Supporting information

Supplementary Table S1. Search strategy.

Data source	Search terms
PubMed	ALL FIELDS (ipilimumab OR MDX-010 OR tremelimumab OR CP-675,206 OR nivolumab OR BMS-963558 OR pembrolizumab OR MK-3475 OR atezolizumab OR MPDL3280A OR avelumab OR MSB0010718C OR durvalumab OR MEDI4736 OR Cemiplimab OR REGN2810 OR Toripalimab OR JS001 OR Sintilimab OR IBI308) AND (phase)
Cochrane library	ALL TEXT ipilimumab OR MDX-010 OR tremelimumab OR CP-675,206 OR nivolumab OR BMS-963558 OR pembrolizumab OR MK-3475 OR atezolizumab OR MPDL3280A OR avelumab OR MSB0010718C OR durvalumab OR MEDI4736 OR Cemiplimab OR REGN2810 OR Toripalimab OR JS001 OR Sintilimab OR IBI308
Embase	ALL FIELDS ('phase '/exp OR 'phase') AND ('ipilimumab'/exp OR 'ipilimumab' OR 'MDX-010'/exp OR 'MDX-010' OR 'tremelimumab'/exp OR 'tremelimumab' OR 'CP-675,206 '/exp OR 'CP-675,206' OR 'nivolumab '/exp OR 'nivolumab' OR 'BMS-963558'/exp OR 'BMS-963558' OR 'pembrolizumab'/exp OR 'pembrolizumab' OR 'MK-3475'/exp OR 'MK-3475' OR 'atezolizumab'/exp OR 'atezolizumab' OR 'MPDL3280A'/exp OR 'MPDL3280A' OR 'avelumab'/exp OR 'avelumab' OR 'MSB0010718C'/exp OR 'MSB0010718C' OR 'pembrolizumab'/exp OR 'pembrolizumab' OR 'MK-3475'/exp OR 'MK-3475' OR 'atezolizumab'/exp OR 'atezolizumab' OR 'MPDL3280A'/exp OR 'MPDL3280A' OR 'avelumab'/exp OR 'avelumab' OR 'MSB0010718C'/exp OR 'MSB0010718C' OR 'durvalumab'/exp OR 'durvalumab' OR 'MEDI4736'/exp OR 'MEDI4736' OR 'Cemiplimab'/exp OR 'Cemiplimab' OR 'REGN2810'/exp OR 'REGN2810' OR 'Toripalimab'/exp OR 'Toripalimab' OR 'JS001'/exp OR 'JS001' OR 'Sintilimab'/exp OR 'Sintilimab' OR 'IBI308'/exp OR 'IBI308')
ClinicalTrials.gov	(ipilimumab OR MDX-010 OR tremelimumab OR CP-675,206 OR nivolumab OR BMS-963558 OR pembrolizumab OR MK-3475 OR atezolizumab OR MPDL3280A OR avelumab OR MSB0010718C OR durvalumab OR MEDI4736 OR Cemiplimab OR REGN2810 OR Toripalimab OR JS001 OR Sintilimab OR IBI308)

Supplementary Table S2. Risk of bias of clinical trials for meta-analysis

No.	Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Sponsorship bias	Other bias
1	Recks, 2013(Reck et al., 2013) NCT00527735	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
2	Kwon, 2014(Kwon et al., 2014) NCT00861614	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
3	Borghaei, 2015(Borghaei et al., 2015) NCT01673867	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
4	Brahmer, 2015(Brahmer et al., 2015) NCT01642004	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
5	Eggermont, 2015(Eggermont et al., 2015) NCT00636168	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
6	Motzer, 2015(Motzer et al., 2015)	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear

7	NCT01668784 Ribas, 2015(Ribas et al., 2015)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
8	NCT01704287 Robert, 2015(Robert et al., 2015)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
9	NCT01721772 Weber, 2015(Weber et al., 2015)	Low	Unclear	High	Low	Unclear	Unclear	High	Unclear
10	NCT01721746 Fehrenbacher, 2016 (Fehrenbacher et al., 2016)	Low	High	High	Unclear	Unclear	Unclear	High	Low
11	NCT01903993 Ferris, 2016 (Ferris et al., 2016)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
12	NCT02105636 Herbst, 2016 (Herbst et al., 2016)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
13	NCT01905657 Langer, 2016(Langer et al.,	Low	Unclear	High	High	Unclear	Unclear	High	Unclear

	2016) NCT02039674								
14	Reck, 2016(Reck et al., 2016a) NCT01450761	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
15	Reck, 2016(Reck et al., 2016b) NCT02142738	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
16	Rittmeyer, 2016(Rittmeyer et al., 2017) NCT02008227	Low	High	High	Unclear	Unclear	Unclear	High	Unclear
17	Antonia, 2017(Antonia et al., 2017) NCT02125461	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
18	Beer, 2017(Beer et al., 2017) NCT01057810	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
19	Bellmunt, 2017(Rogers et al., 2017) NCT02256436	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
20	Carbone, 2017(Carbone et al., 2017)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear

21	NCT02041533 Govindan, 2017(Govindan et al., 2017)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
22	NCT01285609 Kang, 2017(Kang et al., 2017)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
23	NCT02267343 Maio, 2017(Llombart-Cussac et al., 2017)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
24	NCT01843374 Powles, 2017 (Powles et al., 2018)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
25	NCT02302807 Barlesi, 2018(Barlesi et al., 2018)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
26	NCT02395172 Eggermont, 2018(Eggermont et al., 2018)	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
27	NCT02362594 Gandhi, 2018(Gandhi et	Low	Low	Low	Low	Unclear	Unclear	High	Unclear

	al., 2018) NCT02578680								
28	Motzer, 2018 (Motzer et al., 2018) NCT02231749	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
29	Paz-Ares, 2018(Paz-Ares et al., 2018) NCT02775435	Low	Low	Low	Low	Unclear	Unclear	High	Unclear
30	Shitara, 2018(Shitara et al., 2018) NCT02370498	Low	Unclear	High	Low	Unclear	Unclear	High	Unclear
31	Cohen, 2019(Cohen et al., 2019) NCT02252042	Low	Unclear	High	Unclear	Unclear	Unclear	High	Unclear
32	Eng, 2019(Eng et al., 2019) NCT02788279	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
33	Mork, 2019(Mok et al., 2019) NCT02220894	Low	Unclear	High	High	Low	Unclear	High	Unclear
34	Wu, 2019(Wu et al., 2019)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear

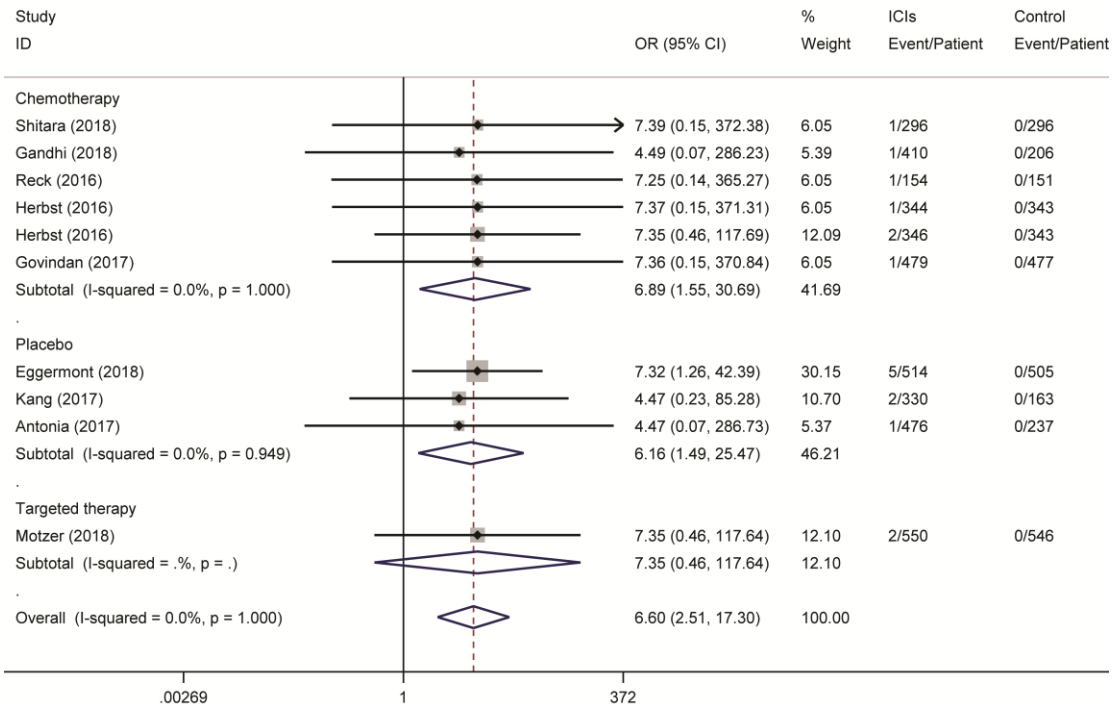
35	NCT02613507 Yang, 2019(Chih-Hsin Yang et al., 2019)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
36	NCT02454933 NCT01585987(Squibb, 2012)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
37	NCT01984242(Roche, 2014)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
38	NCT02367781(Roche, 2015b)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
39	NCT02352948(AstraZeneca, 2015)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear
40	NCT02420821(Roche, 2015a)	Low	Unclear	High	High	Unclear	Unclear	High	Unclear

