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Supplementary Appendix

We used the search terms to search the MEDLINE via PubMed (1 Jan 2010 to 30 June 2021) as follows:

#1 "neoplasms"[MeSH Terms] OR "cancer*"[Title/Abstract] OR "carcinoma*"[Title/Abstract] OR "oncol*"[Title/Abstract] OR "tumor*"[Title/Abstract]

OR "tumour*"[Title/Abstract] OR "adenocarcinoma*"[Title/Abstract] NOT Leukemia[MeSH Terms] NOT Lymphoma[MeSH Terms] NOT "Multiple

Myeloma" [MeSH Terms]

#2 "random*"[Title/Abstract]

#3 "Antineoplastic Agents"[MeSH Terms] OR "immunotherapy"[All Fields] OR "Immune Checkpoint Inhibitors"[All Fields] OR "target therapy"[All

Fields] OR "hormone"[All Fields] OR "chemotherapy"[All Fields]

#4 "humans"[MeSH Terms]

#5"english"[Language]

#6 randomizedcontrolledtrial[Filter]

#7 2010/01/01:2021/06/30[Date - Publication]

#8 adjuvant[Title] OR neoadjuvant[Title]

#9 "placebo"[Title] OR "blind"[Title]

#1 AND #2 AND #3 AND #4 AND #5 AND #6 AND #7 NOT #8 NOT #9

Supplementary Figure 2. The trend in PFS adjudicators from 2010 to 2021

PFS: Adudicator in paper (n = 1,197)
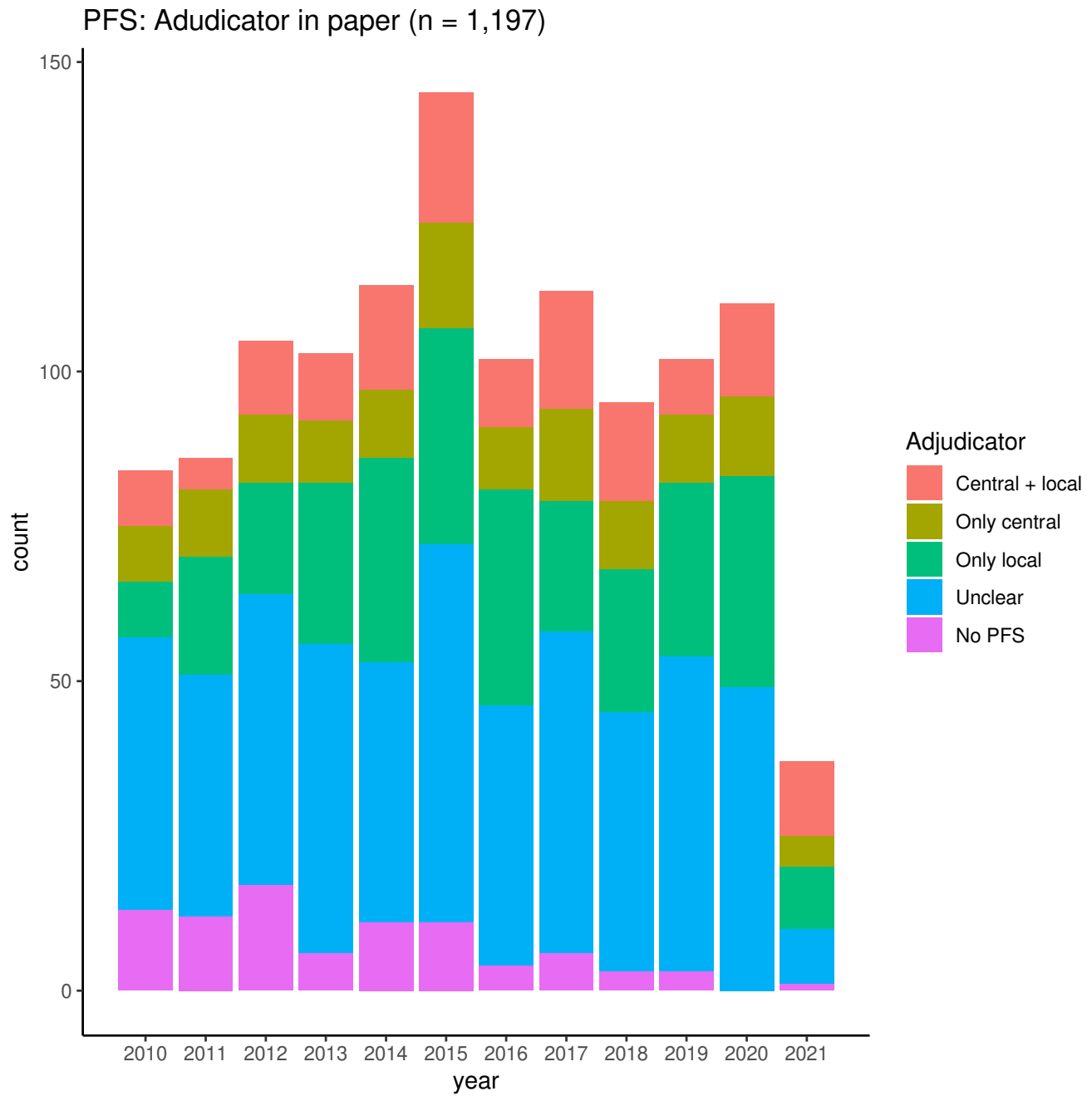
Supplementary Figure 3. The trend in ORR adjudicators from 2010 to 2021

ORR: Adudicator in paper (n = 1,197)

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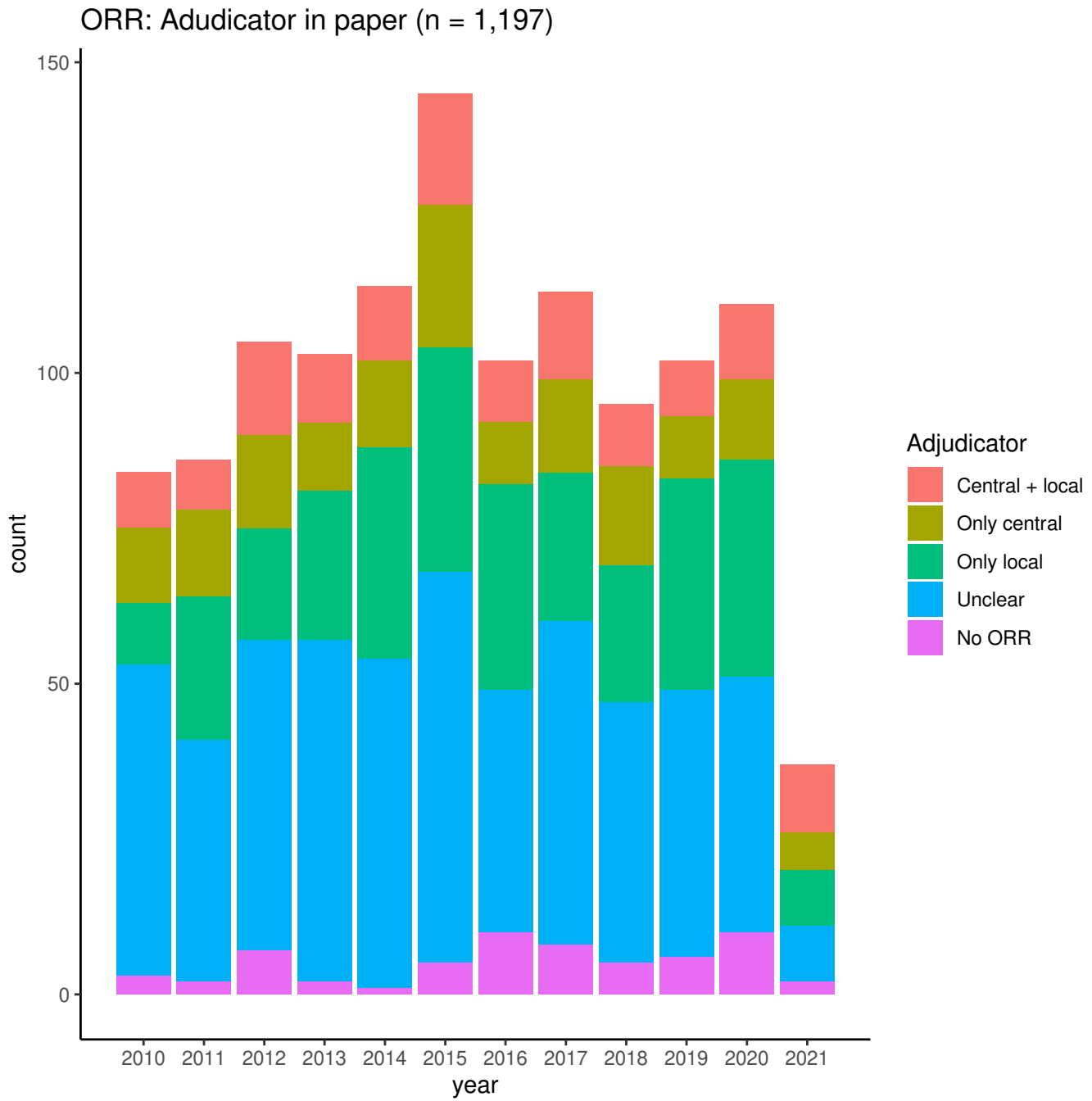
Supplementary Figure 4a. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.25).
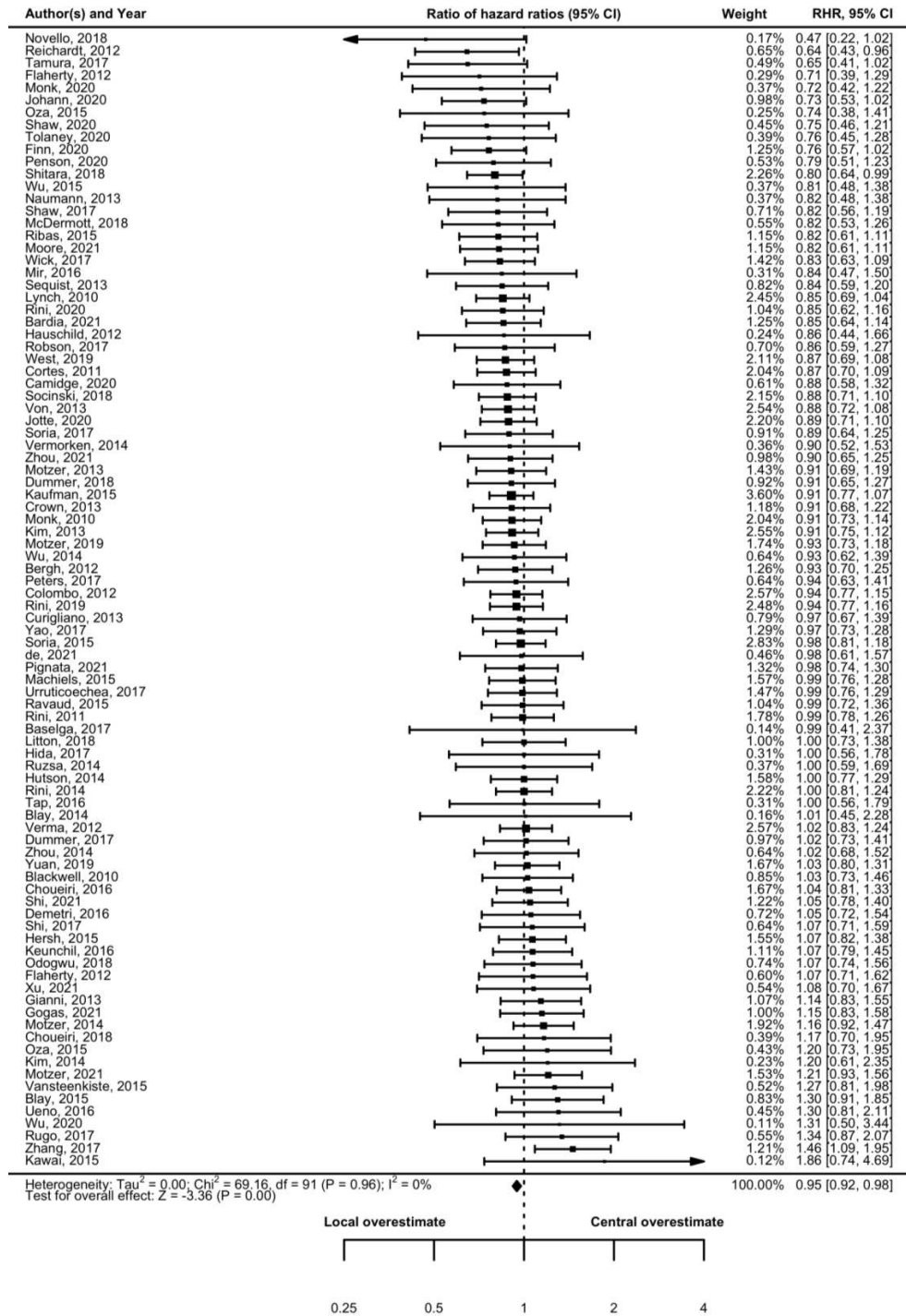
Supplementary Figure 4b. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.50).

