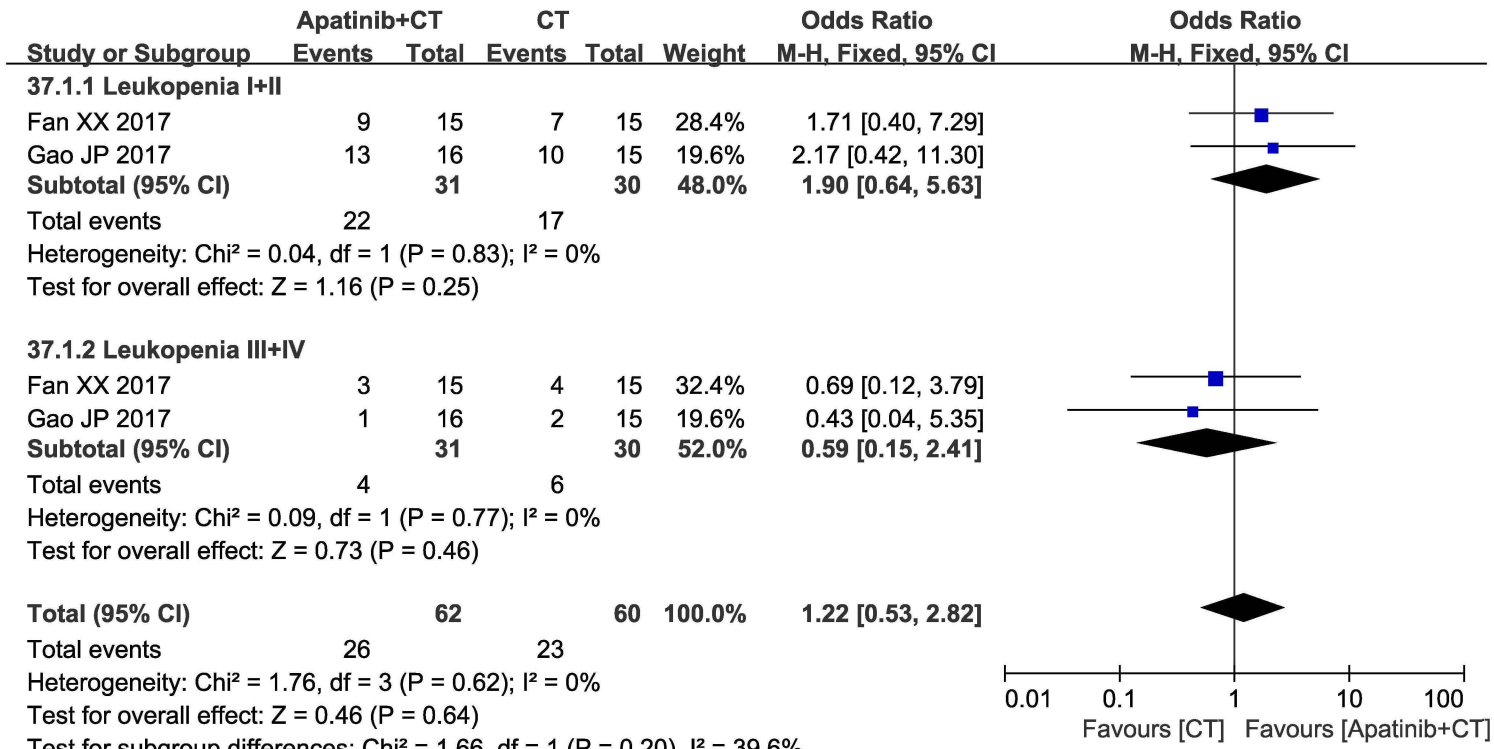
Supplementary Figure 9. Forest plot of the comparison of all-grade oral mucositis between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

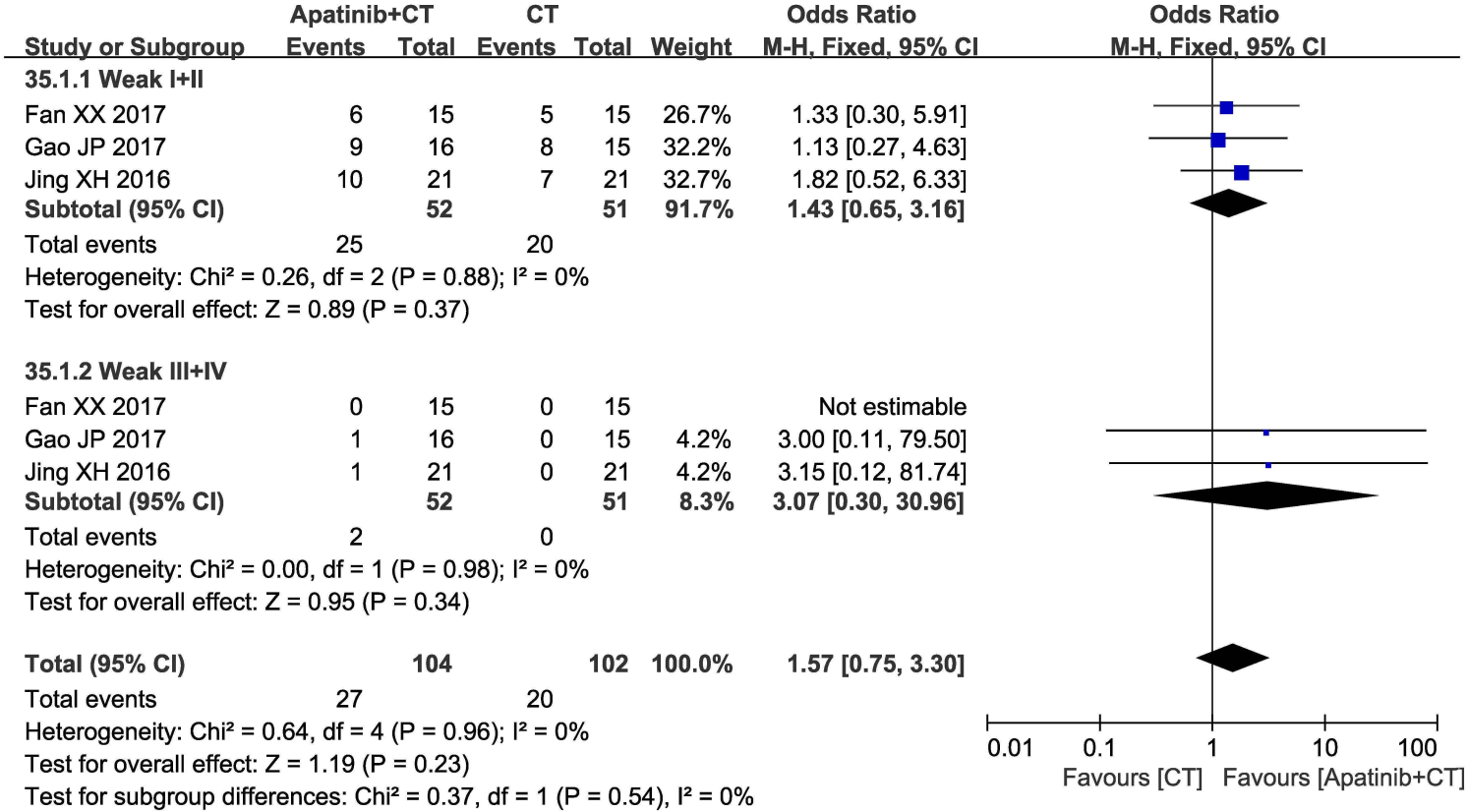
Supplementary Figure 10. Forest plot of the comparison of all-grade weak between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