Supplementary Table S3 The results of publication bias test based on the Egger's test and Begg's test

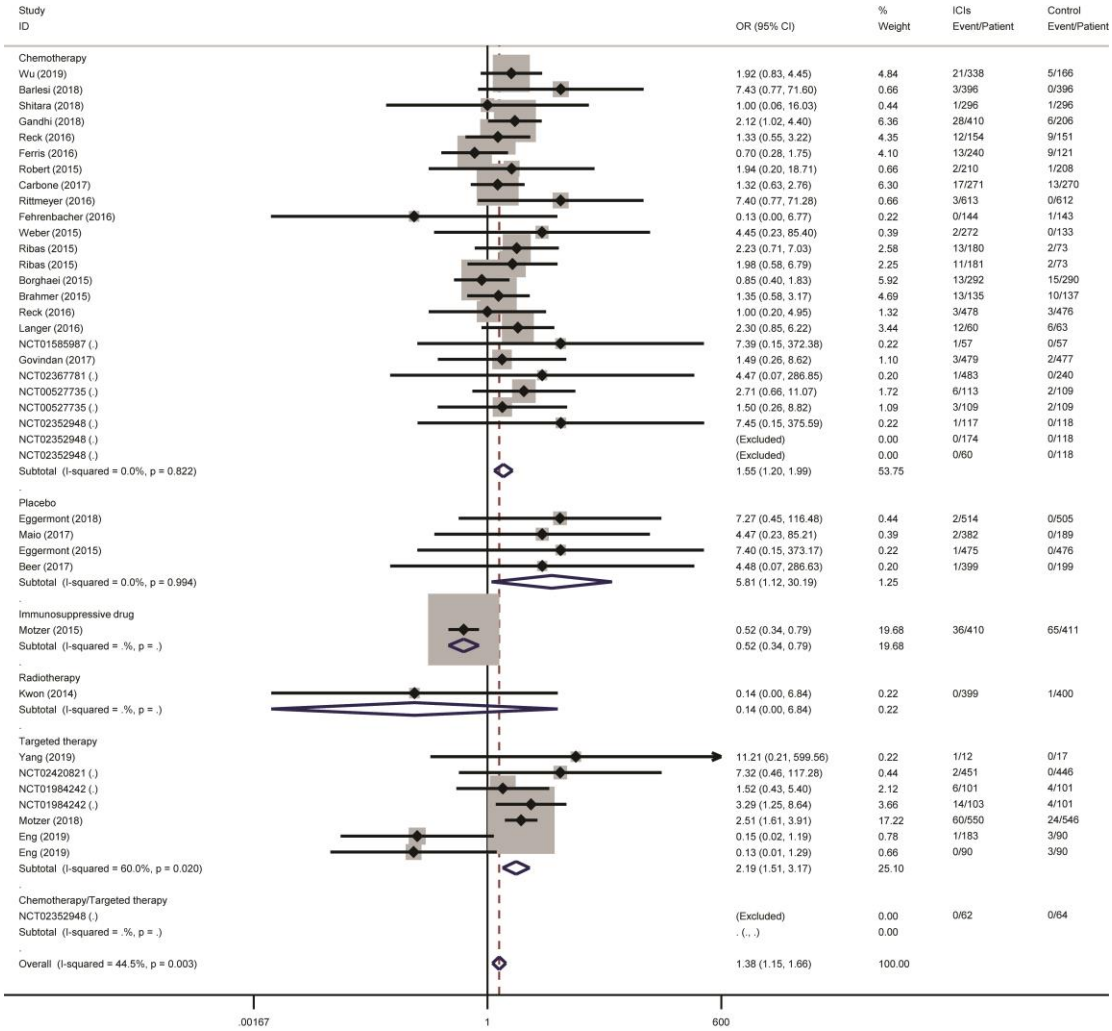
Outcomes	Egger's test	Begg's test
DM	0.994	0.855
All-grade hyperglycemia	0.128	0.733
Serious-grade hyperglycemia	0.325	0.092
T2D	0.310	0.063
All-grade T1D	0.300	0.004
Serious-grade T1D	0.334	0.016

Abbreviations: DM, diabetes mellitus; T1D, type 1 diabetes; T2D, type 2 diabetes.

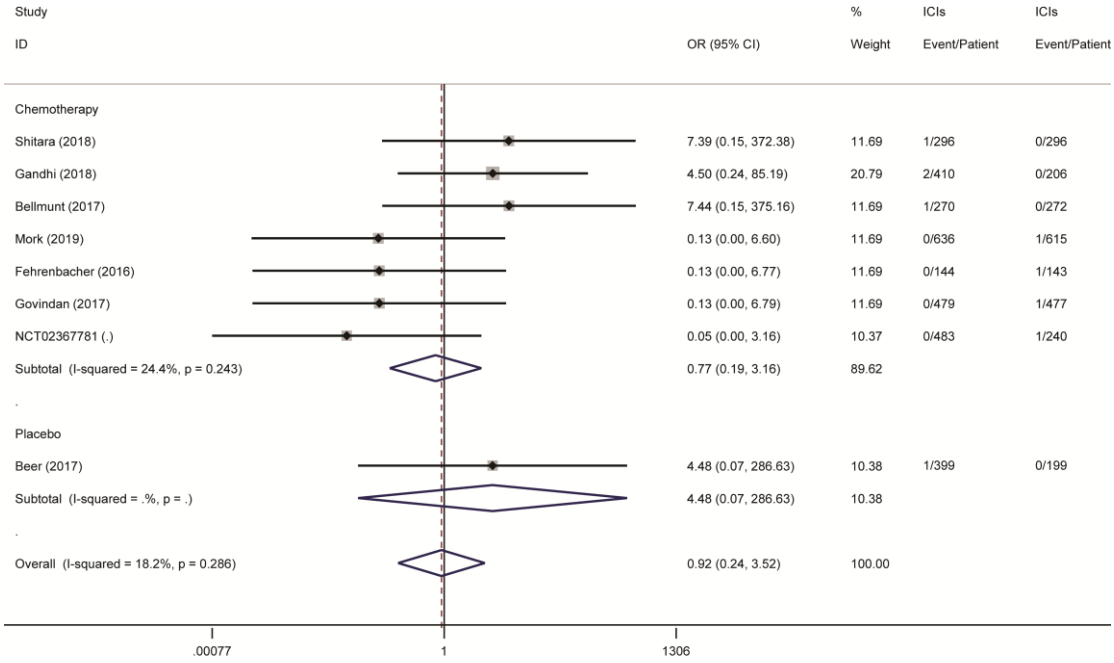
Supplementary Figure S1. Risk of all-grade T1D following the use of ICIs versus control treatment, stratified by the type of control group.