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Supplementary Figure 4c. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Sensitivity analysis ($\rho = 0.75$).

Author(s) and Year	Weight	RHR, 95% CI
Novello, 2018	0.37%	0.47 [0.30, 0.73]
Reichardt, 2012	0.95%	0.64 [0.51, 0.81]
Tamura, 2017	0.81%	0.65 [0.50, 0.84]
Flaherty, 2012	0.55%	0.71 [0.50, 1.01]
Monk, 2020	0.67%	0.72 [0.53, 0.98]
Johann, 2020	1.17%	0.73 [0.61, 0.89]
Oza, 2015	0.50%	0.74 [0.51, 1.07]
Shaw, 2020	0.76%	0.75 [0.57, 0.99]
Tolaney, 2020	0.69%	0.76 [0.56, 1.03]
Finn, 2020	1.30%	0.76 [0.65, 0.90]
Penson, 2020	0.84%	0.79 [0.61, 1.02]
Shitara, 2018	1.59%	0.80 [0.71, 0.90]
Wu, 2015	0.66%	0.81 [0.60, 1.10]
Naumann, 2013	0.68%	0.82 [0.60, 1.10]
Shaw, 2017	1.01%	0.82 [0.66, 1.02]
McDermott, 2018	0.86%	0.82 [0.64, 1.05]
Ribas, 2015	1.26%	0.82 [0.69, 0.98]
Moore, 2021	1.11%	0.82 [0.68, 1.01]
Wick, 2017	1.37%	0.83 [0.71, 0.97]
Mir, 2016	0.59%	0.84 [0.60, 1.18]
Sequist, 2013	1.08%	0.84 [0.69, 1.04]
Lynch, 2010	1.62%	0.85 [0.75, 0.96]
Rini, 2020	1.21%	0.85 [0.71, 1.02]
Bardia, 2021	1.30%	0.85 [0.72, 1.01]
Hauschild, 2012	0.48%	0.86 [0.58, 1.26]
Robson, 2017	0.99%	0.86 [0.69, 1.08]
West, 2019	1.56%	0.87 [0.76, 0.98]
Cortes, 2011	1.53%	0.87 [0.77, 1.00]
Camidge, 2020	0.92%	0.88 [0.69, 1.11]
Socinski, 2018	1.57%	0.88 [0.77, 1.00]
Von, 2013	1.63%	0.88 [0.79, 0.99]
Jotte, 2020	1.58%	0.89 [0.78, 1.01]
Soria, 2017	1.14%	0.89 [0.73, 1.08]
Vermorken, 2014	0.66%	0.90 [0.66, 1.22]
Zhou, 2021	1.16%	0.90 [0.74, 1.09]
Motzer, 2013	1.37%	0.91 [0.78, 1.06]
Dummer, 2018	1.14%	0.91 [0.75, 1.10]
Kaufman, 2015	1.76%	0.91 [0.82, 1.00]
Crown, 2013	1.27%	0.91 [0.77, 1.08]
Monk, 2010	1.54%	0.91 [0.80, 1.04]
Kim, 2013	1.64%	0.91 [0.81, 1.03]
Motzer, 2019	1.47%	0.93 [0.81, 1.07]
Wu, 2014	0.95%	0.93 [0.74, 1.17]
Bergh, 2012	1.29%	0.93 [0.79, 1.11]
Peters, 2017	0.95%	0.94 [0.75, 1.19]
Colombo, 2012	1.64%	0.94 [0.84, 1.06]
Rini, 2019	1.63%	0.94 [0.84, 1.06]
Curigliano, 2013	1.06%	0.97 [0.78, 1.19]
Yao, 2017	1.32%	0.97 [0.82, 1.14]
Soria, 2015	1.67%	0.98 [0.87, 1.09]
de, 2021	0.78%	0.98 [0.75, 1.29]
Pignata, 2021	1.34%	0.98 [0.83, 1.15]
Machiels, 2015	1.42%	0.99 [0.85, 1.15]
Urruticoechea, 2017	1.38%	0.99 [0.85, 1.15]
Ravaud, 2015	1.20%	0.99 [0.82, 1.19]
Rini, 2011	1.48%	0.99 [0.86, 1.14]
Baselga, 2017	0.29%	0.99 [0.59, 1.66]
Litton, 2018	1.18%	1.00 [0.83, 1.20]
Hida, 2017	0.59%	1.00 [0.72, 1.40]
Ruzsa, 2014	0.67%	1.00 [0.74, 1.36]
Hutson, 2014	1.43%	1.00 [0.86, 1.16]
Rini, 2014	1.58%	1.00 [0.88, 1.13]
Tap, 2016	0.57%	1.00 [0.71, 1.41]
Blay, 2014	0.31%	1.01 [0.62, 1.66]
Verma, 2012	1.64%	1.02 [0.90, 1.14]
Dummer, 2017	1.17%	1.02 [0.84, 1.23]
Zhou, 2014	0.94%	1.02 [0.81, 1.29]
Yuan, 2019	1.45%	1.03 [0.89, 1.18]
Blackwell, 2010	1.06%	1.03 [0.83, 1.27]
Choueiri, 2016	1.45%	1.04 [0.90, 1.20]
Shi, 2021	1.29%	1.05 [0.89, 1.24]
Demetri, 2016	1.01%	1.05 [0.85, 1.31]
Shi, 2017	0.93%	1.07 [0.84, 1.35]
Hersh, 2015	1.40%	1.07 [0.92, 1.24]
Keunchil, 2016	1.24%	1.07 [0.90, 1.27]
Odogwu, 2018	1.01%	1.07 [0.86, 1.33]
Flaherty, 2012	0.90%	1.07 [0.84, 1.36]
Xu, 2021	0.86%	1.08 [0.84, 1.39]
Gianni, 2013	1.20%	1.14 [0.95, 1.37]
Gogas, 2021	1.19%	1.15 [0.95, 1.38]
Motzer, 2014	1.52%	1.16 [1.02, 1.33]
Choueiri, 2018	0.69%	1.17 [0.87, 1.57]
Oza, 2015	0.74%	1.20 [0.90, 1.59]
Kim, 2014	0.47%	1.20 [0.81, 1.77]
Motzer, 2021	1.41%	1.21 [1.04, 1.40]
Vansteenkiste, 2015	0.83%	1.27 [0.98, 1.64]
Blay, 2015	1.07%	1.30 [1.05, 1.59]
Ueno, 2016	0.75%	1.30 [0.98, 1.73]
Wu, 2020	0.26%	1.31 [0.75, 2.29]
Rugo, 2017	0.85%	1.34 [1.04, 1.73]
Zhang, 2017	1.29%	1.46 [1.23, 1.73]
Kawai, 2015	0.26%	1.86 [1.07, 3.23]

Heterogeneity: Tau² = 0.01; Chi² = 204.82, df = 91 (P = 0.00); I² = 56%
Test for overall effect: Z = -3.51 (P = 0.00)

Total: 100.00%   0.95 [0.92, 0.98]