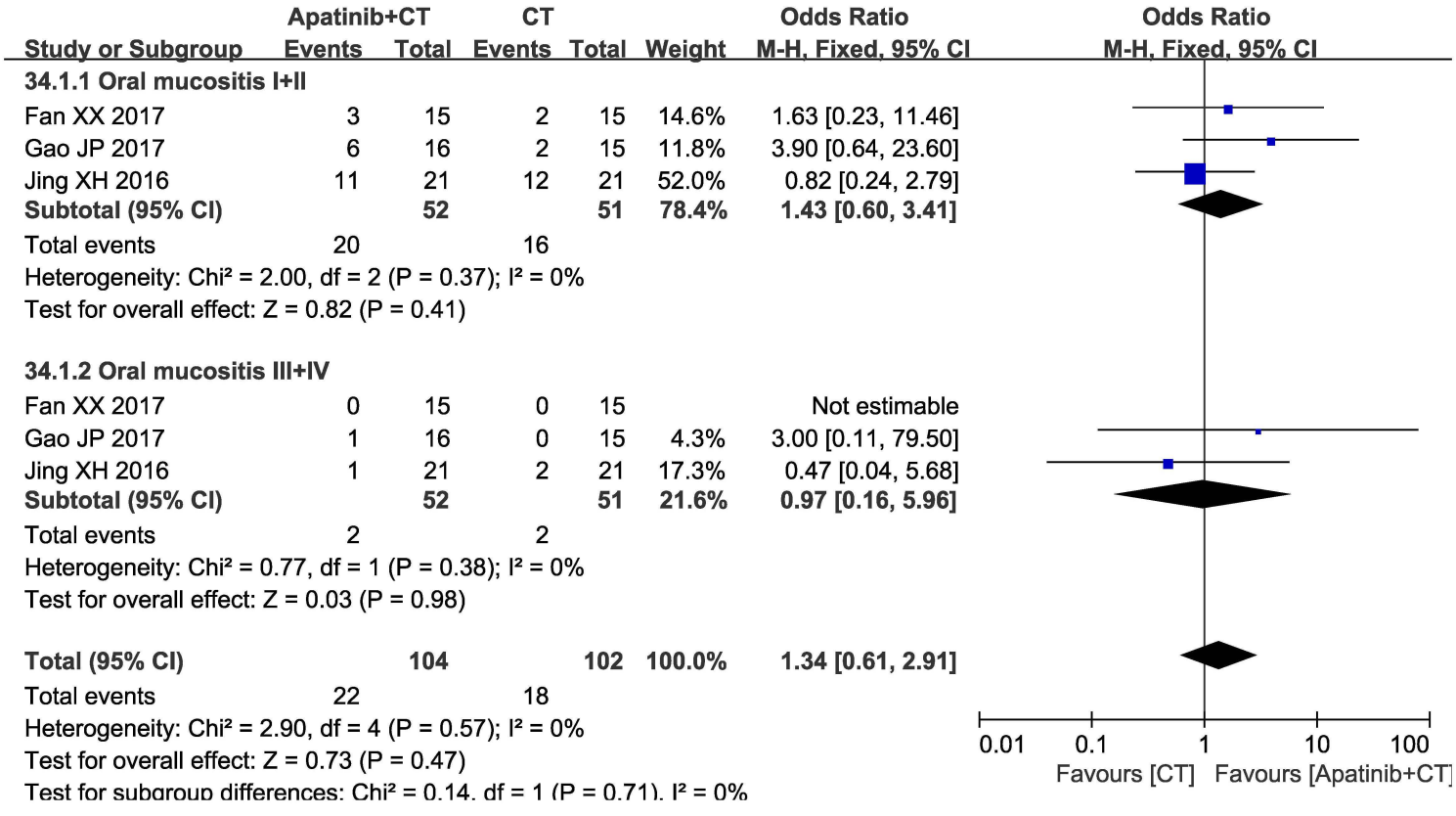
Supplementary Figure 11. Forest plot of the comparison of all-grade leucopenia between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

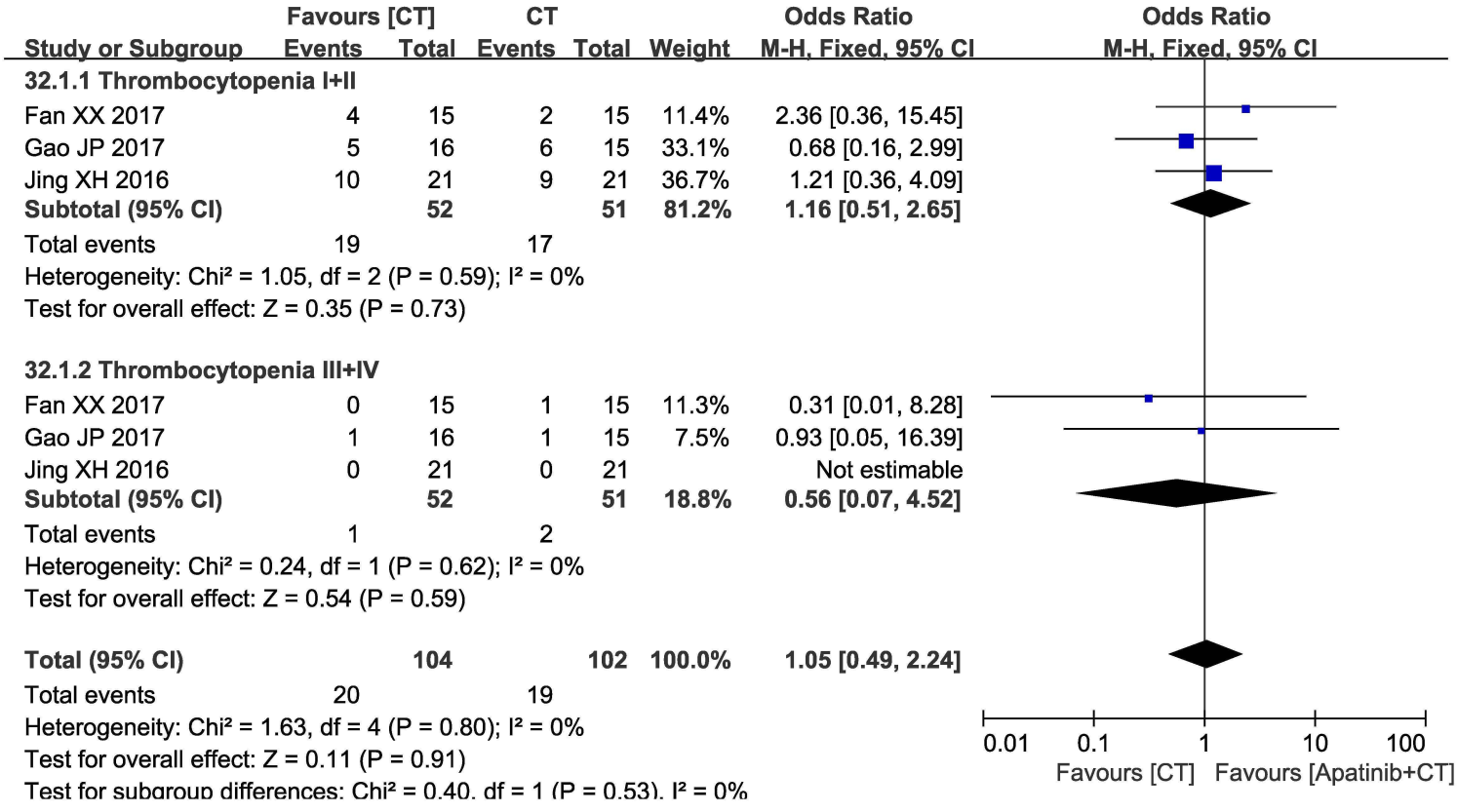
Supplementary Figure 12. Forest plot of the comparison of all-grade neutropenia between the Apatinib+S-1 and S-1 groups. S-1: Gimeracil and Oteracil Porassium Capsules. The fixed-effects meta-analysis model (Mantel–Haenszel method) was used.