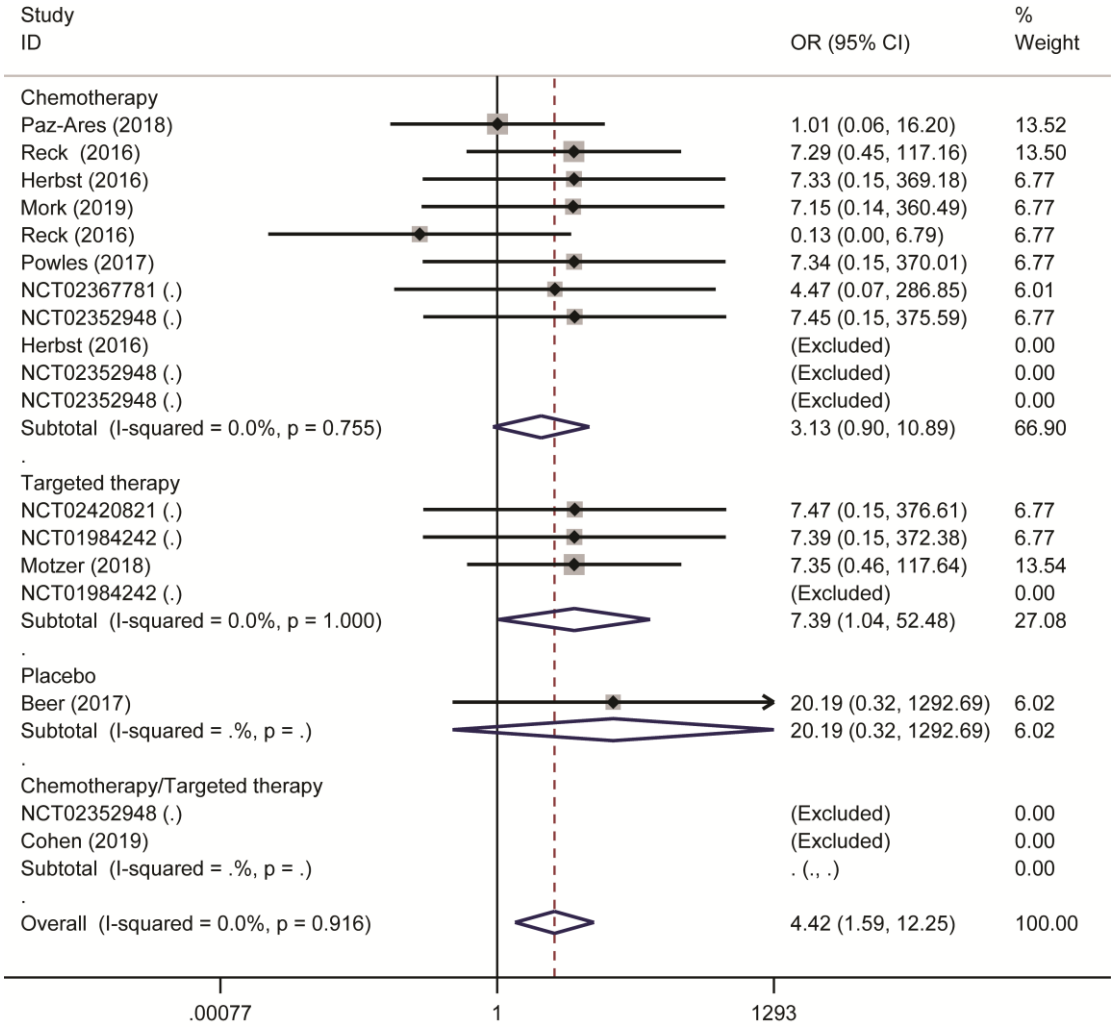
Supplementary Figure S2. Risk of all-grade hyperglycemia following the use of ICIs versus control treatment, stratified by the type of control group.



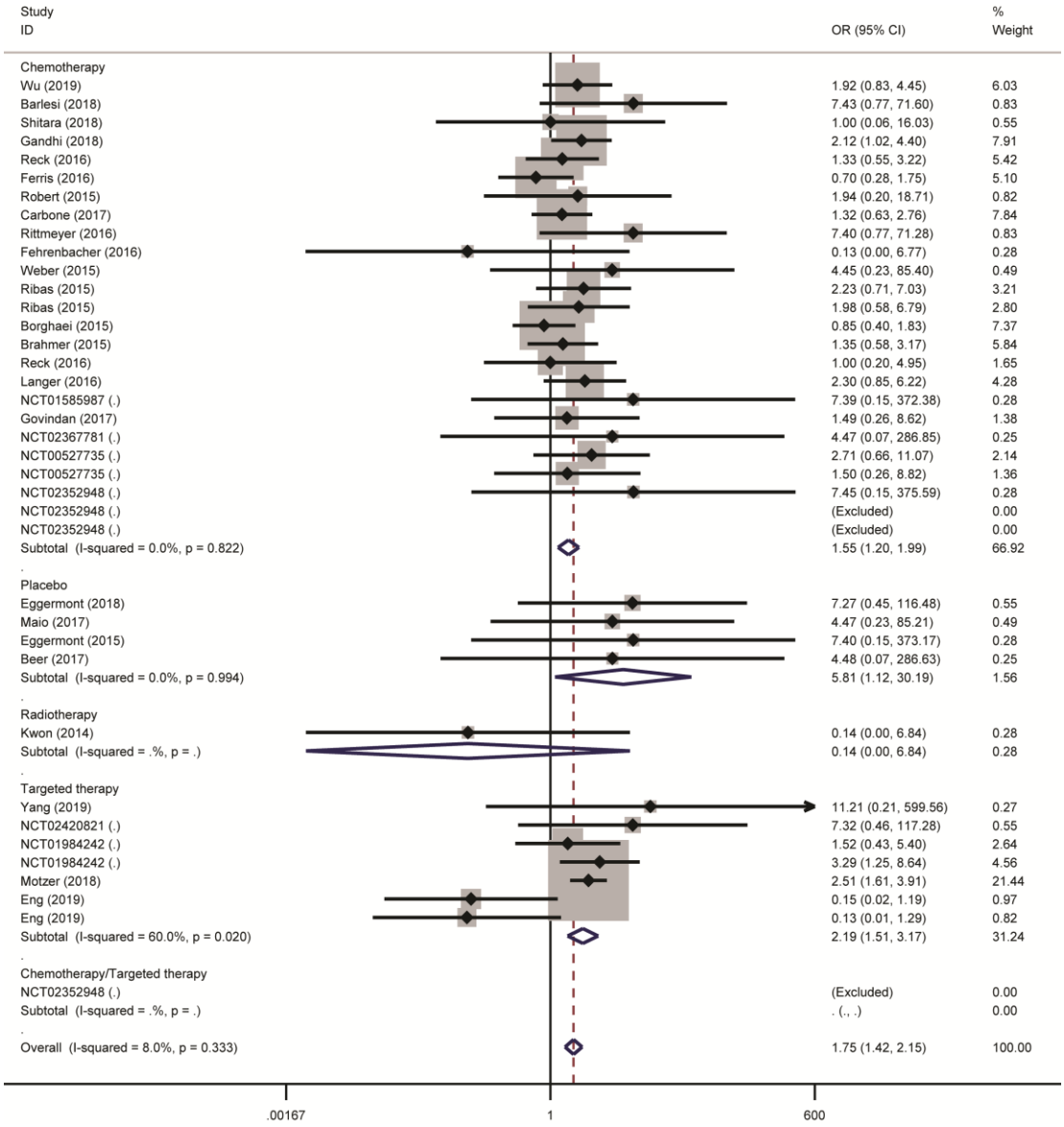
Supplementary Figure S3. Risk of type 2 diabetes following the use ICIs of versus control treatment, stratified by the type of control group.