Local overestimate — Central overestimate

0.25   0.5   1   2   4

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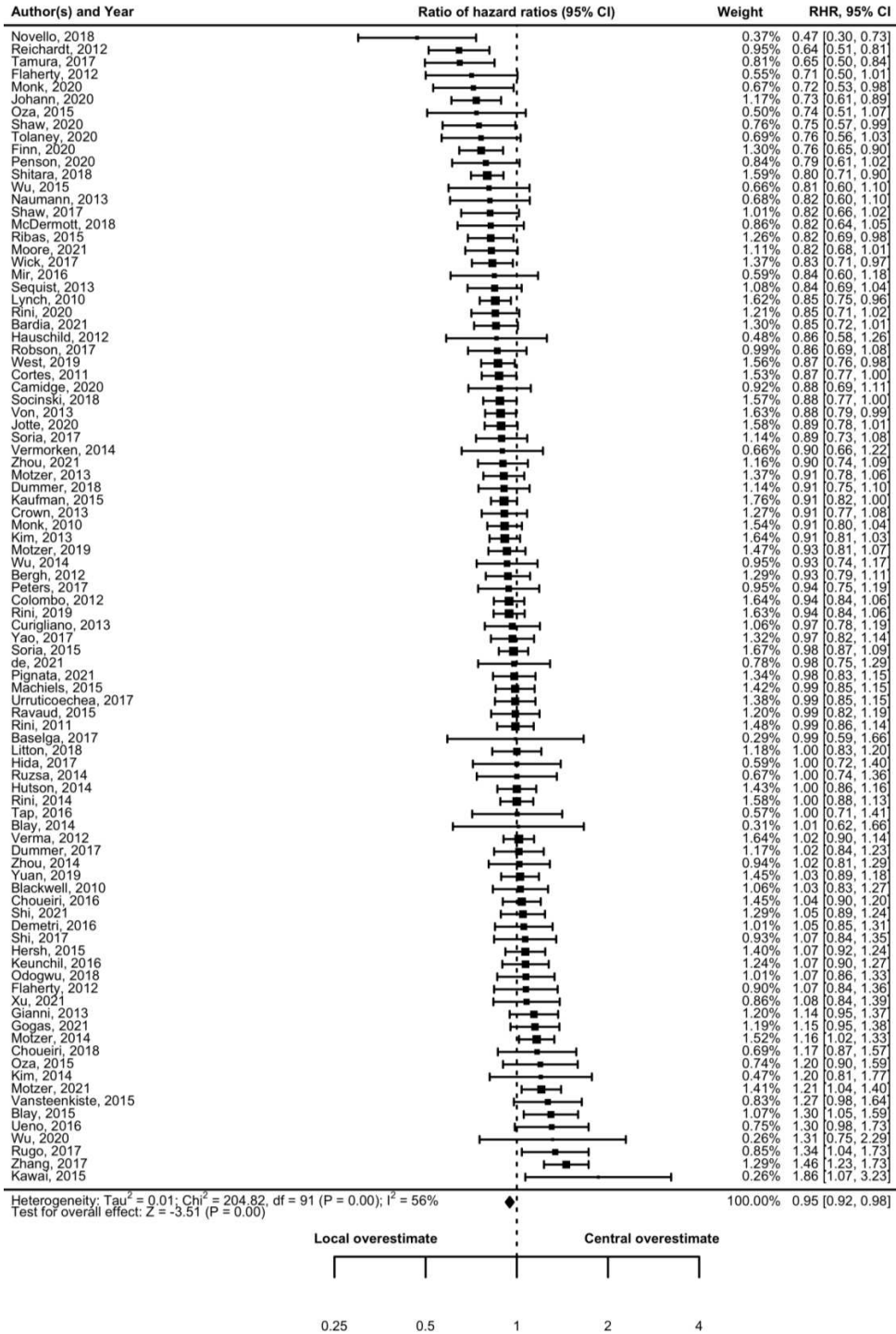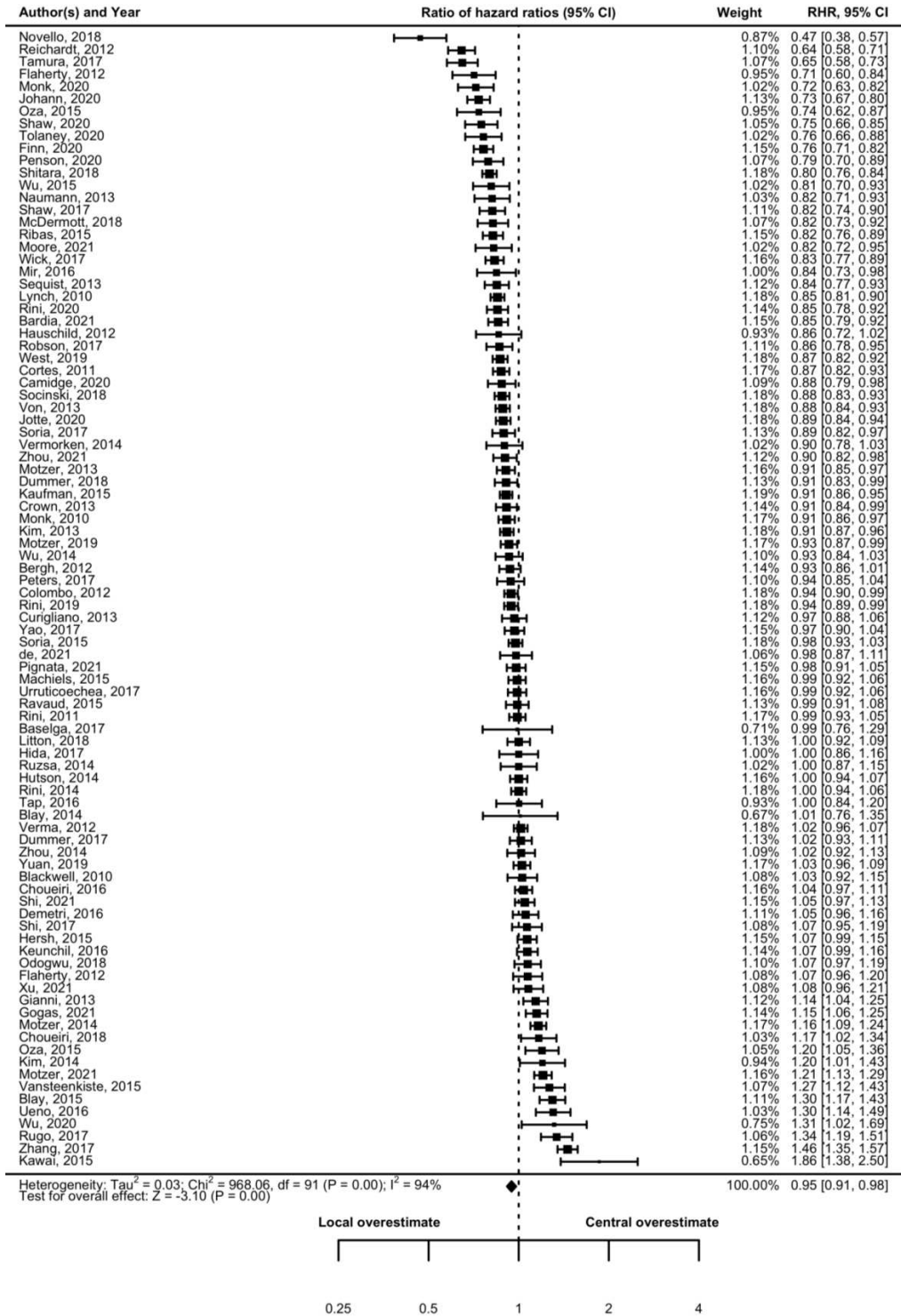
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Supplementary Figure 4d. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Sensitivity analysis ($\rho = 0.95$).
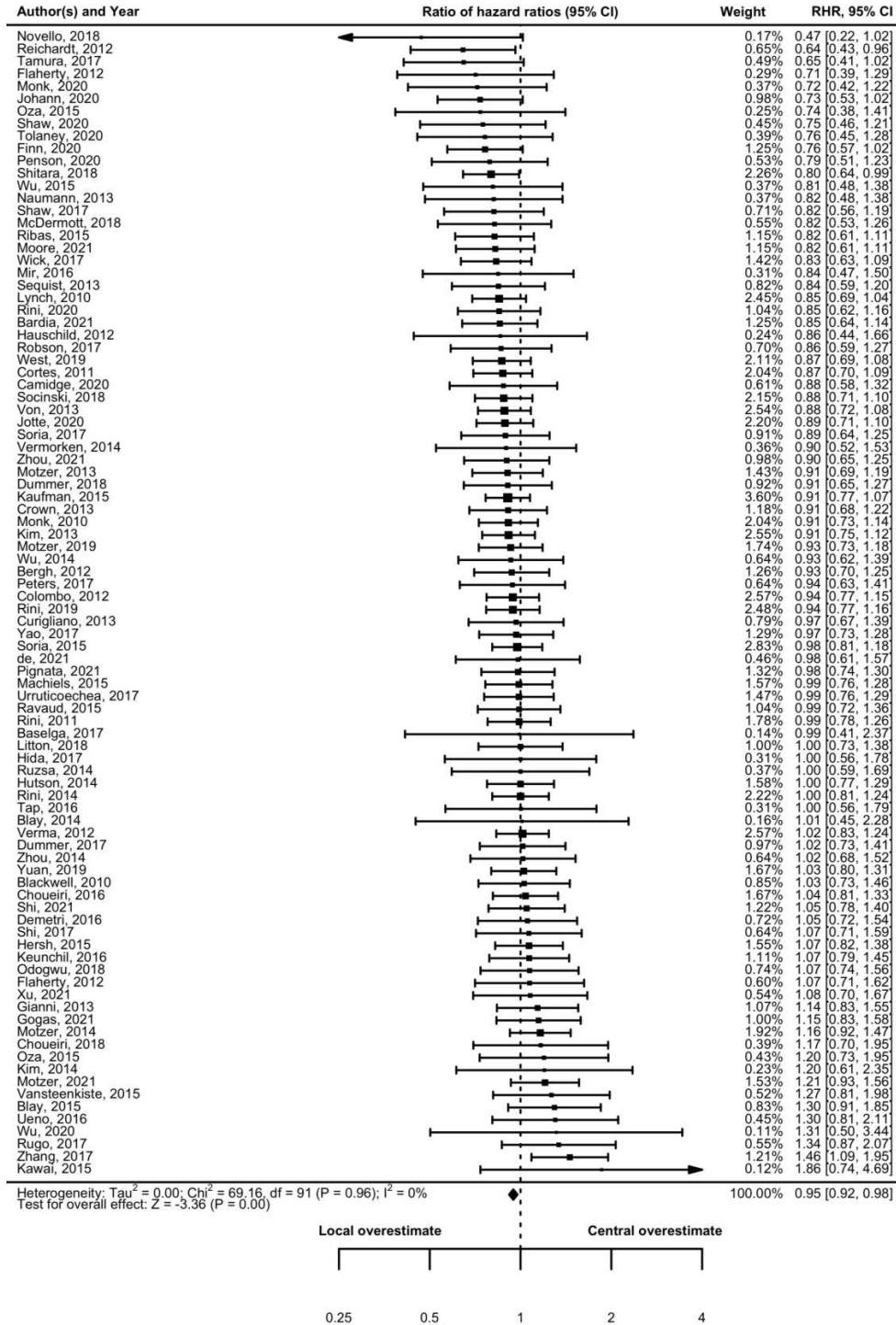
Author(s) and Year	Weight	RHR, 95% CI
Novello, 2018	0.87%	0.47 [0.38, 0.57]
Reichardt, 2012	1.10%	0.64 [0.58, 0.71]
Tamura, 2017	1.07%	0.65 [0.58, 0.73]
Flaherty, 2012	0.95%	0.71 [0.60, 0.84]
Monk, 2020	1.02%	0.72 [0.63, 0.82]
Johann, 2020	1.13%	0.73 [0.67, 0.80]
Oza, 2015	0.95%	0.74 [0.62, 0.87]
Shaw, 2020	1.05%	0.75 [0.66, 0.85]
Tolaney, 2020	1.02%	0.76 [0.66, 0.88]
Finn, 2020	1.15%	0.76 [0.71, 0.82]
Penson, 2020	1.07%	0.79 [0.70, 0.89]
Shitara, 2018	1.18%	0.80 [0.76, 0.84]
Wu, 2015	1.02%	0.81 [0.70, 0.93]
Naumann, 2013	1.03%	0.82 [0.71, 0.93]
Shaw, 2017	1.11%	0.82 [0.74, 0.90]
McDermott, 2018	1.07%	0.82 [0.73, 0.92]
Ribas, 2015	1.15%	0.82 [0.76, 0.89]
Moore, 2021	1.02%	0.82 [0.72, 0.95]
Wick, 2017	1.16%	0.83 [0.77, 0.89]
Mir, 2016	1.00%	0.84 [0.73, 0.98]
Sequist, 2013	1.12%	0.84 [0.77, 0.93]
Lynch, 2010	1.18%	0.85 [0.81, 0.90]
Rini, 2020	1.14%	0.85 [0.78, 0.92]
Bardia, 2021	1.15%	0.85 [0.79, 0.92]
Hauschild, 2012	0.93%	0.86 [0.72, 1.02]
Robson, 2017	1.11%	0.86 [0.78, 0.95]
West, 2019	1.18%	0.87 [0.82, 0.92]
Cortes, 2011	1.17%	0.87 [0.82, 0.93]
Camidge, 2020	1.09%	0.88 [0.79, 0.98]
Socinski, 2018	1.18%	0.88 [0.83, 0.93]
Von, 2013	1.18%	0.88 [0.84, 0.93]
Jotte, 2020	1.18%	0.89 [0.84, 0.94]
Soria, 2017	1.13%	0.89 [0.82, 0.97]
Vermorken, 2014	1.02%	0.90 [0.78, 1.03]
Zhou, 2021	1.12%	0.90 [0.82, 0.98]
Motzer, 2013	1.16%	0.91 [0.85, 0.97]
Dummer, 2018	1.13%	0.91 [0.83, 0.99]
Kaufman, 2015	1.19%	0.91 [0.86, 0.95]
Crown, 2013	1.14%	0.91 [0.84, 0.99]
Monk, 2010	1.17%	0.91 [0.86, 0.97]
Kim, 2013	1.18%	0.91 [0.87, 0.96]
Motzer, 2019	1.17%	0.93 [0.87, 0.99]
Wu, 2014	1.10%	0.93 [0.84, 1.03]
Bergh, 2012	1.14%	0.93 [0.86, 1.01]
Peters, 2017	1.10%	0.94 [0.85, 1.04]
Colombo, 2012	1.18%	0.94 [0.90, 0.99]
Rini, 2019	1.18%	0.94 [0.89, 0.99]
Curigliano, 2013	1.12%	0.97 [0.88, 1.06]
Yao, 2017	1.15%	0.97 [0.90, 1.04]
Soria, 2015	1.18%	0.98 [0.93, 1.03]
de, 2021	1.06%	0.98 [0.87, 1.11]
Pignata, 2021	1.15%	0.98 [0.91, 1.05]
Machiels, 2015	1.16%	0.99 [0.92, 1.06]
Urruticoechea, 2017	1.16%	0.99 [0.92, 1.06]
Ravaud, 2015	1.13%	0.99 [0.91, 1.08]
Rini, 2011	1.17%	0.99 [0.93, 1.05]
Baselga, 2017	0.71%	0.99 [0.76, 1.29]
Litton, 2018	1.13%	1.00 [0.92, 1.09]
Hida, 2017	1.00%	1.00 [0.86, 1.16]
Ruzsa, 2014	1.02%	1.00 [0.87, 1.15]
Hutson, 2014	1.16%	1.00 [0.94, 1.07]
Rini, 2014	1.18%	1.00 [0.94, 1.06]
Tap, 2016	0.93%	1.00 [0.84, 1.20]
Blay, 2014	0.67%	1.01 [0.76, 1.35]
Verma, 2012	1.18%	1.02 [0.96, 1.07]
Dummer, 2017	1.13%	1.02 [0.93, 1.11]
Zhou, 2014	1.09%	1.02 [0.92, 1.13]
Yuan, 2019	1.17%	1.03 [0.96, 1.09]
Blackwell, 2010	1.08%	1.03 [0.92, 1.15]
Choueiri, 2016	1.16%	1.04 [0.97, 1.11]
Shi, 2021	1.15%	1.05 [0.97, 1.13]
Demetri, 2016	1.11%	1.05 [0.96, 1.16]
Shi, 2017	1.08%	1.07 [0.95, 1.19]
Hersh, 2015	1.15%	1.07 [0.99, 1.15]
Keunchil, 2016	1.14%	1.07 [0.99, 1.16]
Odogwu, 2018	1.10%	1.07 [0.97, 1.19]
Flaherty, 2012	1.08%	1.07 [0.96, 1.20]
Xu, 2021	1.08%	1.08 [0.96, 1.21]
Gianni, 2013	1.12%	1.14 [1.04, 1.25]
Gogas, 2021	1.14%	1.15 [1.06, 1.25]
Motzer, 2014	1.17%	1.16 [1.09, 1.24]
Choueiri, 2018	1.03%	1.17 [1.02, 1.34]
Oza, 2015	1.05%	1.20 [1.05, 1.36]
Kim, 2014	0.94%	1.20 [1.01, 1.43]
Motzer, 2021	1.16%	1.21 [1.13, 1.29]
Vansteenkiste, 2015	1.07%	1.27 [1.12, 1.43]
Blay, 2015	1.11%	1.30 [1.17, 1.43]
Ueno, 2016	1.03%	1.30 [1.14, 1.49]
Wu, 2020	0.75%	1.31 [1.02, 1.69]
Rugo, 2017	1.06%	1.34 [1.19, 1.51]
Zhang, 2017	1.15%	1.46 [1.35, 1.57]
Kawai, 2015	0.65%	1.86 [1.38, 2.50]

Heterogeneity: Tau² = 0.03; Chi² = 968.06, df = 91 (P = 0.00); I² = 94%
Test for overall effect: Z = -3.10 (P = 0.00)

100.00%   0.95 [0.91, 0.98]

Local overestimate | Central overestimate

0.25   0.5   1   2   4

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Supplementary Figure 5a. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.25).