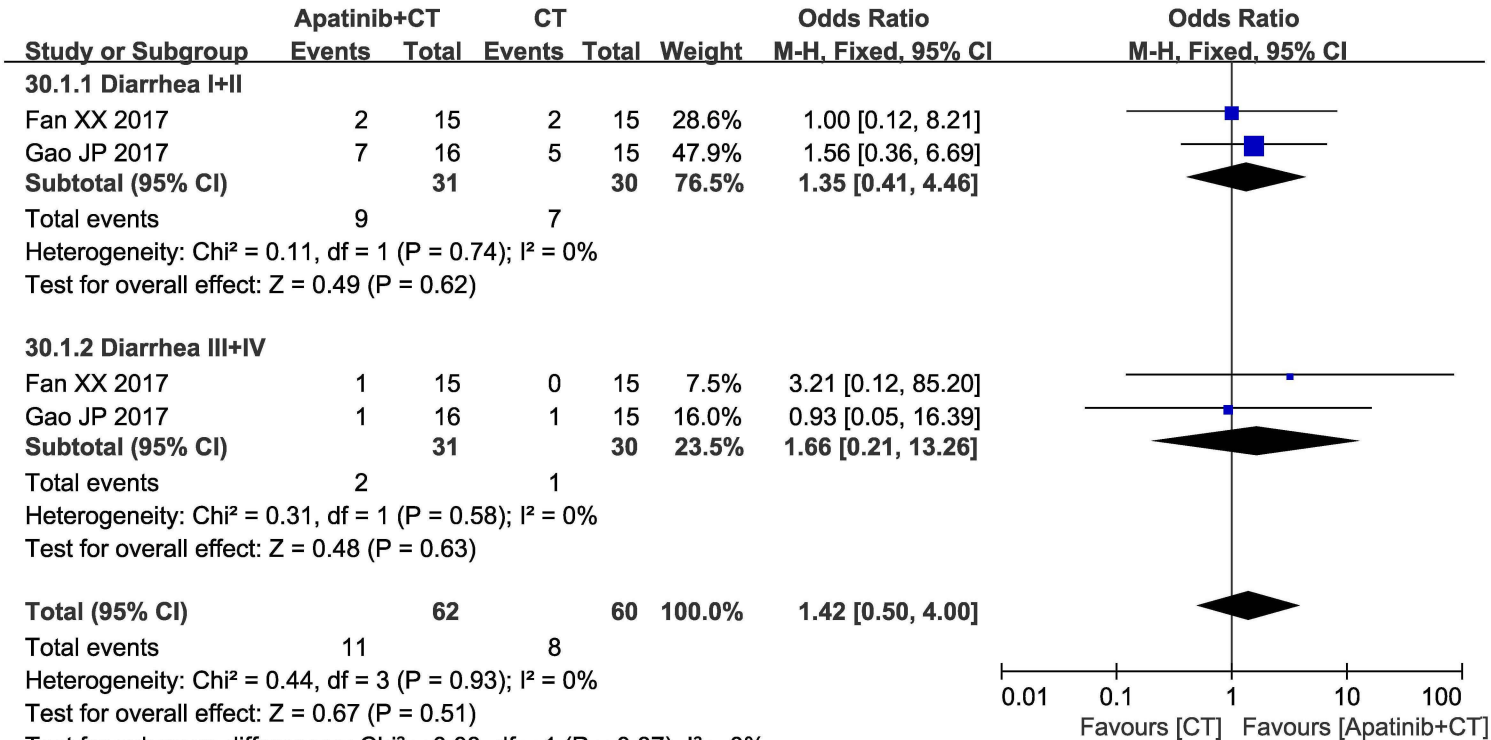
Supplementary Figure 13. Funnel plot of percentage of complete response rates (CR, A), partial response rates (PR, B) stable disease rates (SD, C) and progressive disease rates (PD, D).

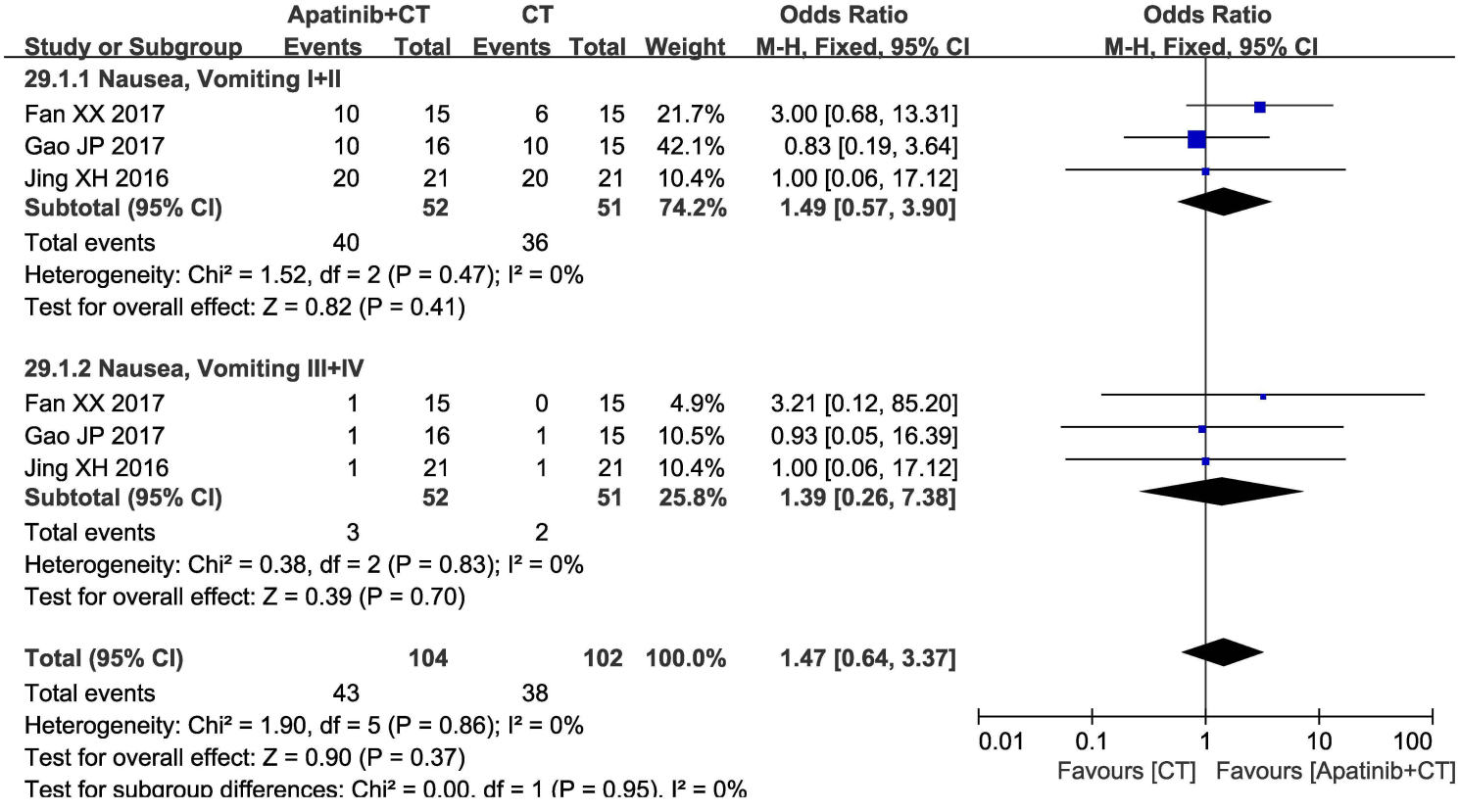

Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
37.1.1 Leukopenia I+II
Fan XX 2017 9 15 7 15 28.4% 1.71 [0.40, 7.29]
Gao JP 2017 13 16 10 15 19.6% 2.17 [0.42, 11.30]
Subtotal (95% CI) 31 30 48.0% 1.90 [0.64, 5.63]
Total events 22 17
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 1.16 (P = 0.25)
37.1.2 Leukopenia III+IV
Fan XX 2017 3 15 4 15 32.4% 0.69 [0.12, 3.79]
Gao JP 2017 1 16 2 15 19.6% 0.43 [0.04, 5.35]
Subtotal (95% CI) 31 30 52.0% 0.59 [0.15, 2.41]
Total events 4 6
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.73 (P = 0.46)
Total (95% CI) 62 60 100.0% 1.22 [0.53, 2.82]
Total events 26 23
Heterogeneity: Chi² = 1.76, df = 3 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.46 (P = 0.64)
Test for subgroup differences: Chi² = 1.66, df = 1 (P = 0.20), I² = 39.6%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]