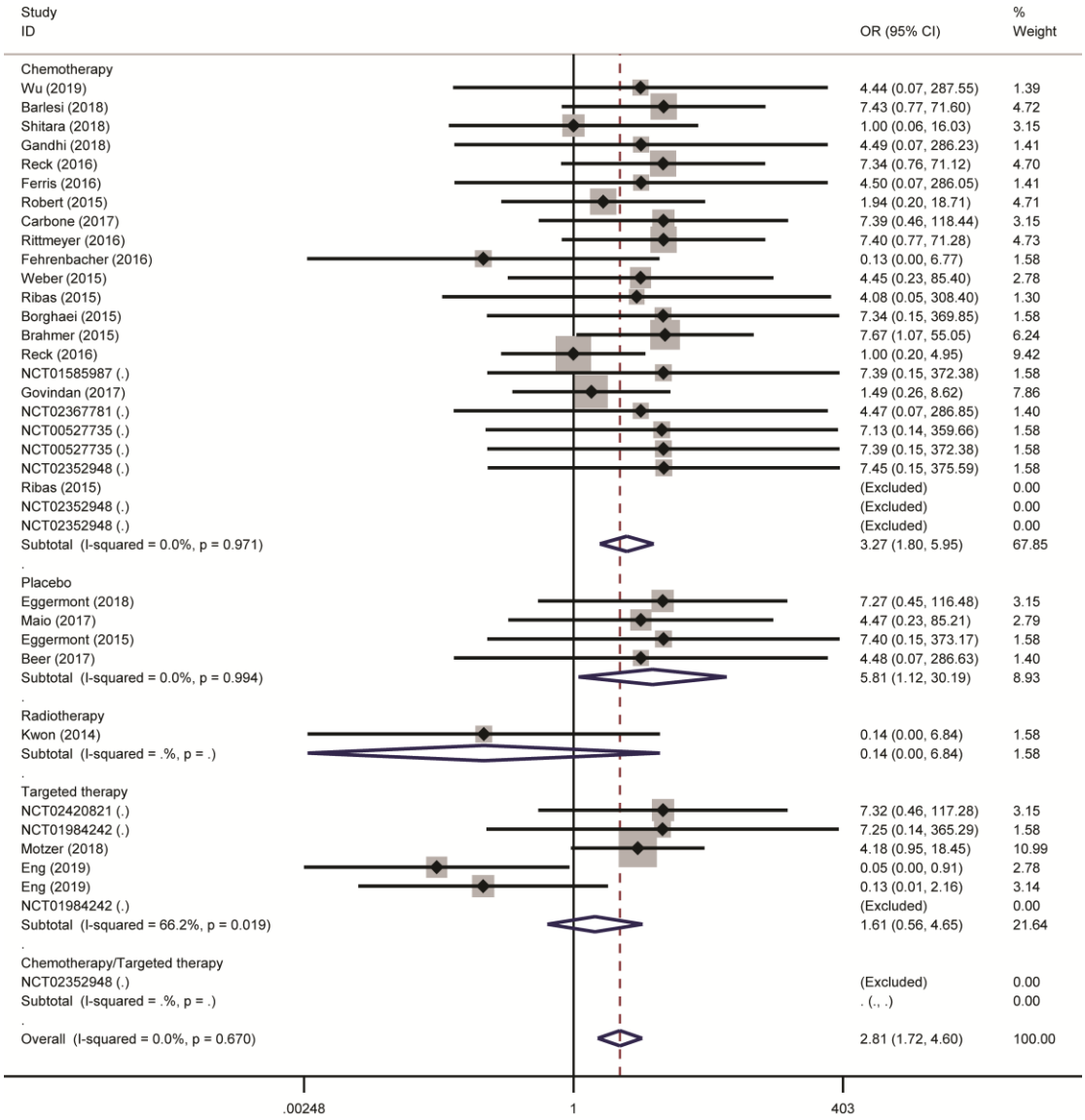
Supplementary Figure S4. Risk of diabetes mellitus following the use of ICIs versus control treatment, after excluding everolimus-based control group.



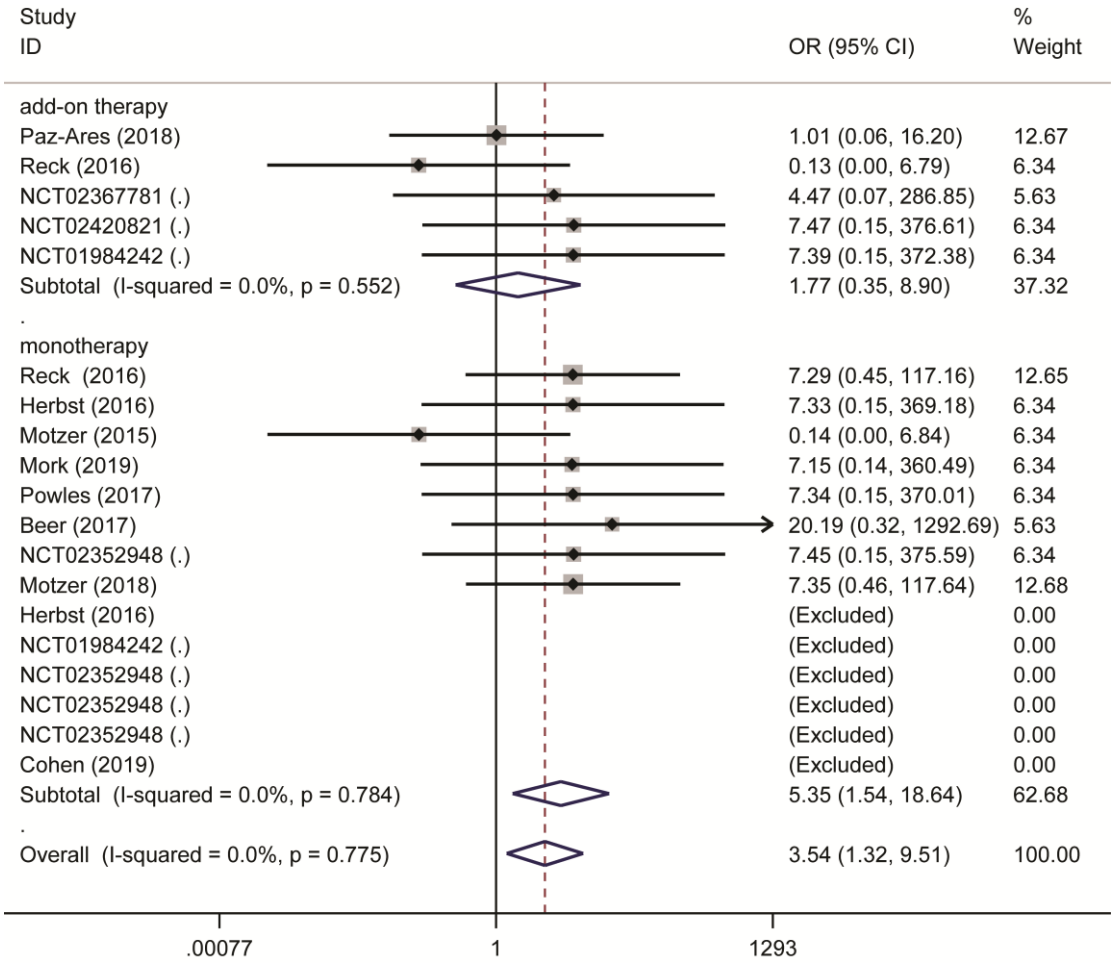
Supplementary Figure S5. Risk of all-grade hyperglycemia following the use of ICIs versus control treatment, after excluding everolimus-based control group.