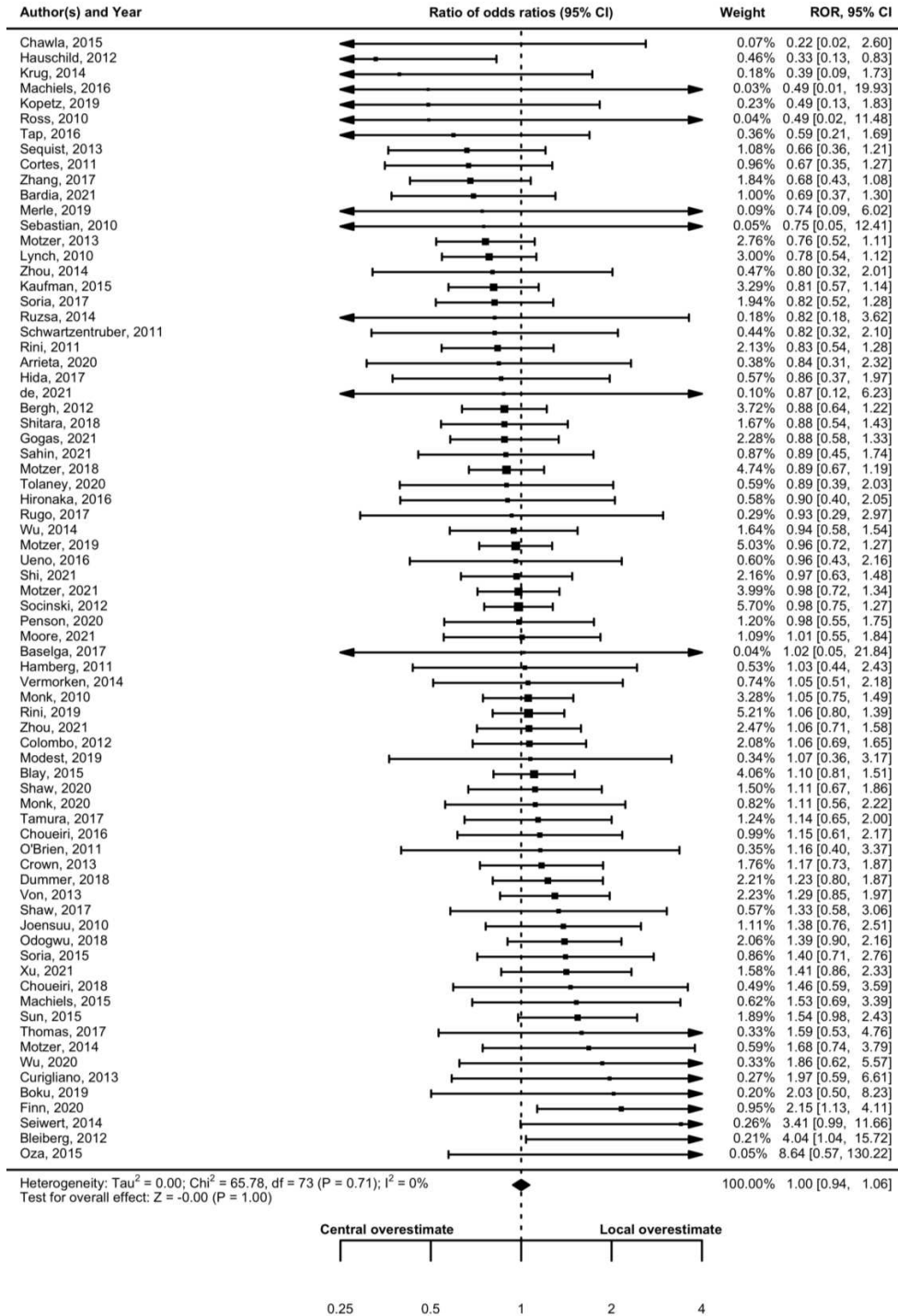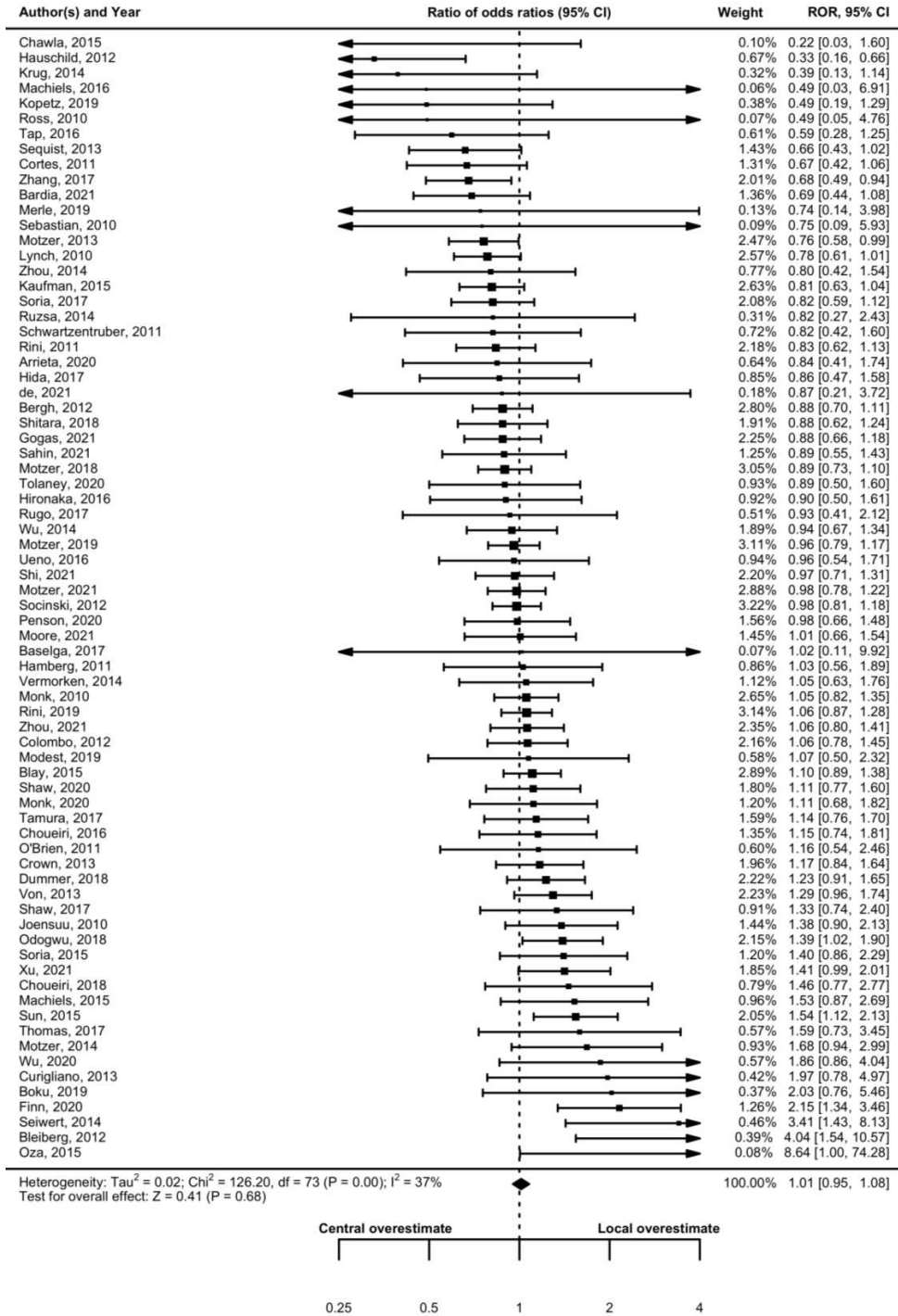**Supplementary Figure 5b. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.50).**

Author(s) and Year	Ratio of odds ratios (95% CI)	Weight	ROR, 95% CI
Chawla, 2015		0.07%	0.22 [0.02, 2.60]
Hauschild, 2012		0.46%	0.33 [0.13, 0.83]
Krug, 2014		0.18%	0.39 [0.09, 1.73]
Machiels, 2016		0.03%	0.49 [0.01, 19.93]
Kopetz, 2019		0.23%	0.49 [0.13, 1.83]
Ross, 2010		0.04%	0.49 [0.02, 11.48]
Tap, 2016		0.36%	0.59 [0.21, 1.69]
Sequist, 2013		1.08%	0.66 [0.36, 1.21]
Cortes, 2011		0.96%	0.67 [0.35, 1.27]
Zhang, 2017		1.84%	0.68 [0.43, 1.08]
Bardia, 2021		1.00%	0.69 [0.37, 1.30]
Merle, 2019		0.09%	0.74 [0.09, 6.02]
Sebastian, 2010		0.05%	0.75 [0.05, 12.41]
Motzer, 2013		2.76%	0.76 [0.52, 1.11]
Lynch, 2010		3.00%	0.78 [0.54, 1.12]
Zhou, 2014		0.47%	0.80 [0.32, 2.01]
Kaufman, 2015		3.29%	0.81 [0.57, 1.14]
Soria, 2017		1.94%	0.82 [0.52, 1.28]
Ruzsa, 2014		0.18%	0.82 [0.18, 3.62]
Schwartzentruber, 2011		0.44%	0.82 [0.32, 2.10]
Rini, 2011		2.13%	0.83 [0.54, 1.28]
Arrieta, 2020		0.38%	0.84 [0.31, 2.32]
Hida, 2017		0.57%	0.86 [0.37, 1.97]
de, 2021		0.10%	0.87 [0.12, 6.23]
Bergh, 2012		3.72%	0.88 [0.64, 1.22]
Shitara, 2018		1.67%	0.88 [0.54, 1.43]
Gogas, 2021		2.28%	0.88 [0.58, 1.33]
Sahin, 2021		0.87%	0.89 [0.45, 1.74]
Motzer, 2018		4.74%	0.89 [0.67, 1.19]
Tolaney, 2020		0.59%	0.89 [0.39, 2.03]
Hironaka, 2016		0.58%	0.90 [0.40, 2.05]
Rugo, 2017		0.29%	0.93 [0.29, 2.97]
Wu, 2014		1.64%	0.94 [0.58, 1.54]
Motzer, 2019		5.03%	0.96 [0.72, 1.27]
Ueno, 2016		0.60%	0.96 [0.43, 2.16]
Shi, 2021		2.16%	0.97 [0.63, 1.48]
Motzer, 2021		3.99%	0.98 [0.72, 1.34]
Socinski, 2012		5.70%	0.98 [0.75, 1.27]
Penson, 2020		1.20%	0.98 [0.55, 1.75]
Moore, 2021		1.09%	1.01 [0.55, 1.84]
Baselga, 2017		0.04%	1.02 [0.05, 21.84]
Hamberg, 2011		0.53%	1.03 [0.44, 2.43]
Vermorken, 2014		0.74%	1.05 [0.51, 2.18]
Monk, 2010		3.28%	1.05 [0.75, 1.49]
Rini, 2019		5.21%	1.06 [0.80, 1.39]
Zhou, 2021		2.47%	1.06 [0.71, 1.58]
Colombo, 2012		2.08%	1.06 [0.69, 1.65]
Modest, 2019		0.34%	1.07 [0.36, 3.17]
Blay, 2015		4.06%	1.10 [0.81, 1.51]
Shaw, 2020		1.50%	1.11 [0.67, 1.86]
Monk, 2020		0.82%	1.11 [0.56, 2.22]
Tamura, 2017		1.24%	1.14 [0.65, 2.00]
Choueiri, 2016		0.99%	1.15 [0.61, 2.17]
O'Brien, 2011		0.35%	1.16 [0.40, 3.37]
Crown, 2013		1.76%	1.17 [0.73, 1.87]
Dummer, 2018		2.21%	1.23 [0.80, 1.87]
Von, 2013		2.23%	1.29 [0.85, 1.97]
Shaw, 2017		0.57%	1.33 [0.58, 3.06]
Joensuu, 2010		1.11%	1.38 [0.76, 2.51]
Odogwu, 2018		2.06%	1.39 [0.90, 2.16]
Soria, 2015		0.86%	1.40 [0.71, 2.76]
Xu, 2021		1.58%	1.41 [0.86, 2.33]
Choueiri, 2018		0.49%	1.46 [0.59, 3.59]
Machiels, 2015		0.62%	1.53 [0.69, 3.39]
Sun, 2015		1.89%	1.54 [0.98, 2.43]
Thomas, 2017		0.33%	1.59 [0.53, 4.76]
Motzer, 2014		0.59%	1.68 [0.74, 3.79]
Wu, 2020		0.33%	1.86 [0.62, 5.57]
Curigliano, 2013		0.27%	1.97 [0.59, 6.61]
Boku, 2019		0.20%	2.03 [0.50, 8.23]
Finn, 2020		0.95%	2.15 [1.13, 4.11]
Seiwert, 2014		0.26%	3.41 [0.99, 11.66]
Bleiberg, 2012		0.21%	4.04 [1.04, 15.72]
Oza, 2015		0.05%	8.64 [0.57, 130.22]
Heterogeneity: Tau² = 0.00; Chi² = 65.78, df = 73 (P = 0.71); I² = 0% Test for overall effect: Z = -0.00 (P = 1.00)		100.00%	1.00 [0.94, 1.06]