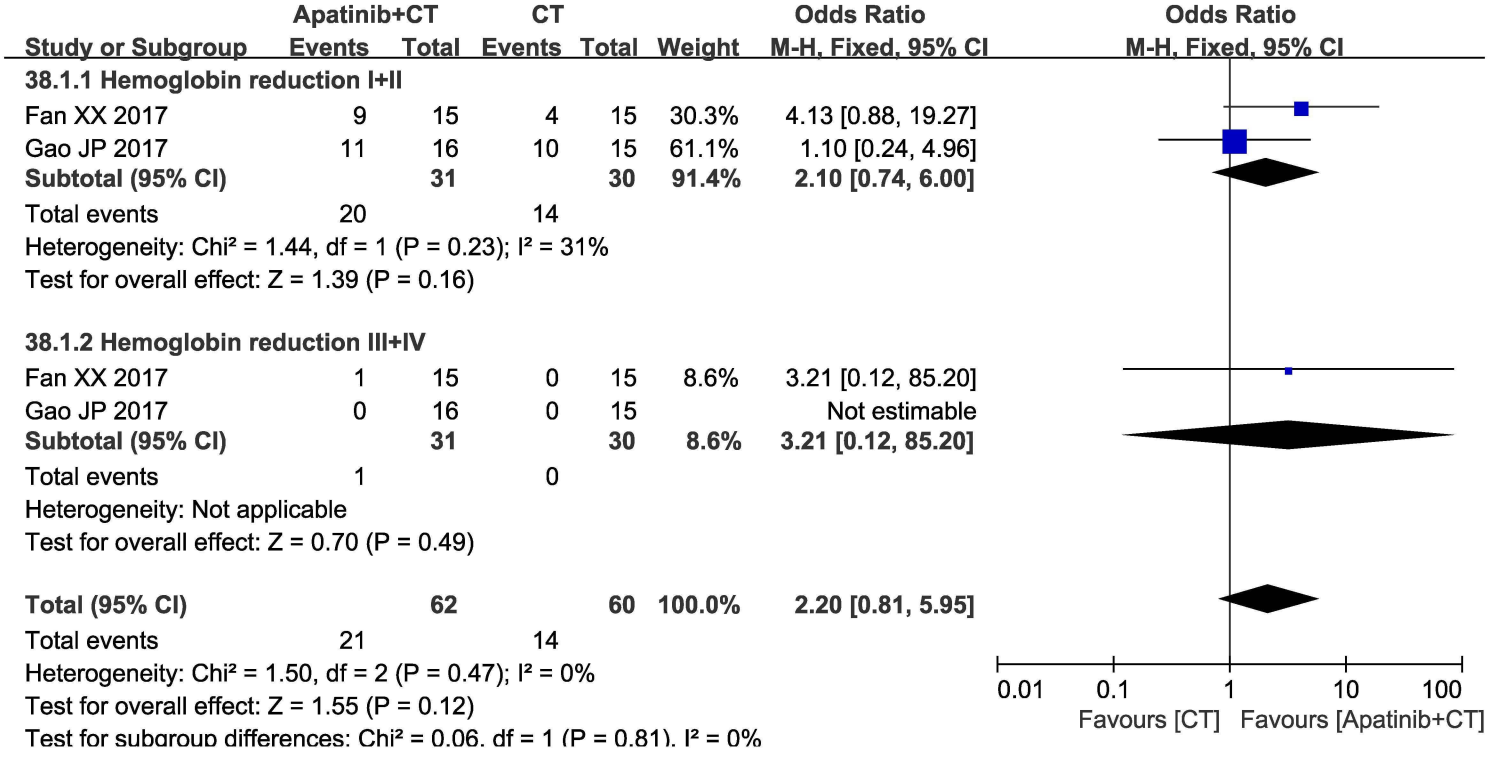

Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
35.1.1 Weak I+II
Fan XX 2017 6 15 5 15 26.7% 1.33 [0.30, 5.91]
Gao JP 2017 9 16 8 15 32.2% 1.13 [0.27, 4.63]
Jing XH 2016 10 21 7 21 32.7% 1.82 [0.52, 6.33]
Subtotal (95% CI) 52 51 91.7% 1.43 [0.65, 3.16]
Total events 25 20
Heterogeneity: Chi² = 0.26, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.37)
35.1.2 Weak III+IV
Fan XX 2017 0 15 0 15 Not estimable
Gao JP 2017 1 16 0 15 4.2% 3.00 [0.11, 79.50]
Jing XH 2016 1 21 0 21 4.2% 3.15 [0.12, 81.74]
Subtotal (95% CI) 52 51 8.3% 3.07 [0.30, 30.96]
Total events 2 0
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)
Total (95% CI) 104 102 100.0% 1.57 [0.75, 3.30]
Total events 27 20
Heterogeneity: Chi² = 0.64, df = 4 (P = 0.96); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.23)
Test for subgroup differences: Chi² = 0.37, df = 1 (P = 0.54), I² = 0%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]

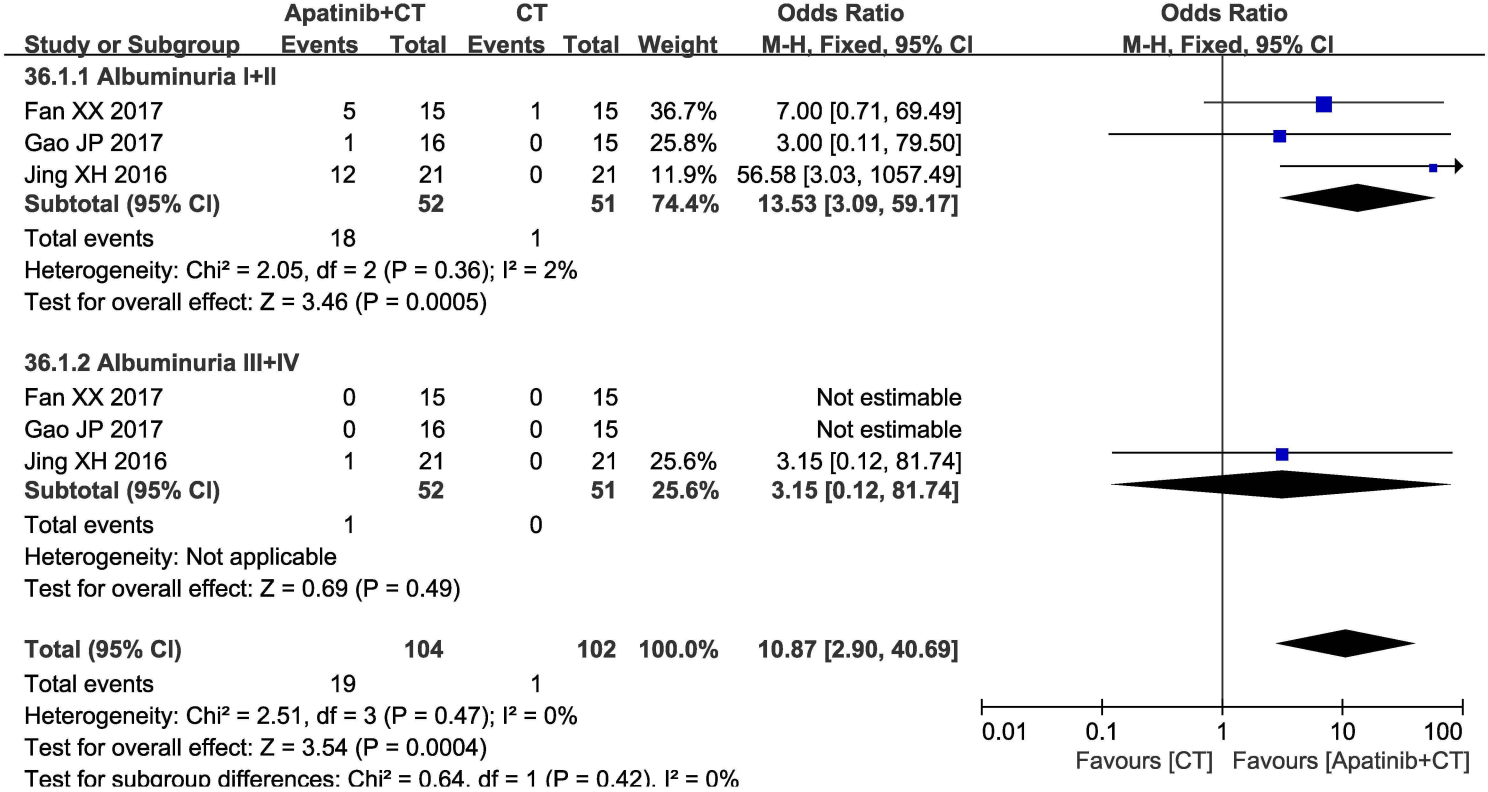

Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
34.1.1 Oral mucositis I+II
Fan XX 2017 3 15 2 15 14.6% 1.63 [0.23, 11.46]
Gao JP 2017 6 16 2 15 11.8% 3.90 [0.64, 23.60]
Jing XH 2016 11 21 12 21 52.0% 0.82 [0.24, 2.79]
Subtotal (95% CI) 52 51 78.4% 1.43 [0.60, 3.41]
Total events 20 16
Heterogeneity: Chi² = 2.00, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.82 (P = 0.41)
34.1.2 Oral mucositis III+IV
Fan XX 2017 0 15 0 15 Not estimable
Gao JP 2017 1 16 0 15 4.3% 3.00 [0.11, 79.50]
Jing XH 2016 1 21 2 21 17.3% 0.47 [0.04, 5.68]
Subtotal (95% CI) 52 51 21.6% 0.97 [0.16, 5.96]
Total events 2 2
Heterogeneity: Chi² = 0.77, df = 1 (P = 0.38); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.98)
Total (95% CI) 104 102 100.0% 1.34 [0.61, 2.91]
Total events 22 18
Heterogeneity: Chi² = 2.90, df = 4 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%
0.01 0.1 1 10 100
Favours [CT] Favours [Apatinib+CT]