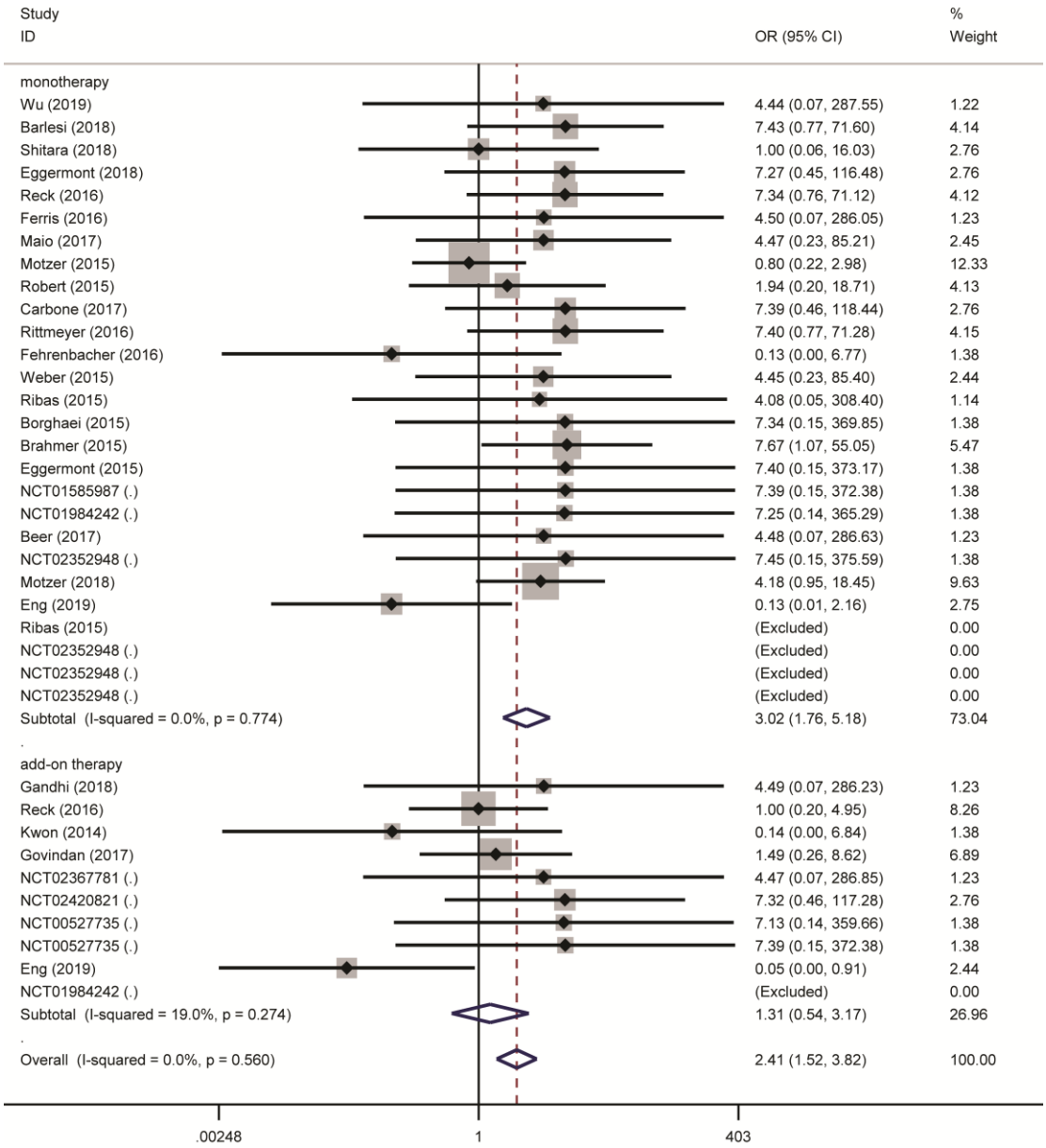
Supplementary Figure S6. Risk of serious-grade hyperglycemia following the use of ICIs versus control treatment, after excluding everolimus-based control group.



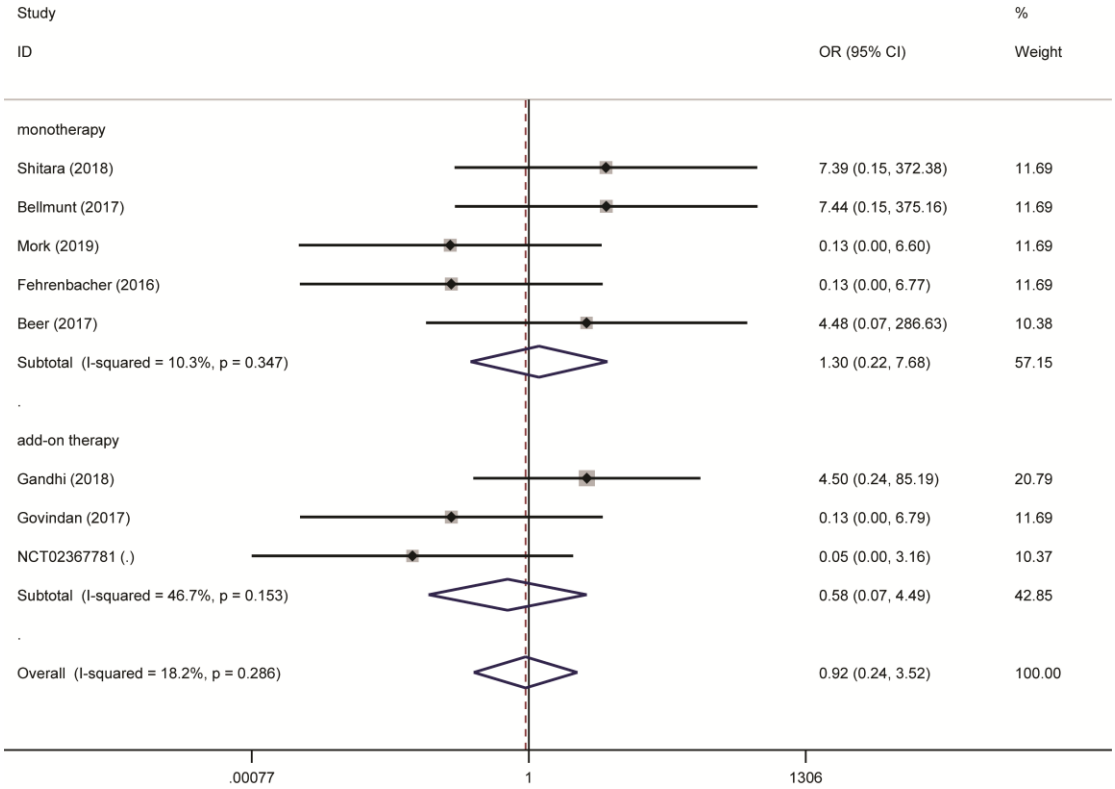
Supplementary Figure S7. Risk of diabetes mellitus following the use of ICIs versus control treatment, stratified by the mode of treatment (monotherapy v add-on therapy).



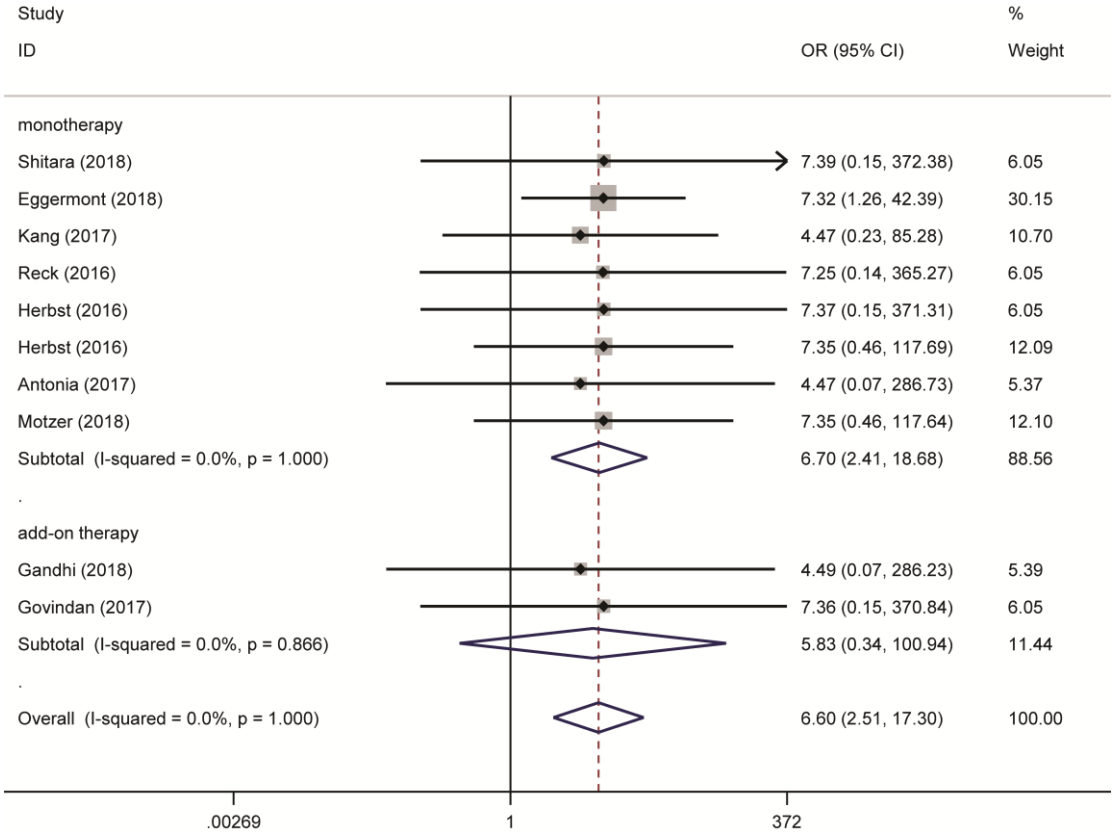
Supplementary Figure S8. Risk of serious-grade hyperglycemia following the use of ICIs versus control treatment, stratified by the mode of treatment (monotherapy v add-on therapy).