Heterogeneity: Tau^2 = 0.00; Chi^2 = 65.78, df = 73 (P = 0.71); I^2 = 0%
Test for overall effect: Z = -0.00 (P = 1.00)

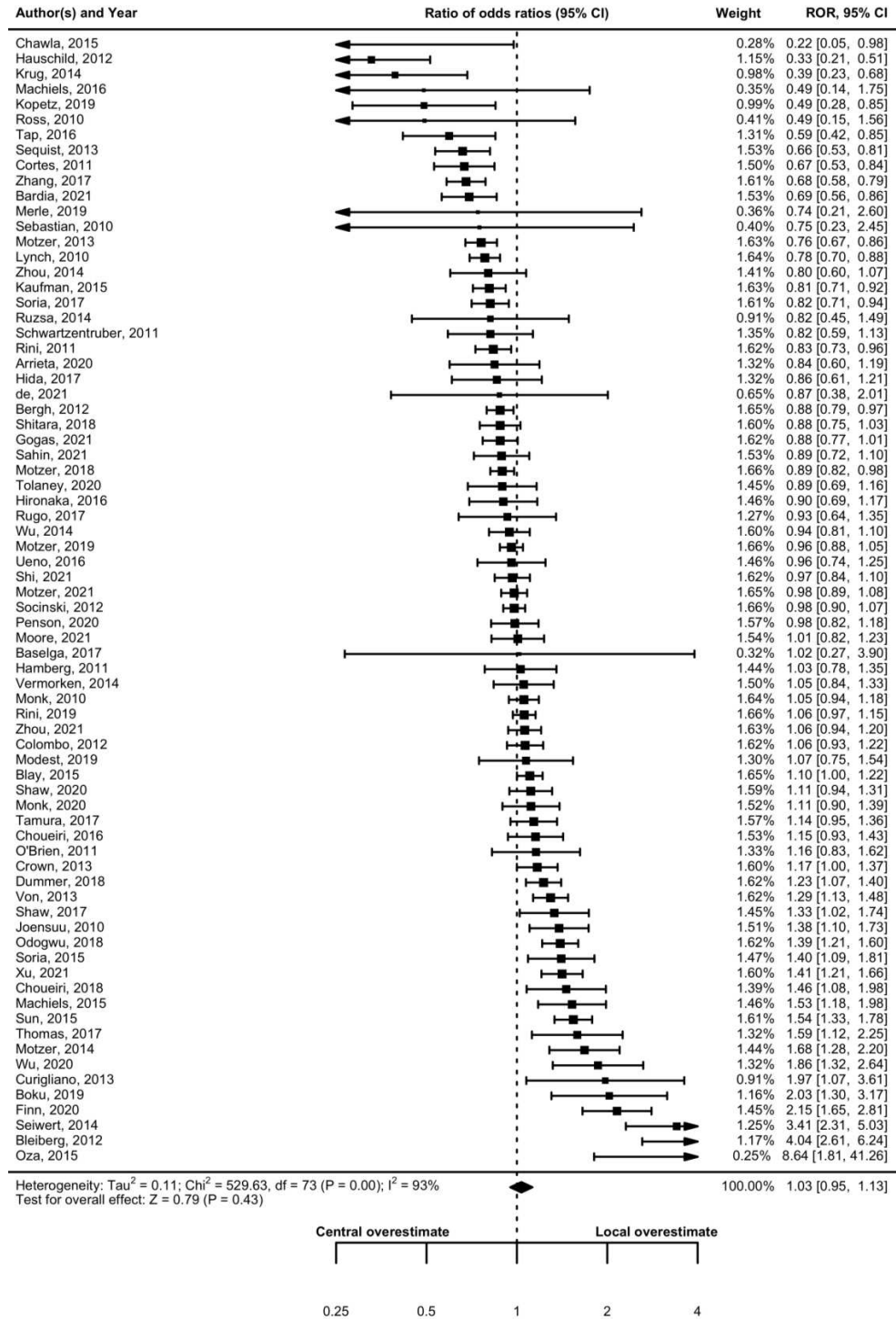Central overestimate — Local overestimate
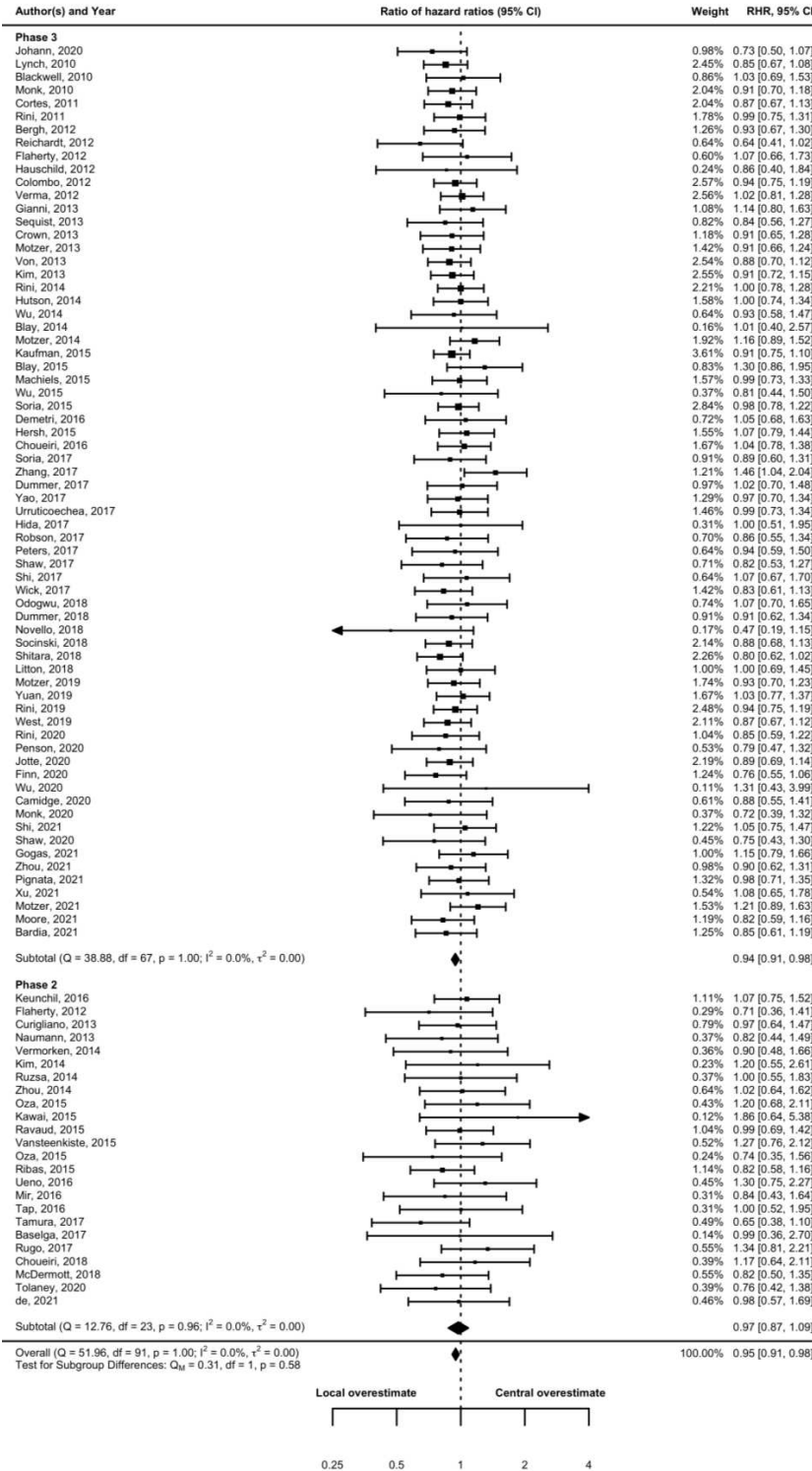
0.25 0.5 1 2 4

Supplementary Figure 5c. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.75).

Author(s) and Year	Weight	ROR, 95% CI
Chawla, 2015	0.10%	0.22 [0.03, 1.60]
Hauschild, 2012	0.67%	0.33 [0.16, 0.66]
Krug, 2014	0.32%	0.39 [0.13, 1.14]
Machiels, 2016	0.06%	0.49 [0.03, 6.91]
Kopetz, 2019	0.38%	0.49 [0.19, 1.29]
Ross, 2010	0.07%	0.49 [0.05, 4.76]
Tap, 2016	0.61%	0.59 [0.28, 1.25]
Sequist, 2013	1.43%	0.66 [0.43, 1.02]
Cortes, 2011	1.31%	0.67 [0.42, 1.06]
Zhang, 2017	2.01%	0.68 [0.49, 0.94]
Bardia, 2021	1.36%	0.69 [0.44, 1.08]
Merle, 2019	0.13%	0.74 [0.14, 3.98]
Sebastian, 2010	0.09%	0.75 [0.09, 5.93]
Motzer, 2013	2.47%	0.76 [0.58, 0.99]
Lynch, 2010	2.57%	0.78 [0.61, 1.01]
Zhou, 2014	0.77%	0.80 [0.42, 1.54]
Kaufman, 2015	2.63%	0.81 [0.63, 1.04]
Soria, 2017	2.08%	0.82 [0.59, 1.12]
Ruzsa, 2014	0.31%	0.82 [0.27, 2.43]
Schwartzentruber, 2011	0.72%	0.82 [0.42, 1.60]
Rini, 2011	2.18%	0.83 [0.62, 1.13]
Arrieta, 2020	0.64%	0.84 [0.41, 1.74]
Hida, 2017	0.85%	0.86 [0.47, 1.58]
de, 2021	0.18%	0.87 [0.21, 3.72]
Bergh, 2012	2.80%	0.88 [0.70, 1.11]
Shitara, 2018	1.91%	0.88 [0.62, 1.24]
Gogas, 2021	2.25%	0.88 [0.66, 1.18]
Sahin, 2021	1.25%	0.89 [0.55, 1.43]
Motzer, 2018	3.05%	0.89 [0.73, 1.10]
Tolaney, 2020	0.93%	0.89 [0.50, 1.60]
Hironaka, 2016	0.92%	0.90 [0.50, 1.61]
Rugo, 2017	0.51%	0.93 [0.41, 2.12]
Wu, 2014	1.89%	0.94 [0.67, 1.34]
Motzer, 2019	3.11%	0.96 [0.79, 1.17]
Ueno, 2016	0.94%	0.96 [0.54, 1.71]
Shi, 2021	2.20%	0.97 [0.71, 1.31]
Motzer, 2021	2.88%	0.98 [0.78, 1.22]
Socinski, 2012	3.22%	0.98 [0.81, 1.18]
Penson, 2020	1.56%	0.98 [0.66, 1.48]
Moore, 2021	1.45%	1.01 [0.66, 1.54]
Baselga, 2017	0.07%	1.02 [0.11, 9.92]
Hamberg, 2011	0.86%	1.03 [0.56, 1.89]
Vermorken, 2014	1.12%	1.05 [0.63, 1.76]
Monk, 2010	2.65%	1.05 [0.82, 1.35]
Rini, 2019	3.14%	1.06 [0.87, 1.28]
Zhou, 2021	2.35%	1.06 [0.80, 1.41]
Colombo, 2012	2.16%	1.06 [0.78, 1.45]
Modest, 2019	0.58%	1.07 [0.50, 2.32]
Blay, 2015	2.89%	1.10 [0.89, 1.38]
Shaw, 2020	1.80%	1.11 [0.77, 1.60]
Monk, 2020	1.20%	1.11 [0.68, 1.82]
Tamura, 2017	1.59%	1.14 [0.76, 1.70]
Choueiri, 2016	1.35%	1.15 [0.74, 1.81]
O'Brien, 2011	0.60%	1.16 [0.54, 2.46]
Crown, 2013	1.96%	1.17 [0.84, 1.64]
Dummer, 2018	2.22%	1.23 [0.91, 1.65]
Von, 2013	2.23%	1.29 [0.96, 1.74]
Shaw, 2017	0.91%	1.33 [0.74, 2.40]
Joensuu, 2010	1.44%	1.38 [0.90, 2.13]
Odogwu, 2018	2.15%	1.39 [1.02, 1.90]
Soria, 2015	1.20%	1.40 [0.86, 2.29]
Xu, 2021	1.85%	1.41 [0.99, 2.01]
Choueiri, 2018	0.79%	1.46 [0.77, 2.77]
Machiels, 2015	0.96%	1.53 [0.87, 2.69]
Sun, 2015	2.05%	1.54 [1.12, 2.13]
Thomas, 2017	0.57%	1.59 [0.73, 3.45]
Motzer, 2014	0.93%	1.68 [0.94, 2.99]
Wu, 2020	0.57%	1.86 [0.86, 4.04]
Curigliano, 2013	0.42%	1.97 [0.78, 4.97]
Boku, 2019	0.37%	2.03 [0.76, 5.46]
Finn, 2020	1.26%	2.15 [1.34, 3.46]
Seiwert, 2014	0.46%	3.41 [1.43, 8.13]
Bleiberg, 2012	0.39%	4.04 [1.54, 10.57]
Oza, 2015	0.08%	8.64 [1.00, 74.28]