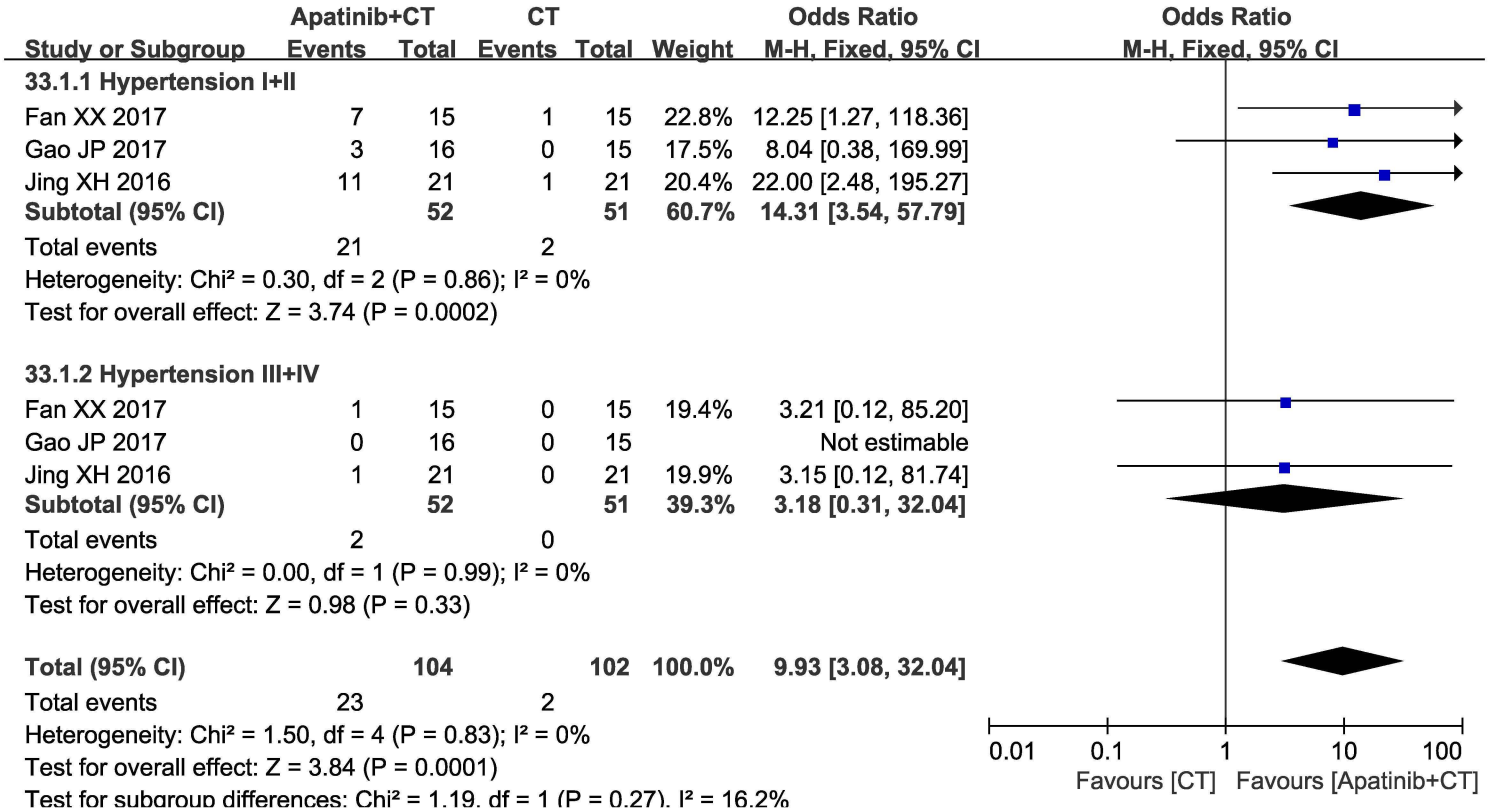

Favours [CT]
CT
Odds Ratio
Odds Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
32.1.1 Thrombocytopenia I+II
Fan XX 2017 4 15 2 15 11.4% 2.36 [0.36, 15.45]
Gao JP 2017 5 16 6 15 33.1% 0.68 [0.16, 2.99]
Jing XH 2016 10 21 9 21 36.7% 1.21 [0.36, 4.09]
Subtotal (95% CI) 52 51 81.2% 1.16 [0.51, 2.65]
Total events 19 17
Heterogeneity: Chi² = 1.05, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.35 (P = 0.73)
32.1.2 Thrombocytopenia III+IV
Fan XX 2017 0 15 1 15 11.3% 0.31 [0.01, 8.28]
Gao JP 2017 1 16 1 15 7.5% 0.93 [0.05, 16.39]
Jing XH 2016 0 21 0 21 Not estimable
Subtotal (95% CI) 52 51 18.8% 0.56 [0.07, 4.52]
Total events 1 2
Heterogeneity: Chi² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)
Total (95% CI) 104 102 100.0% 1.05 [0.49, 2.24]
Total events 20 19
Heterogeneity: Chi² = 1.63, df = 4 (P = 0.80); I² = 0%
Test for overall effect: Z = 0.11 (P = 0.91)
Test for subgroup differences: Chi² = 0.40, df = 1 (P = 0.53), I² = 0%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]