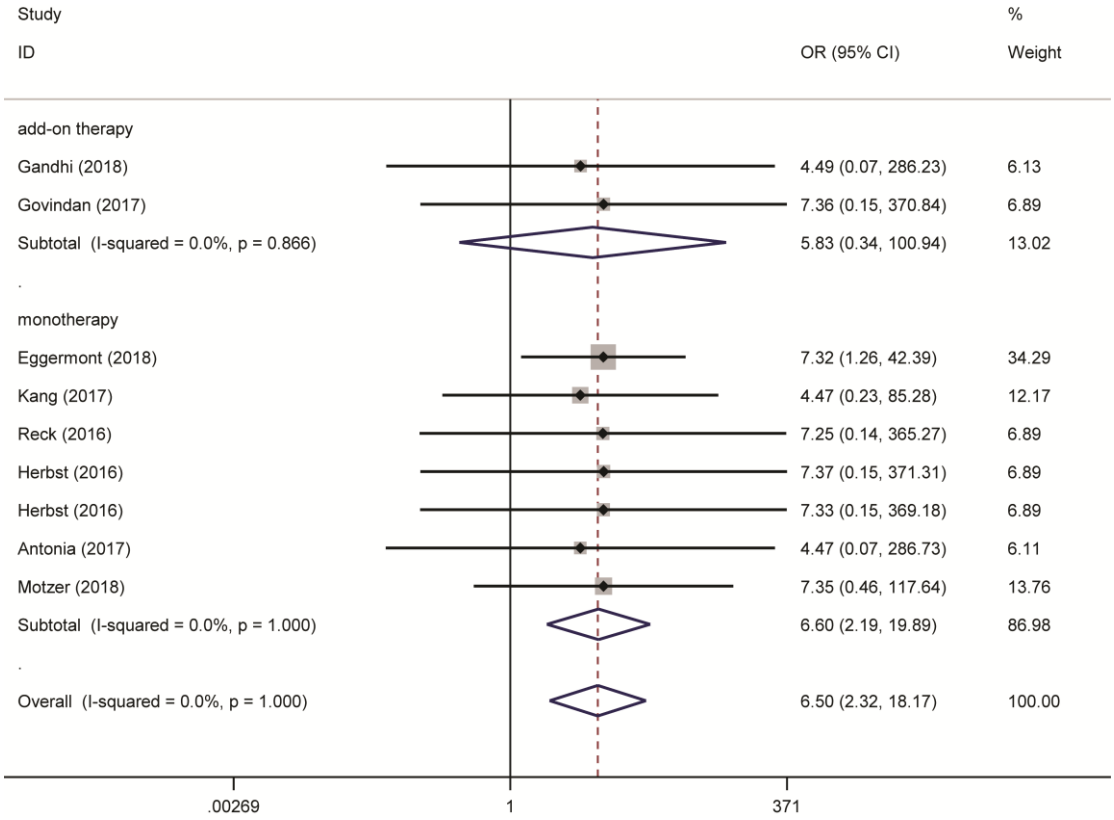
Supplementary Figure S9. Risk of type 2 diabetes following the use of ICIs versus control treatment, stratified by the mode of treatment (monotherapy v add-on therapy).



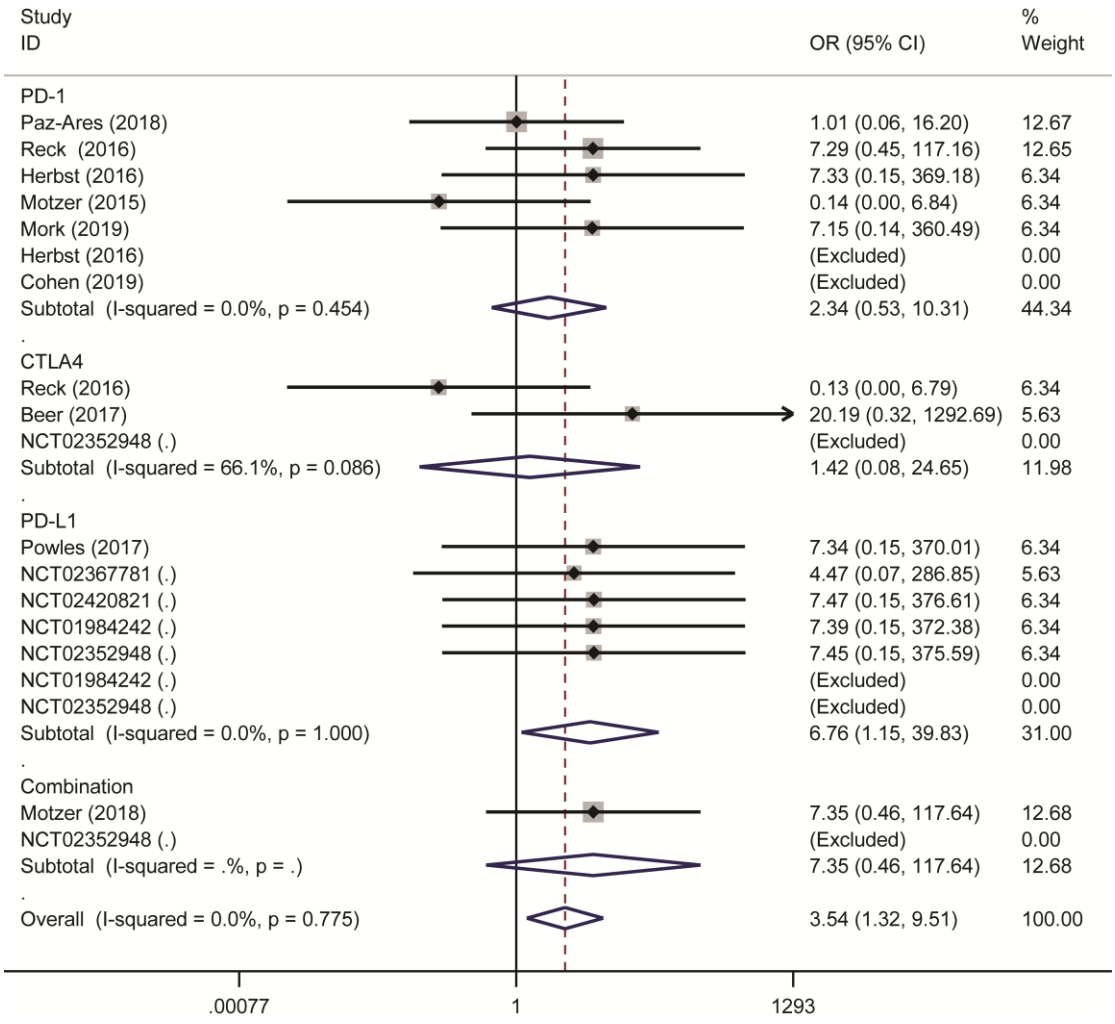
Supplementary Figure S10. Risk of all-grade type 1 diabetes following the use of ICIs versus control treatment, stratified by the mode of treatment (monotherapy v add-on therapy).