Heterogeneity: Tau² = 0.02; Chi² = 126.20, df = 73 (P = 0.00); I² = 37%
Test for overall effect: Z = 0.41 (P = 0.68)

100.00% 1.01 [0.95, 1.08]

Central overestimate   Local overestimate

0.25   0.5   1   2   4

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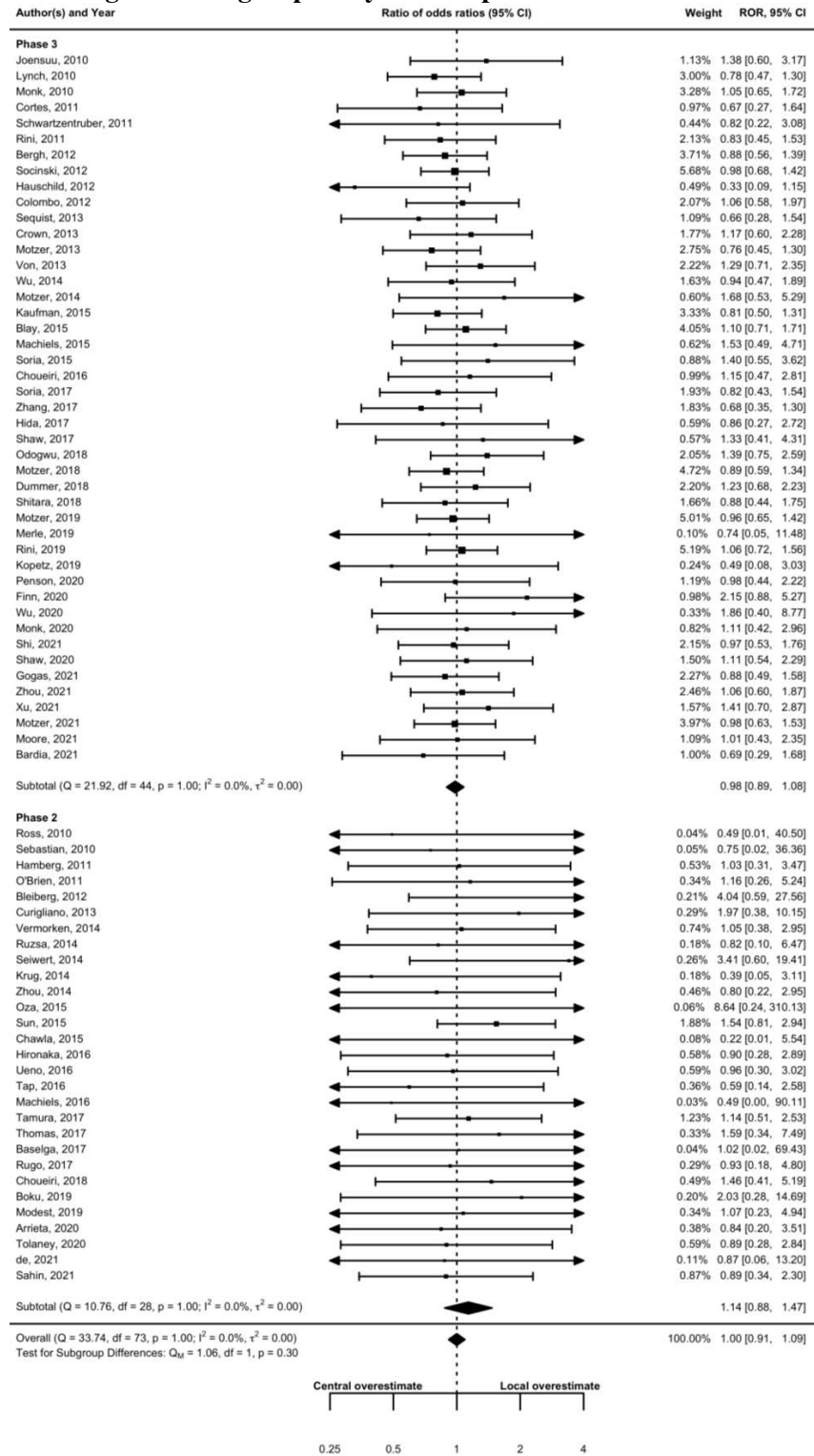
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Supplementary Figure 5d. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Sensitivity analysis (ρ = 0.95).
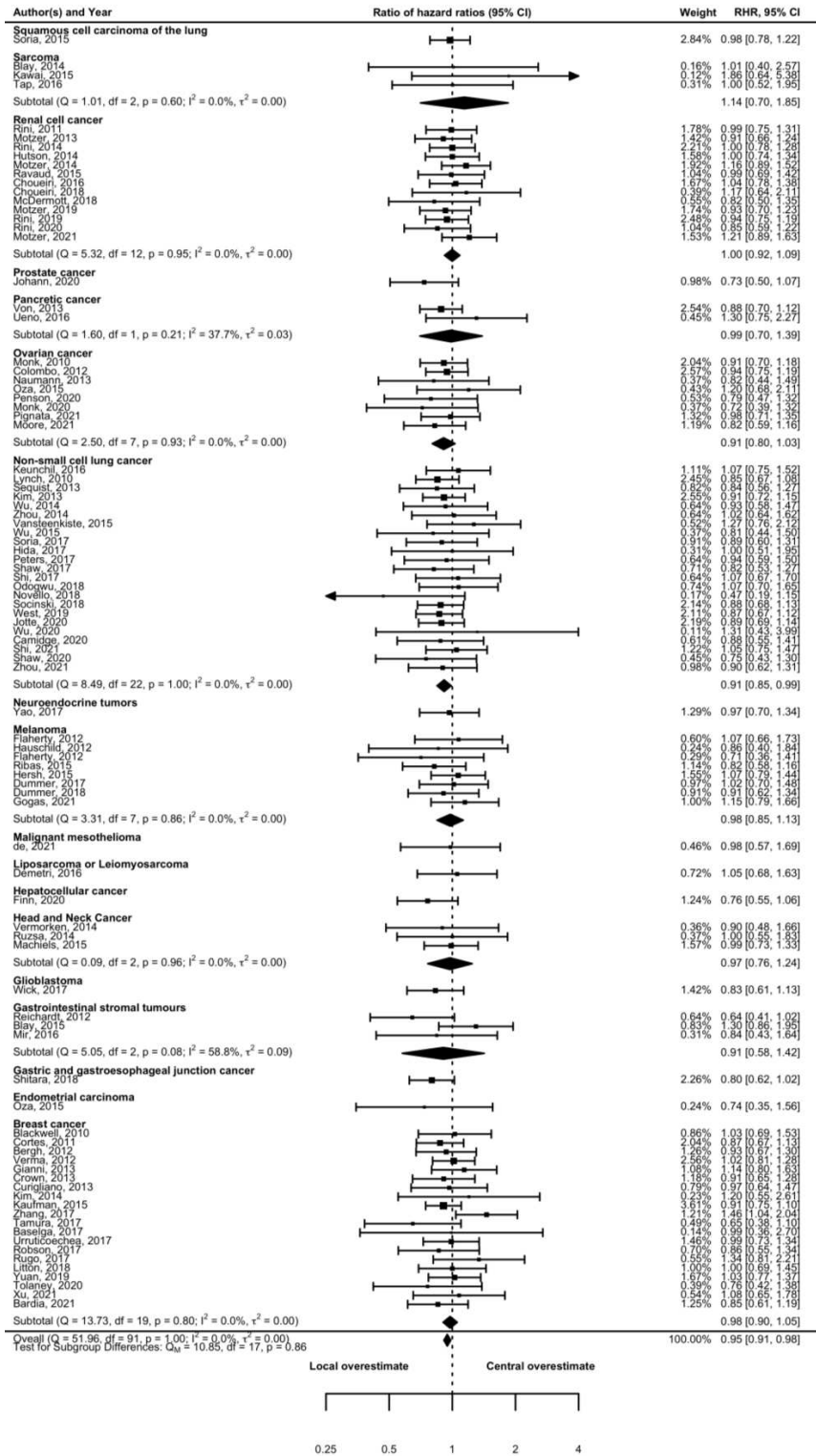