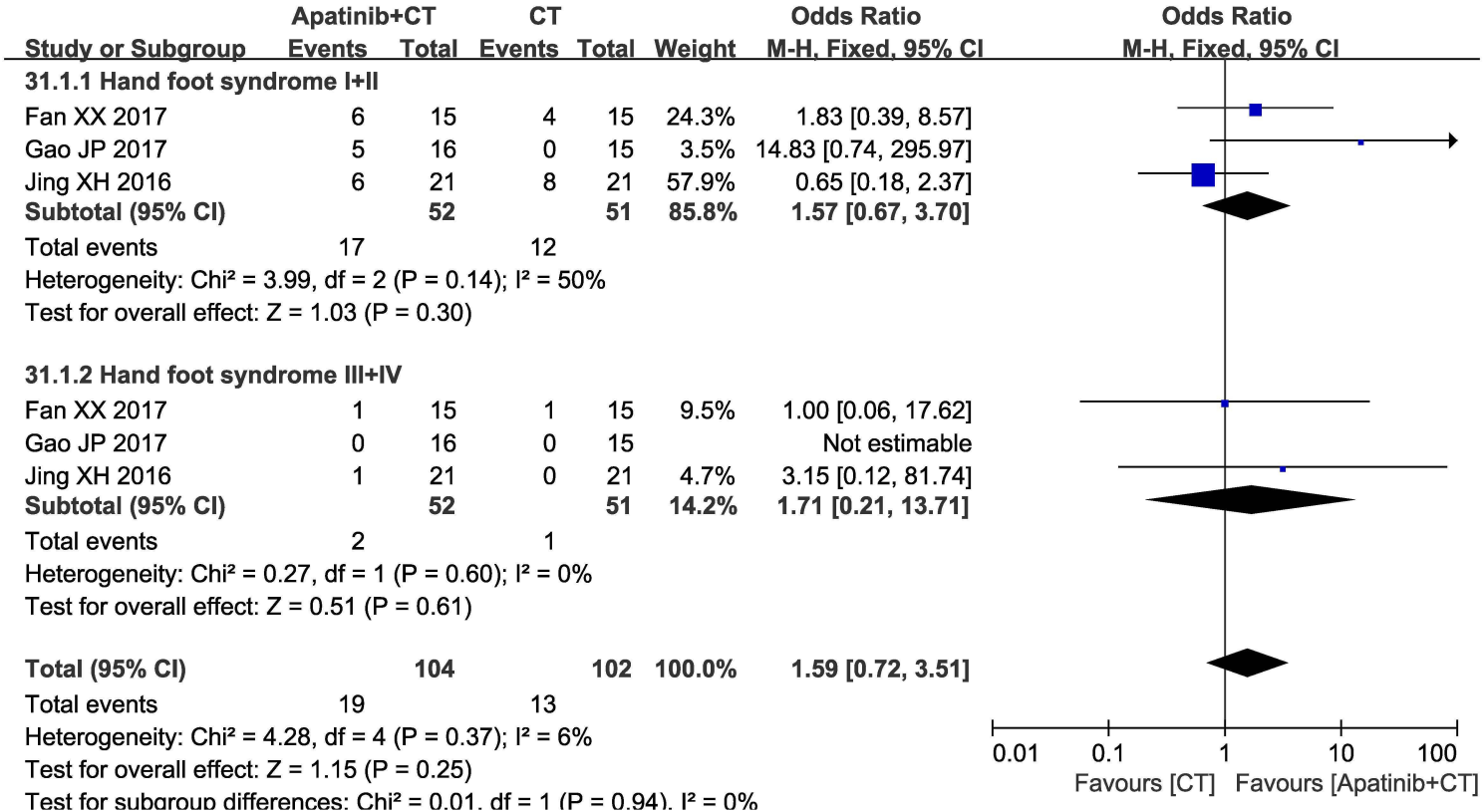

Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
30.1.1 Diarrhea I+II
Fan XX 2017 2 15 2 15 28.6% 1.00 [0.12, 8.21]
Gao JP 2017 7 16 5 15 47.9% 1.56 [0.36, 6.69]
Subtotal (95% CI) 31 30 76.5% 1.35 [0.41, 4.46]
Total events 9 7
Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.49 (P = 0.62)
30.1.2 Diarrhea III+IV
Fan XX 2017 1 15 0 15 7.5% 3.21 [0.12, 85.20]
Gao JP 2017 1 16 1 15 16.0% 0.93 [0.05, 16.39]
Subtotal (95% CI) 31 30 23.5% 1.66 [0.21, 13.26]
Total events 2 1
Heterogeneity: Chi² = 0.31, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.48 (P = 0.63)
Total (95% CI) 62 60 100.0% 1.42 [0.50, 4.00]
Total events 11 8
Heterogeneity: Chi² = 0.44, df = 3 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.67 (P = 0.51)
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.87), I² = 0%
0.01 0.1 1 10 100
Favours [CT] Favours [Apatinib+CT]


Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
29.1.1 Nausea, Vomiting I+II
Fan XX 2017 10 15 6 15 21.7% 3.00 [0.68, 13.31]
Gao JP 2017 10 16 10 15 42.1% 0.83 [0.19, 3.64]
Jing XH 2016 20 21 20 21 10.4% 1.00 [0.06, 17.12]
Subtotal (95% CI) 52 51 74.2% 1.49 [0.57, 3.90]
Total events 40 36
Heterogeneity: Chi² = 1.52, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.82 (P = 0.41)
29.1.2 Nausea, Vomiting III+IV
Fan XX 2017 1 15 0 15 4.9% 3.21 [0.12, 85.20]
Gao JP 2017 1 16 1 15 10.5% 0.93 [0.05, 16.39]
Jing XH 2016 1 21 1 21 10.4% 1.00 [0.06, 17.12]
Subtotal (95% CI) 52 51 25.8% 1.39 [0.26, 7.38]
Total events 3 2
Heterogeneity: Chi² = 0.38, df = 2 (P = 0.83); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)
Total (95% CI) 104 102 100.0% 1.47 [0.64, 3.37]
Total events 43 38
Heterogeneity: Chi² = 1.90, df = 5 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%
0.01 0.1 1 10 100
Favours [CT] Favours [Apatinib+CT]


Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
38.1.1 Hemoglobin reduction I+II
Fan XX 2017 9 15 4 15 30.3% 4.13 [0.88, 19.27]
Gao JP 2017 11 16 10 15 61.1% 1.10 [0.24, 4.96]
Subtotal (95% CI) 31 30 91.4% 2.10 [0.74, 6.00]
Total events 20 14
Heterogeneity: Chi² = 1.44, df = 1 (P = 0.23); I² = 31%
Test for overall effect: Z = 1.39 (P = 0.16)
38.1.2 Hemoglobin reduction III+IV
Fan XX 2017 1 15 0 15 8.6% 3.21 [0.12, 85.20]
Gao JP 2017 0 16 0 15 Not estimable
Subtotal (95% CI) 31 30 8.6% 3.21 [0.12, 85.20]
Total events 1 0
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.49)
Total (95% CI) 62 60 100.0% 2.20 [0.81, 5.95]
Total events 21 14
Heterogeneity: Chi² = 1.50, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 1.55 (P = 0.12)
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]


Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
36.1.1 Albuminuria I+II
Fan XX 2017 5 15 1 15 36.7% 7.00 [0.71, 69.49]
Gao JP 2017 1 16 0 15 25.8% 3.00 [0.11, 79.50]
Jing XH 2016 12 21 0 21 11.9% 56.58 [3.03, 1057.49]
Subtotal (95% CI) 52 51 74.4% 13.53 [3.09, 59.17]
Total events 18 1
Heterogeneity: Chi² = 2.05, df = 2 (P = 0.36); I² = 2%
Test for overall effect: Z = 3.46 (P = 0.0005)
36.1.2 Albuminuria III+IV
Fan XX 2017 0 15 0 15 Not estimable
Gao JP 2017 0 16 0 15 Not estimable
Jing XH 2016 1 21 0 21 25.6% 3.15 [0.12, 81.74]
Subtotal (95% CI) 52 51 25.6% 3.15 [0.12, 81.74]
Total events 1 0
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)
Total (95% CI) 104 102 100.0% 10.87 [2.90, 40.69]
Total events 19 1
Heterogeneity: Chi² = 2.51, df = 3 (P = 0.47); I² = 0%
Test for overall effect: Z = 3.54 (P = 0.0004)
Test for subgroup differences: Chi² = 0.64, df = 1 (P = 0.42), I² = 0%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]

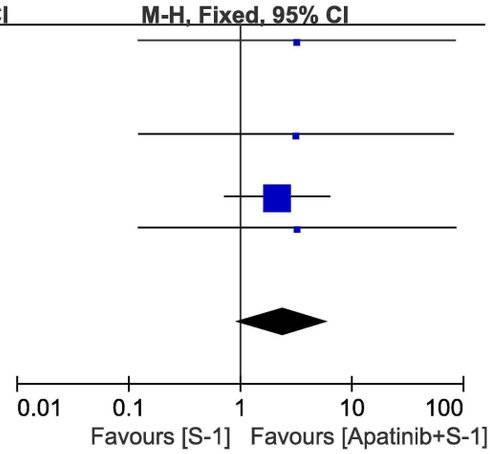

Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
33.1.1 Hypertension I+II
Fan XX 2017 7 15 1 15 22.8% 12.25 [1.27, 118.36]
Gao JP 2017 3 16 0 15 17.5% 8.04 [0.38, 169.99]
Jing XH 2016 11 21 1 21 20.4% 22.00 [2.48, 195.27]
Subtotal (95% CI) 52 51 60.7% 14.31 [3.54, 57.79]
Total events 21 2
Heterogeneity: Chi² = 0.30, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 3.74 (P = 0.0002)
33.1.2 Hypertension III+IV
Fan XX 2017 1 15 0 15 19.4% 3.21 [0.12, 85.20]
Gao JP 2017 0 16 0 15 Not estimable
Jing XH 2016 1 21 0 21 19.9% 3.15 [0.12, 81.74]
Subtotal (95% CI) 52 51 39.3% 3.18 [0.31, 32.04]
Total events 2 0
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)
Total (95% CI) 104 102 100.0% 9.93 [3.08, 32.04]
Total events 23 2
Heterogeneity: Chi² = 1.50, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 3.84 (P = 0.0001)
Test for subgroup differences: Chi² = 1.19, df = 1 (P = 0.27), I² = 16.2%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]


Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
31.1.1 Hand foot syndrome I+II
Fan XX 2017 6 15 4 15 24.3% 1.83 [0.39, 8.57]
Gao JP 2017 5 16 0 15 3.5% 14.83 [0.74, 295.97]
Jing XH 2016 6 21 8 21 57.9% 0.65 [0.18, 2.37]
Subtotal (95% CI) 52 51 85.8% 1.57 [0.67, 3.70]
Total events 17 12
Heterogeneity: Chi² = 3.99, df = 2 (P = 0.14); I² = 50%
Test for overall effect: Z = 1.03 (P = 0.30)
31.1.2 Hand foot syndrome III+IV
Fan XX 2017 1 15 1 15 9.5% 1.00 [0.06, 17.62]
Gao JP 2017 0 16 0 15 Not estimable
Jing XH 2016 1 21 0 21 4.7% 3.15 [0.12, 81.74]
Subtotal (95% CI) 52 51 14.2% 1.71 [0.21, 13.71]
Total events 2 1
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 0.51 (P = 0.61)
Total (95% CI) 104 102 100.0% 1.59 [0.72, 3.51]
Total events 19 13
Heterogeneity: Chi² = 4.28, df = 4 (P = 0.37); I² = 6%
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%
0.01 0.1 1 10 100
Favours [CT] Favours [Apatinib+CT]

A

Study or Subgroup	Apatinib+S-1 Events	Total	S-1 Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Fan XX 2017	1	15	0	15	7.8%	3.21 [0.12, 85.20]
Gao JP 2017	0	16	0	15		Not estimable
Hu SS 2016	0	23	0	23		Not estimable
Jing XH 2016	1	21	0	21	8.1%	3.15 [0.12, 81.74]
Sheng HM 2017	0	59	0	59		Not estimable
Wang DP 2016	13	29	8	29	76.3%	2.13 [0.71, 6.37]
Wu ZW 2017	1	14	0	14	7.8%	3.22 [0.12, 86.09]
Zhou L 2018	0	20	0	20		Not estimable
Total (95% CI)		**197**		**196**	**100.0%**	**2.38 [0.93, 6.12]**
Total events	16		8			

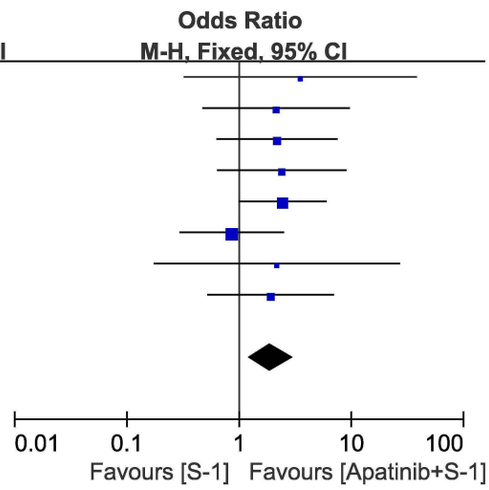
Heterogeneity: Chi² = 0.13, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.81 (P = 0.07)



B

Study or Subgroup	Apatinib+S-1 Events	Total	S-1 Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Fan XX 2017	3	15	1	15	3.0%	3.50 [0.32, 38.23]
Gao JP 2017	7	16	4	15	8.6%	2.14 [0.47, 9.70]
Hu SS 2016	10	23	6	23	12.6%	2.18 [0.63, 7.56]
Jing XH 2016	9	21	5	21	10.6%	2.40 [0.64, 9.03]
Sheng HM 2017	18	59	9	59	23.2%	2.44 [0.99, 6.00]
Wang DP 2016	10	29	11	29	26.7%	0.86 [0.29, 2.52]
Wu ZW 2017	2	14	1	14	3.2%	2.17 [0.17, 27.08]
Zhou L 2018	9	20	6	20	12.2%	1.91 [0.52, 7.01]
Total (95% CI)		**197**		**196**	**100.0%**	**1.91 [1.21, 3.02]**
Total events	68		43			

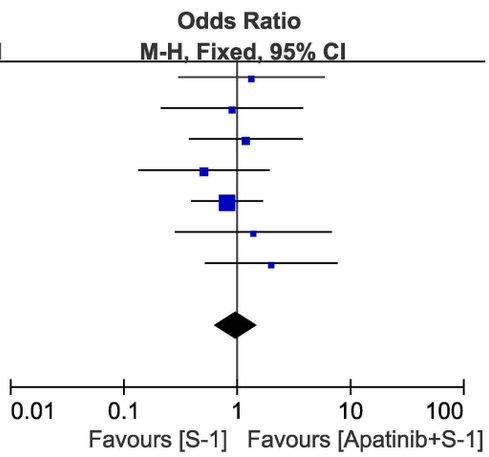
Heterogeneity: Chi² = 2.84, df = 7 (P = 0.90); I² = 0%
Test for overall effect: Z = 2.78 (P = 0.005)



C

Study or Subgroup	Apatinib+S-1 Events	Total	S-1 Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Fan XX 2017	10	15	9	15	7.5%	1.33 [0.30, 5.91]
Gao JP 2017	6	16	6	15	9.7%	0.90 [0.21, 3.82]
Hu SS 2016	12	23	11	23	13.2%	1.19 [0.37, 3.78]
Jing XH 2016	5	21	8	21	15.3%	0.51 [0.13, 1.93]
Sheng HM 2017	32	59	35	59	40.2%	0.81 [0.39, 1.69]
Wu ZW 2017	10	14	9	14	6.5%	1.39 [0.28, 6.84]
Zhou L 2018	8	20	5	20	7.5%	2.00 [0.52, 7.72]
Total (95% CI)		**168**		**167**	**100.0%**	**0.99 [0.64, 1.54]**
Total events	83		83			

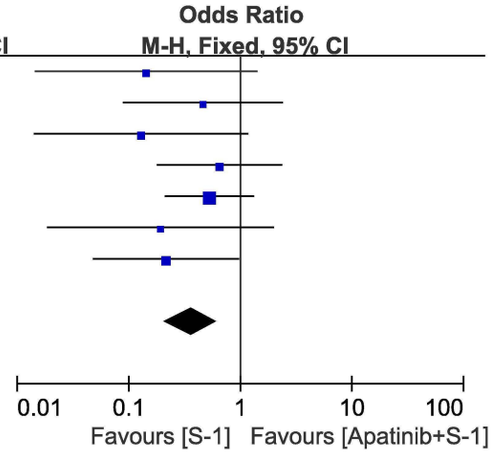
Heterogeneity: Chi² = 2.72, df = 6 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)