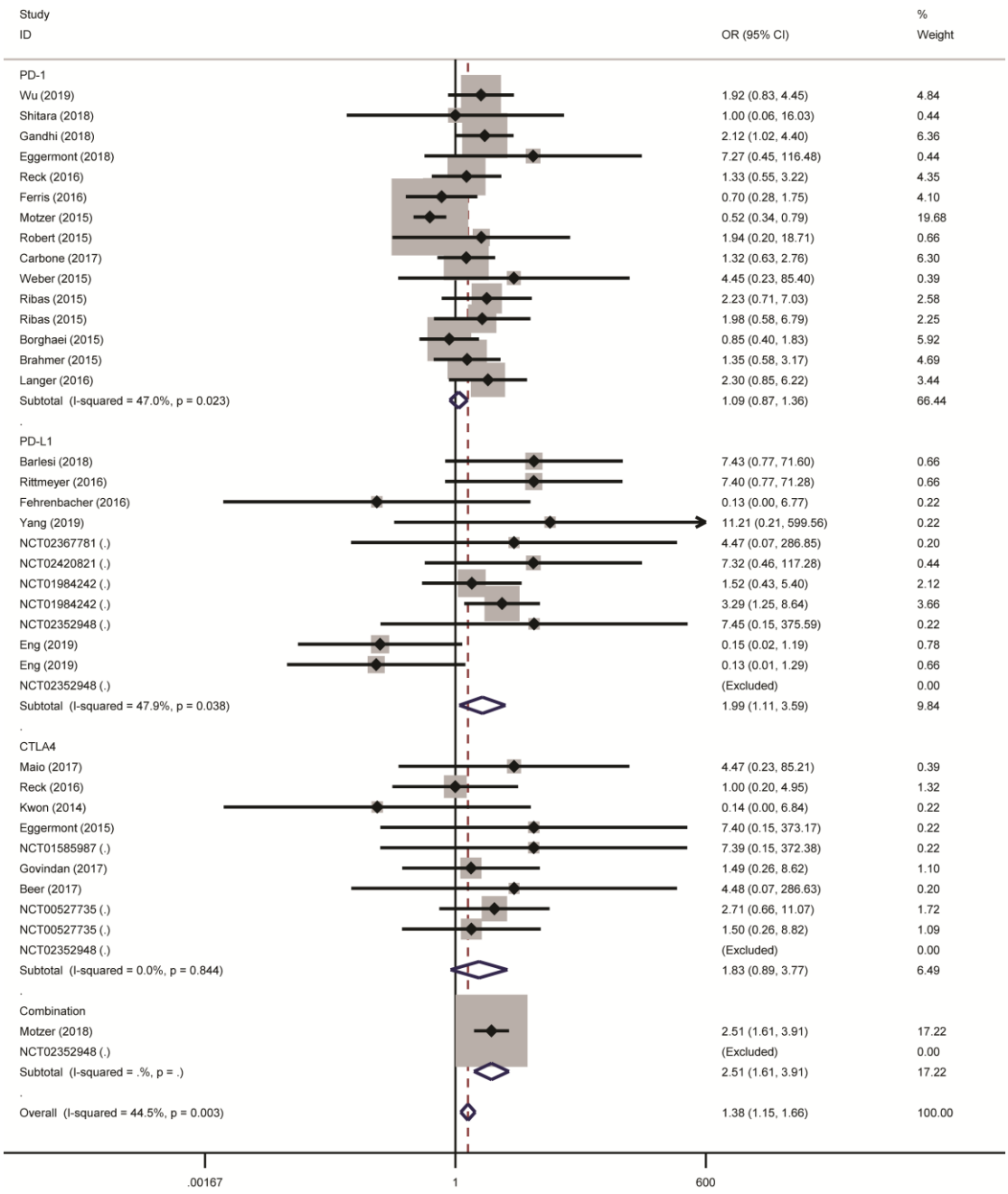
Supplementary Figure S11. Risk of serious type 1 diabetes following the use of ICIs versus control treatment, stratified by the mode of treatment (monotherapy v add-on therapy).



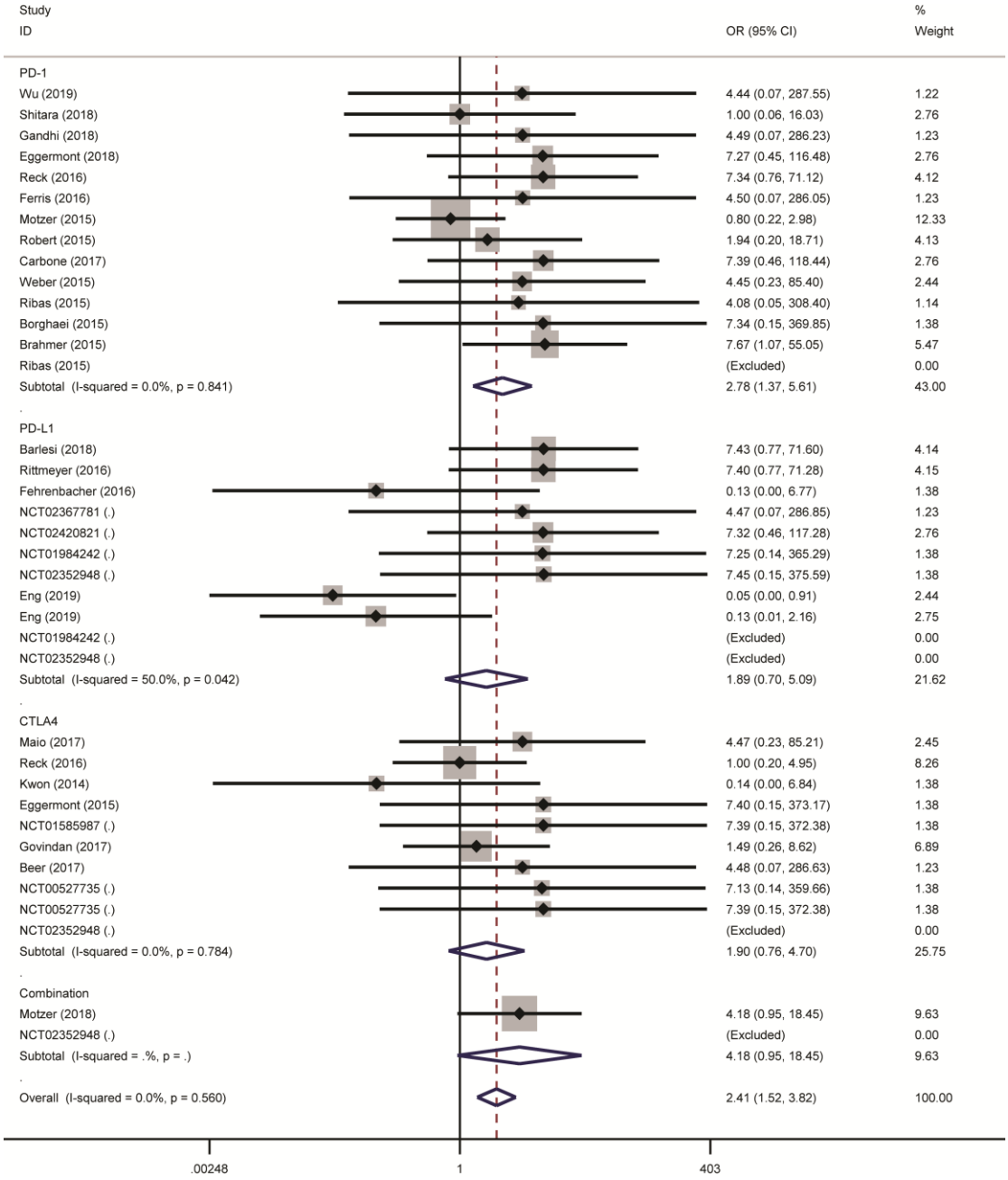
Supplementary Figure S12. Risk of diabetes mellitus following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