Author(s) and Year	Weight	ROR, 95% CI
Chawla, 2015	0.28%	0.22 [0.05, 0.98]
Hauschild, 2012	1.15%	0.33 [0.21, 0.51]
Krug, 2014	0.98%	0.39 [0.23, 0.68]
Machiels, 2016	0.35%	0.49 [0.14, 1.75]
Kopetz, 2019	0.99%	0.49 [0.28, 0.85]
Ross, 2010	0.41%	0.49 [0.15, 1.56]
Tap, 2016	1.31%	0.59 [0.42, 0.85]
Sequist, 2013	1.53%	0.66 [0.53, 0.81]
Cortes, 2011	1.50%	0.67 [0.53, 0.84]
Zhang, 2017	1.61%	0.68 [0.58, 0.79]
Bardia, 2021	1.53%	0.69 [0.56, 0.86]
Merle, 2019	0.36%	0.74 [0.21, 2.60]
Sebastian, 2010	0.40%	0.75 [0.23, 2.45]
Motzer, 2013	1.63%	0.76 [0.67, 0.86]
Lynch, 2010	1.64%	0.78 [0.70, 0.88]
Zhou, 2014	1.41%	0.80 [0.60, 1.07]
Kaufman, 2015	1.63%	0.81 [0.71, 0.92]
Soria, 2017	1.61%	0.82 [0.71, 0.94]
Ruzsa, 2014	0.91%	0.82 [0.45, 1.49]
Schwartzentruber, 2011	1.35%	0.82 [0.59, 1.13]
Rini, 2011	1.62%	0.83 [0.73, 0.96]
Arrieta, 2020	1.32%	0.84 [0.60, 1.19]
Hida, 2017	1.32%	0.86 [0.61, 1.21]
de, 2021	0.65%	0.87 [0.38, 2.01]
Bergh, 2012	1.65%	0.88 [0.79, 0.97]
Shitara, 2018	1.60%	0.88 [0.75, 1.03]
Gogas, 2021	1.62%	0.88 [0.77, 1.01]
Sahin, 2021	1.53%	0.89 [0.72, 1.10]
Motzer, 2018	1.66%	0.89 [0.82, 0.98]
Tolaney, 2020	1.45%	0.89 [0.69, 1.16]
Hironaka, 2016	1.46%	0.90 [0.69, 1.17]
Rugo, 2017	1.27%	0.93 [0.64, 1.35]
Wu, 2014	1.60%	0.94 [0.81, 1.10]
Motzer, 2019	1.66%	0.96 [0.88, 1.05]
Ueno, 2016	1.46%	0.96 [0.74, 1.25]
Shi, 2021	1.62%	0.97 [0.84, 1.10]
Motzer, 2021	1.65%	0.98 [0.89, 1.08]
Socinski, 2012	1.66%	0.98 [0.90, 1.07]
Penson, 2020	1.57%	0.98 [0.82, 1.18]
Moore, 2021	1.54%	1.01 [0.82, 1.23]
Baselga, 2017	0.32%	1.02 [0.27, 3.90]
Hamberg, 2011	1.44%	1.03 [0.78, 1.35]
Vermorken, 2014	1.50%	1.05 [0.84, 1.33]
Monk, 2010	1.64%	1.05 [0.94, 1.18]
Rini, 2019	1.66%	1.06 [0.97, 1.15]
Zhou, 2021	1.63%	1.06 [0.94, 1.20]
Colombo, 2012	1.62%	1.06 [0.93, 1.22]
Modest, 2019	1.30%	1.07 [0.75, 1.54]
Blay, 2015	1.65%	1.10 [1.00, 1.22]
Shaw, 2020	1.59%	1.11 [0.94, 1.31]
Monk, 2020	1.52%	1.11 [0.90, 1.39]
Tamura, 2017	1.57%	1.14 [0.95, 1.36]
Choueiri, 2016	1.53%	1.15 [0.93, 1.43]
O'Brien, 2011	1.33%	1.16 [0.83, 1.62]
Crown, 2013	1.60%	1.17 [1.00, 1.37]
Dummer, 2018	1.62%	1.23 [1.07, 1.40]
Von, 2013	1.62%	1.29 [1.13, 1.48]
Shaw, 2017	1.45%	1.33 [1.02, 1.74]
Joensuu, 2010	1.51%	1.38 [1.10, 1.73]
Odogwu, 2018	1.62%	1.39 [1.21, 1.60]
Soria, 2015	1.47%	1.40 [1.09, 1.81]
Xu, 2021	1.60%	1.41 [1.21, 1.66]
Choueiri, 2018	1.39%	1.46 [1.08, 1.98]
Machiels, 2015	1.46%	1.53 [1.18, 1.98]
Sun, 2015	1.61%	1.54 [1.33, 1.78]
Thomas, 2017	1.32%	1.59 [1.12, 2.25]
Motzer, 2014	1.44%	1.68 [1.28, 2.20]
Wu, 2020	1.32%	1.86 [1.32, 2.64]
Curigliano, 2013	0.91%	1.97 [1.07, 3.61]
Boku, 2019	1.16%	2.03 [1.30, 3.17]
Finn, 2020	1.45%	2.15 [1.65, 2.81]
Seiwert, 2014	1.25%	3.41 [2.31, 5.03]
Bleiberg, 2012	1.17%	4.04 [2.61, 6.24]
Oza, 2015	0.25%	8.64 [1.81, 41.26]
	100.00%	1.03 [0.95, 1.13]

Heterogeneity: Tau² = 0.11; Chi² = 529.63, df = 73 (P = 0.00); I² = 93%
Test for overall effect: Z = 0.79 (P = 0.43)

Central overestimate   Local overestimate

0.25   0.5   1   2   4

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Supplementary Figure 6a. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Subgroup analysis: trial phase.
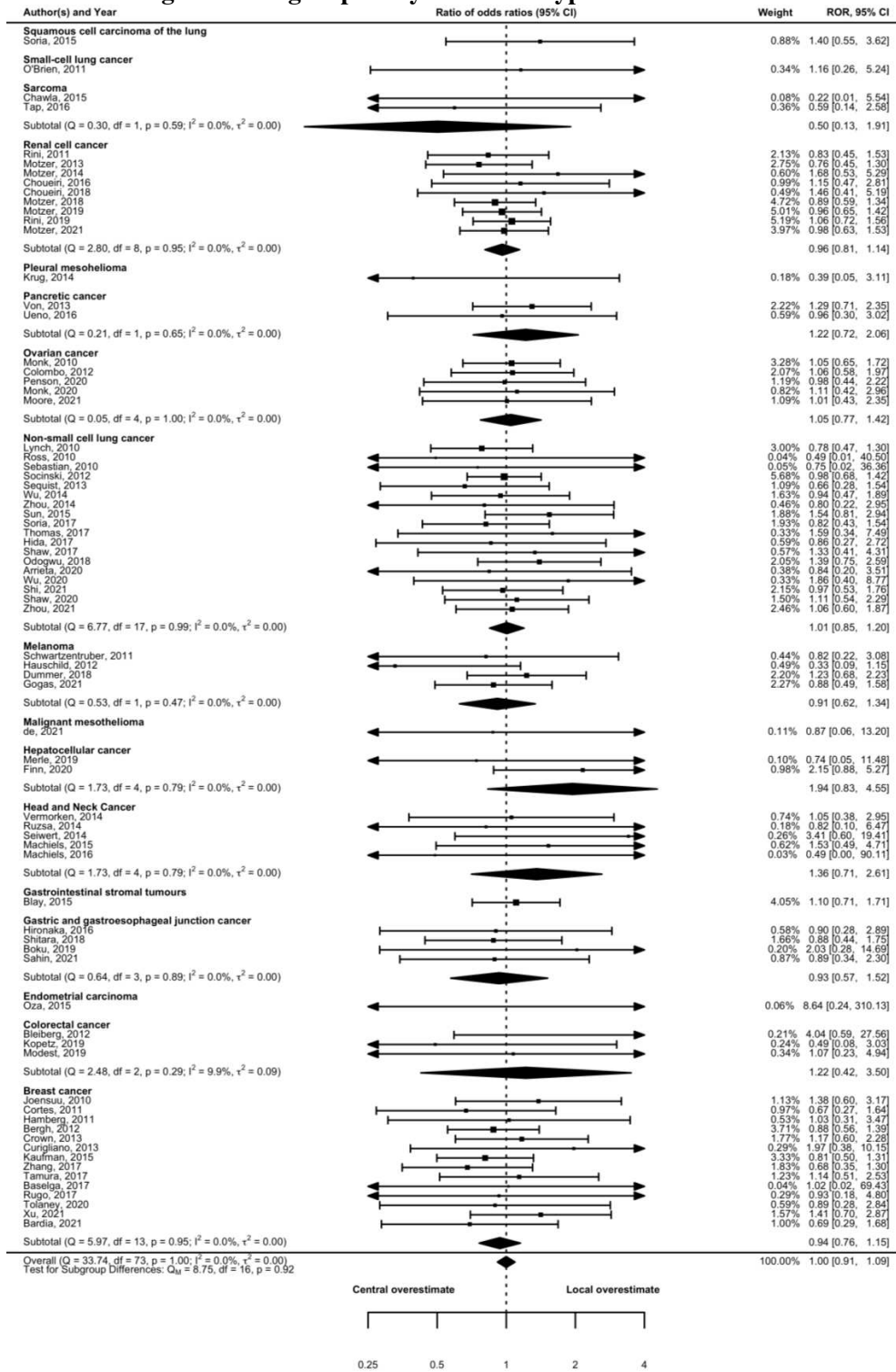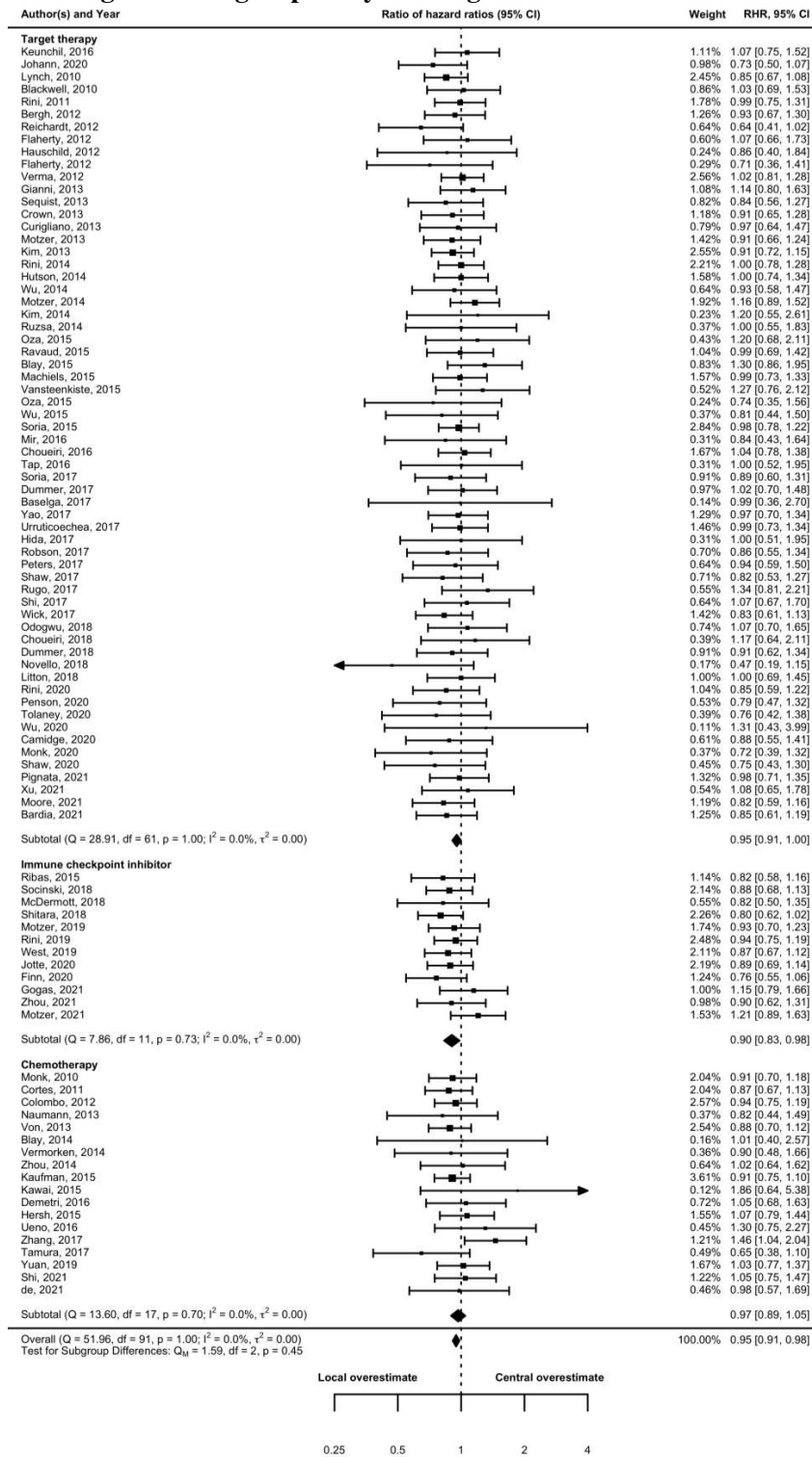
Supplementary Figure 6b. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Subgroup analysis: trial phase.