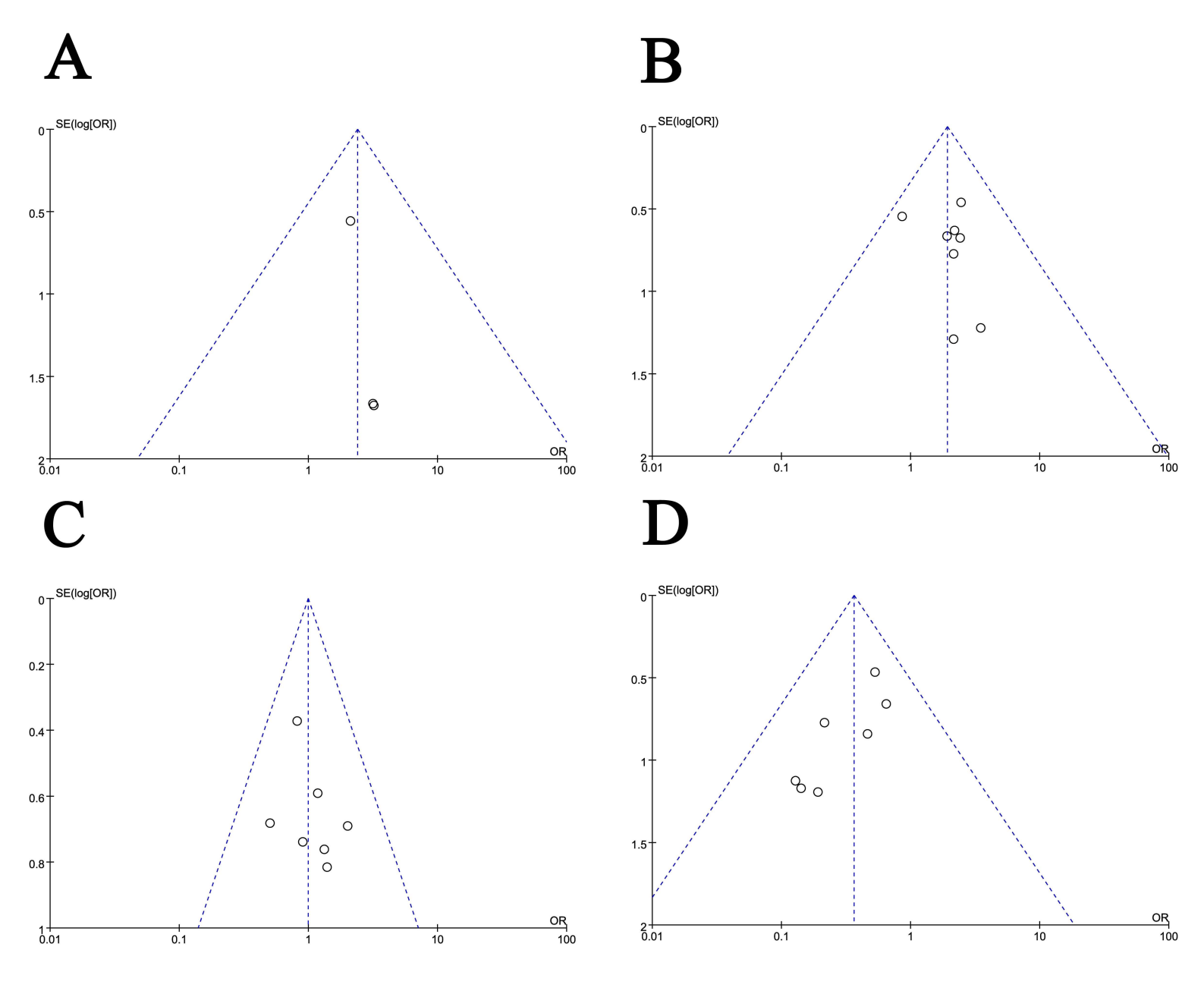


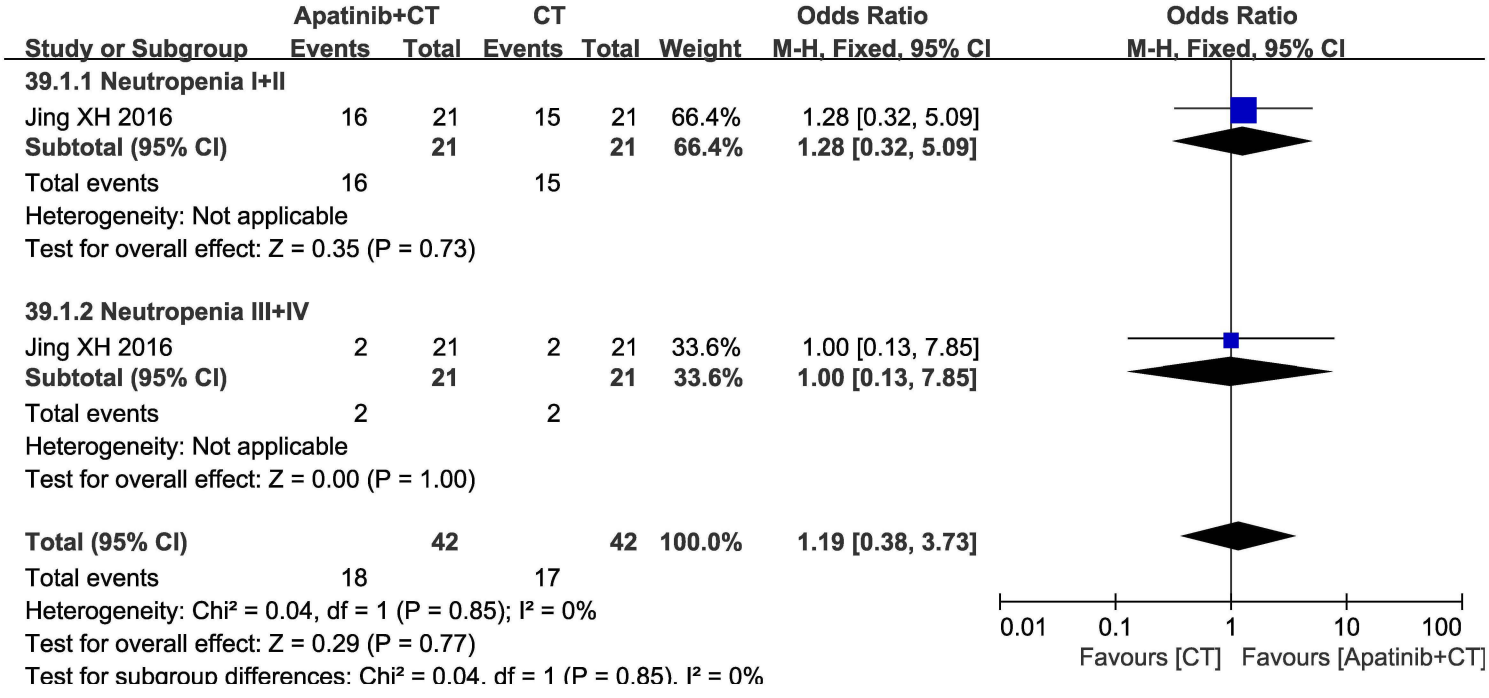
D

Study or Subgroup	Apatinib+S-1 Events	Total	S-1 Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Fan XX 2017	1	15	5	15	10.5%	0.14 [0.01, 1.42]
Gao JP 2017	3	16	5	15	9.4%	0.46 [0.09, 2.41]
Hu SS 2016	1	23	6	23	12.9%	0.13 [0.01, 1.17]
Jing XH 2016	6	21	8	21	12.9%	0.65 [0.18, 2.37]
Sheng HM 2017	9	59	15	59	28.6%	0.53 [0.21, 1.33]
Wu ZW 2017	1	14	4	14	8.4%	0.19 [0.02, 2.00]
Zhou L 2018	3	20	9	20	17.2%	0.22 [0.05, 0.98]
Total (95% CI)		**168**		**167**	**100.0%**	**0.36 [0.21, 0.63]**
Total events	24		52			

Heterogeneity: Chi² = 3.71, df = 6 (P = 0.72); I² = 0%
Test for overall effect: Z = 3.62 (P = 0.0003)




A
SE(log[OR])
0
0.5
1
1.5
2
0.01
0.1
1
10
100
OR
B
SE(log[OR])
0
0.5
1
1.5
2
0.01
0.1
1
10
100
OR
C
SE(log[OR])
0
0.2
0.4
0.6
0.8
1
0.01
0.1
1
10
100
OR
D
SE(log[OR])
0
0.5
1
1.5
2
0.01
0.1
1
10
100
OR


Apatinib+CT
CT
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
39.1.1 Neutropenia I+II
Jing XH 2016 16 21 15 21 66.4% 1.28 [0.32, 5.09]
Subtotal (95% CI) 21 21 66.4% 1.28 [0.32, 5.09]
Total events 16 15
Heterogeneity: Not applicable
Test for overall effect: Z = 0.35 (P = 0.73)
39.1.2 Neutropenia III+IV
Jing XH 2016 2 21 2 21 33.6% 1.00 [0.13, 7.85]
Subtotal (95% CI) 21 21 33.6% 1.00 [0.13, 7.85]
Total events 2 2
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Total (95% CI) 42 42 100.0% 1.19 [0.38, 3.73]
Total events 18 17
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.85), I² = 0%
0.01
0.1
1
10
100
Favours [CT]
Favours [Apatinib+CT]

Supplementary Table 1. Clinical information from the eligible trials in the meta-analysis.

Included studies	Blinding methods	Tumor stage	Gender (F/M)		Number of metastatic sites (No.)	Follow-up time	IT or RR	Other treatments before S-1/Apatinib+S-1
			S-1	Apatinib+S-1				
Fan XX	ND	III-IV	11/4	12/3	≥1	ND	Both	ND
Gao JP 2017	ND	Advanced	ND	ND	≥1	ND	Both	ND
Hu SS 2016	double-blinded	Advanced	18/5	19/4	≥1	ND	ND	ND
Jing XH	ND	Advanced	13/8	12/9	≥1, ≥2(18)	ND	Both	ND
Sheng HM	ND	III-IV	41/18	38/21	ND	ND	RR	ND
Wang DP	ND	Advanced	13/16	15/14	ND	ND	ND	ND
Wu ZW	ND	III-IV	10/4	12/2	≥1	ND	RR	FOLFOX, DCF, XELOX
Zhou L 2018	ND	IV	11/9	13/7	≥1	ND	RR	ND

Abbreviations: ND: No description; S-1: Gimeracil and Oteracil Porassium Capsules; IT: initial treatment; RR: refractory relapsed; FOLFOX: Oxaliplatin+Calcium folinate+5-Fluorouracil; XELOX: Oxaliplatin+Capecitabine; DCF: Cisplatin+5-fluorouracil +docetaxel.