Supplementary Figure 7a. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Subgroup analysis: cancer type.
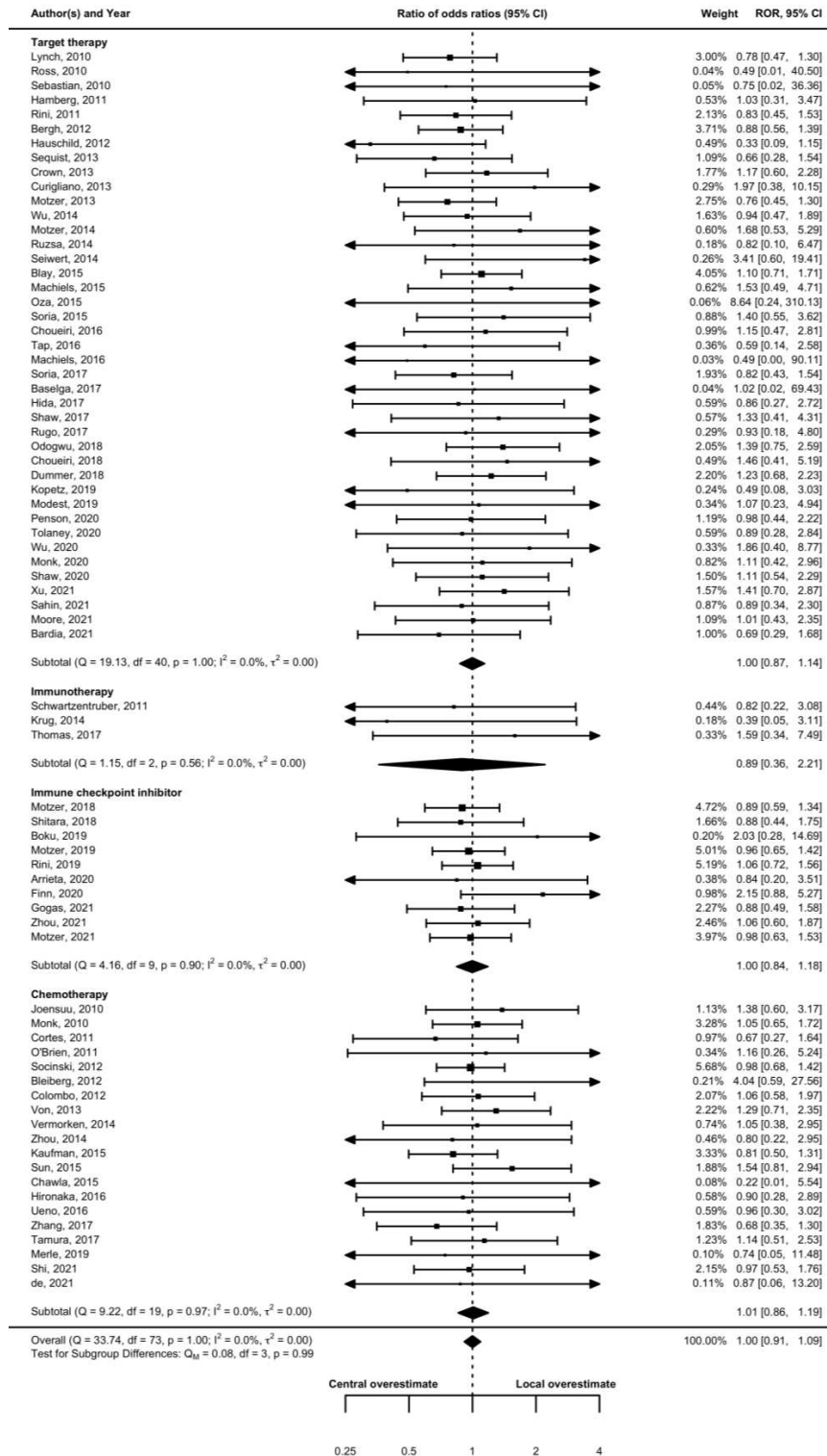

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Supplementary Figure 7b. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Subgroup analysis: cancer type.

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Supplementary Figure 8a. Comparison of treatment effect estimates (Hazard Ratio) between central reviewers and local investigators. Subgroup analysis: drug classification.

Author(s) and Year	Ratio of hazard ratios (95% CI)	Weight	RHR, 95% CI
Target therapy			
Keunchil, 2016		1.11%	1.07 [0.75, 1.52]
Johann, 2020		0.98%	0.73 [0.50, 1.07]
Lynch, 2010		2.45%	0.85 [0.67, 1.08]
Blackwell, 2010		0.86%	1.03 [0.69, 1.53]
Rini, 2011		1.78%	0.99 [0.75, 1.31]
Bergh, 2012		1.26%	0.93 [0.67, 1.30]
Reichardt, 2012		0.64%	0.64 [0.41, 1.02]
Flaherty, 2012		0.60%	1.07 [0.66, 1.73]
Hauschild, 2012		0.24%	0.86 [0.40, 1.84]
Flaherty, 2012		0.29%	0.71 [0.36, 1.41]
Verma, 2012		2.56%	1.02 [0.81, 1.28]
Gianni, 2013		1.08%	1.14 [0.80, 1.63]
Sequist, 2013		0.82%	0.84 [0.56, 1.27]
Crown, 2013		1.18%	0.91 [0.65, 1.28]
Curigliano, 2013		0.79%	0.97 [0.64, 1.47]
Motzer, 2013		1.42%	0.91 [0.66, 1.24]
Kim, 2013		2.55%	0.91 [0.72, 1.15]
Rini, 2014		2.21%	1.00 [0.78, 1.28]
Hutson, 2014		1.58%	1.00 [0.74, 1.34]
Wu, 2014		0.64%	0.93 [0.58, 1.47]
Motzer, 2014		1.92%	1.16 [0.89, 1.52]
Kim, 2014		0.23%	1.20 [0.55, 2.61]
Ruzsa, 2014		0.37%	1.00 [0.55, 1.83]
Oza, 2015		0.43%	1.20 [0.68, 2.11]
Ravaud, 2015		1.04%	0.99 [0.69, 1.42]
Blay, 2015		0.83%	1.30 [0.86, 1.95]
Machiels, 2015		1.57%	0.99 [0.73, 1.33]
Vansteenkiste, 2015		0.52%	1.27 [0.76, 2.12]
Oza, 2015		0.24%	0.74 [0.35, 1.56]
Wu, 2015		0.37%	0.81 [0.44, 1.50]
Soria, 2015		2.84%	0.98 [0.78, 1.22]
Mir, 2016		0.31%	0.84 [0.43, 1.64]
Choueiri, 2016		1.67%	1.04 [0.78, 1.38]
Tap, 2016		0.31%	1.00 [0.52, 1.95]
Soria, 2017		0.91%	0.89 [0.60, 1.31]
Dummer, 2017		0.97%	1.02 [0.70, 1.48]
Baselga, 2017		0.14%	0.99 [0.36, 2.70]
Yao, 2017		1.29%	0.97 [0.70, 1.34]
Urruticoechea, 2017		1.46%	0.99 [0.73, 1.34]
Hida, 2017		0.31%	1.00 [0.51, 1.95]
Robson, 2017		0.70%	0.86 [0.55, 1.34]
Peters, 2017		0.64%	0.94 [0.59, 1.50]
Shaw, 2017		0.71%	0.82 [0.53, 1.27]
Rugo, 2017		0.55%	1.34 [0.81, 2.21]
Shi, 2017		0.64%	1.07 [0.67, 1.70]
Wick, 2017		1.42%	0.83 [0.61, 1.13]
Odogwu, 2018		0.74%	1.07 [0.70, 1.65]
Choueiri, 2018		0.39%	1.17 [0.64, 2.11]
Dummer, 2018		0.91%	0.91 [0.62, 1.34]
Novello, 2018		0.17%	0.47 [0.19, 1.15]
Litton, 2018		1.00%	1.00 [0.69, 1.45]
Rini, 2020		1.04%	0.85 [0.59, 1.22]
Penson, 2020		0.53%	0.79 [0.47, 1.32]
Tolaney, 2020		0.39%	0.76 [0.42, 1.38]
Wu, 2020		0.11%	1.31 [0.43, 3.99]
Camidge, 2020		0.61%	0.88 [0.55, 1.41]
Monk, 2020		0.37%	0.72 [0.39, 1.32]
Shaw, 2020		0.45%	0.75 [0.43, 1.30]
Pignata, 2021		1.32%	0.98 [0.71, 1.35]
Xu, 2021		0.54%	1.08 [0.65, 1.78]
Moore, 2021		1.19%	0.82 [0.59, 1.16]
Bardia, 2021		1.25%	0.85 [0.61, 1.19]
Subtotal (Q = 28.91, df = 61, p = 1.00; I² = 0.0%, τ² = 0.00)			0.95 [0.91, 1.00]
Immune checkpoint inhibitor			
Ribas, 2015		1.14%	0.82 [0.58, 1.16]
Socinski, 2018		2.14%	0.88 [0.68, 1.13]
McDermott, 2018		0.55%	0.82 [0.50, 1.35]
Shitara, 2018		2.26%	0.80 [0.62, 1.02]
Motzer, 2019		1.74%	0.93 [0.70, 1.23]
Rini, 2019		2.48%	0.94 [0.75, 1.19]
West, 2019		2.11%	0.87 [0.67, 1.12]
Jotte, 2020		2.19%	0.89 [0.69, 1.14]
Finn, 2020		1.24%	0.76 [0.55, 1.06]
Gogas, 2021		1.00%	1.15 [0.79, 1.66]
Zhou, 2021		0.98%	0.90 [0.62, 1.31]
Motzer, 2021		1.53%	1.21 [0.89, 1.63]
Subtotal (Q = 7.86, df = 11, p = 0.73; I² = 0.0%, τ² = 0.00)			0.90 [0.83, 0.98]
Chemotherapy			
Monk, 2010		2.04%	0.91 [0.70, 1.18]
Cortes, 2011		2.04%	0.87 [0.67, 1.13]
Colombo, 2012		2.57%	0.94 [0.75, 1.19]
Naumann, 2013		0.37%	0.82 [0.44, 1.49]
Von, 2013		2.54%	0.88 [0.70, 1.12]
Blay, 2014		0.16%	1.01 [0.40, 2.57]
Vermorken, 2014		0.36%	0.90 [0.48, 1.66]
Zhou, 2014		0.64%	1.02 [0.64, 1.62]
Kaufman, 2015		3.61%	0.91 [0.75, 1.10]
Kawai, 2015		0.12%	1.86 [0.64, 5.38]
Demetri, 2016		0.72%	1.05 [0.68, 1.63]
Hersh, 2015		1.55%	1.07 [0.79, 1.44]
Ueno, 2016		0.45%	1.30 [0.75, 2.27]
Zhang, 2017		1.21%	1.46 [1.04, 2.04]
Tamura, 2017		0.49%	0.65 [0.38, 1.10]
Yuan, 2019		1.67%	1.03 [0.77, 1.37]
Shi, 2021		1.22%	1.05 [0.75, 1.47]
de, 2021		0.46%	0.98 [0.57, 1.69]
Subtotal (Q = 13.60, df = 17, p = 0.70; I² = 0.0%, τ² = 0.00)			0.97 [0.89, 1.05]
Overall (Q = 51.96, df = 91, p = 1.00; I² = 0.0%, τ² = 0.00)		100.00%	0.95 [0.91, 0.98]
Test for Subgroup Differences: Q_M = 1.59, df = 2, p = 0.45			

Local overestimate   Central overestimate

0.25   0.5   1   2   4

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Supplementary Figure 8b. Comparison of treatment effect estimates (Odds Ratio) between central reviewers and local investigators. Subgroup analysis: drug classification.

Supplementary Table 1. Adjudicators of open-label trials of anticancer drugs (n = 1,197)

PFS	
Central + local	157 (13.1)
Only central	134 (11.2)
Only local	291 (24.3)
Unclear	528 (44.1)
No PFS	87 (7.3)
ORR	
Central + local	141 (11.8)
Only central	158 (13.2)
Only local	301 (25.2)
Unclear	536 (44.8)
No ORR	61 (5.1)

Abbreviations: ORR, objective response rate; PFS, progression-free survival.

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Supplementary Table 2. Effect of correlation between central and local adjudications (sensitivity analysis).

PFS

ρ	RHR (95%CI)	Tau^2	I^2	P value for heterogeneity
0	0.95 (0.91 to 0.98)	0.00	0%	>0.99
0.25	0.95 (0.92 to 0.98)	0.00	0%	0.96
0.50	0.95 (0.92 to 0.97)	0.00	7.0%	0.18
0.75	0.95 (0.92 to 0.98)	0.01	56.0%	< .0001
0.95	0.95 (0.91 to 0.98)	0.03	94.0%	< .0001

ORR

ρ	ROR (95%CI)	Tau^2	I^2	P value for heterogeneity
0	1.00 (0.91 to 1.09)	0.00	0%	>0.99
0.25	1.00 (0.93 to 1.08)	0.00	0%	>0.99
0.50	1.00 (0.94 to 1.06)	0.00	0%	0.71
0.75	1.01 (0.95 to 1.08)	0.02	37.0%	< .0001
0.95	1.03 (0.95 to 1.13)	0.11	93.0%	< .0001

Abbreviations: ORR, objective response rate; PFS, progression-free survival; RHR, ratios of hazard ratio; ROR, ratios of odds ratio.

A ρ is correlation coefficients between central and local adjudications in each trial.

A ρ of 0 indicates no dependency and a r of 0.95 indicates almost complete dependency.

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