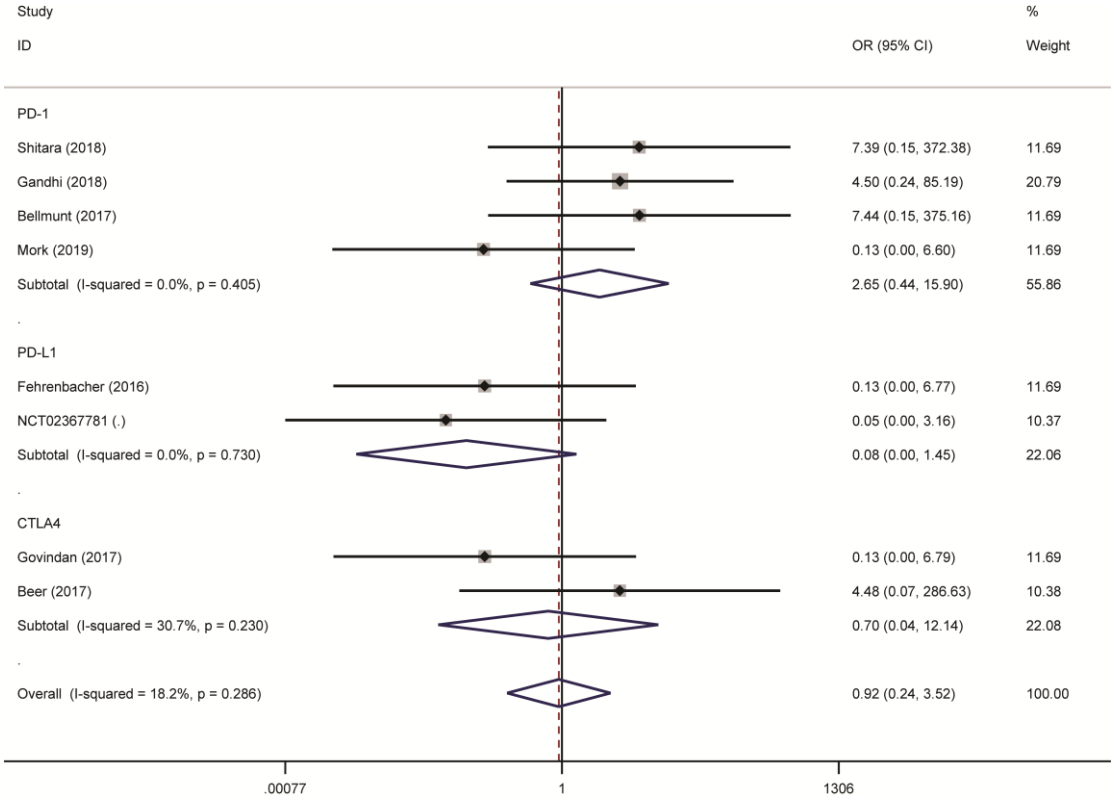
Supplementary Figure S13. Risk of all-grade hyperglycemia following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



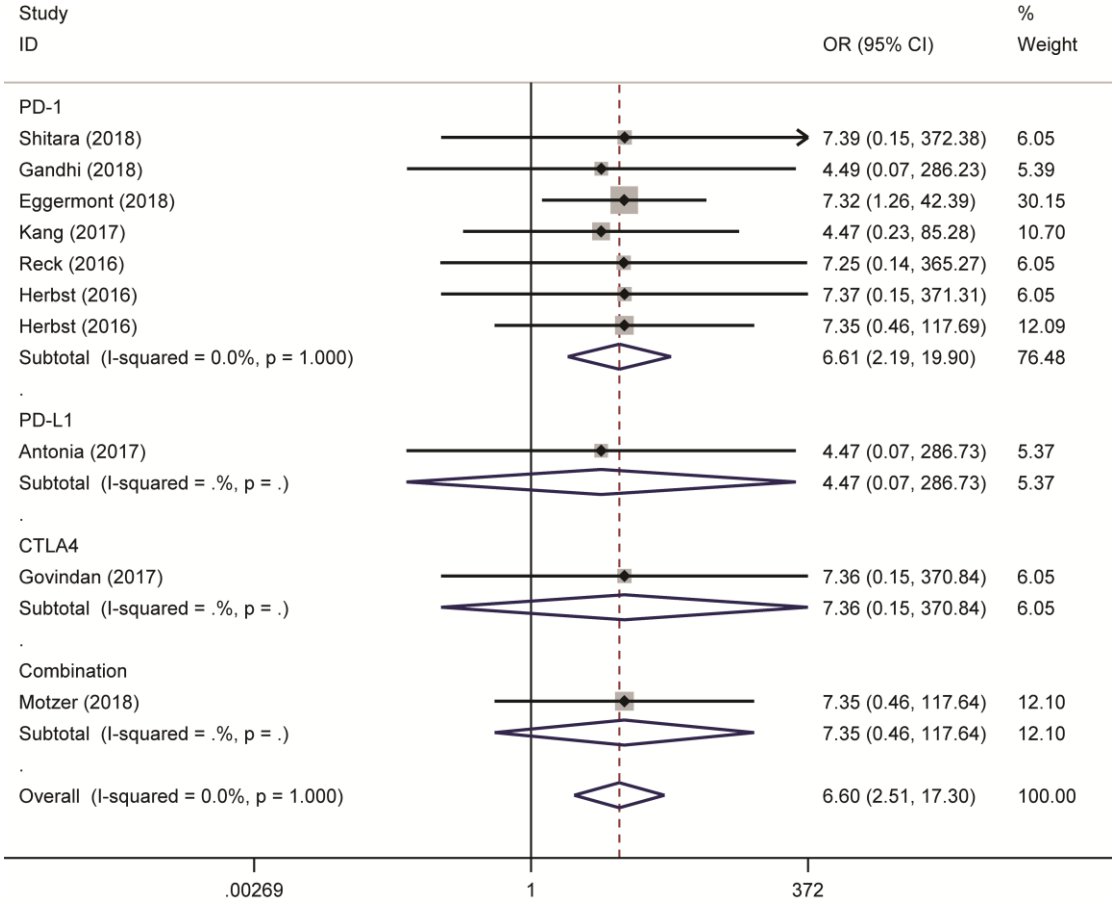
Supplementary Figure S14. Risk of serious-grade hyperglycemia following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



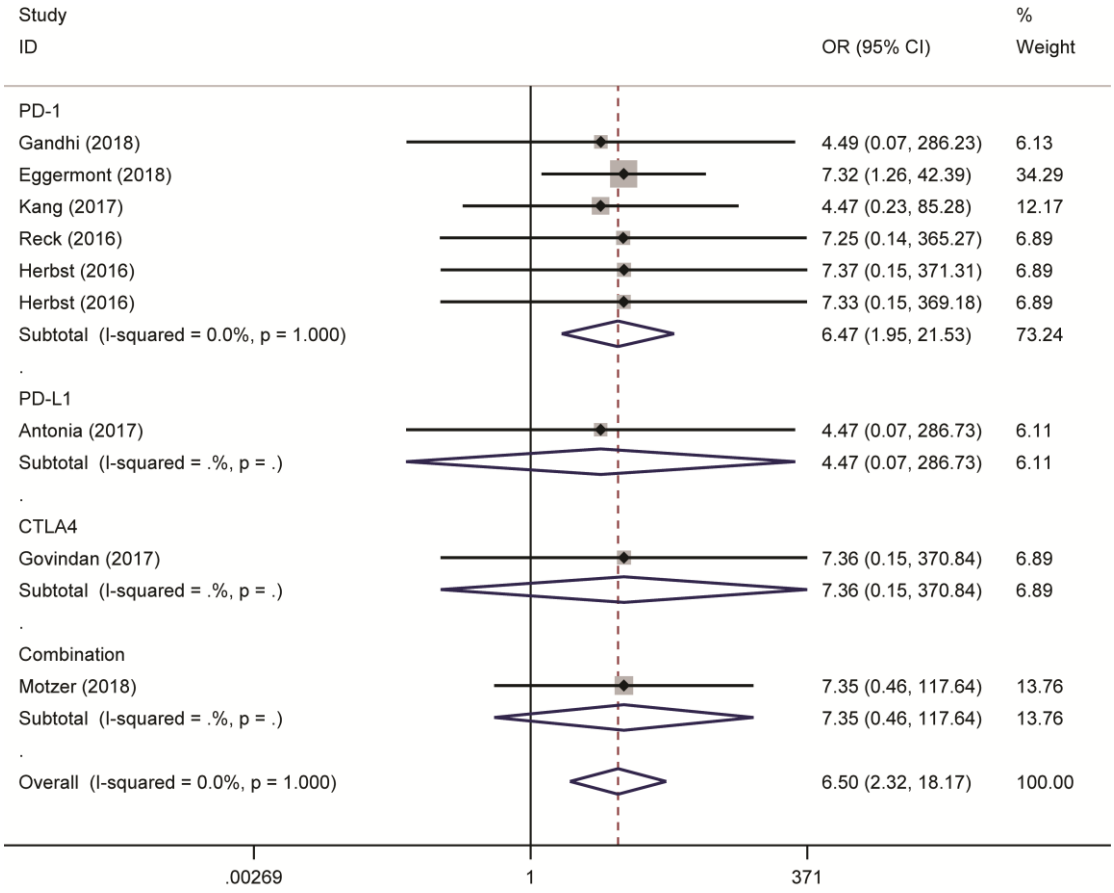
Supplementary Figure S15. Risk of type 2 diabetes following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



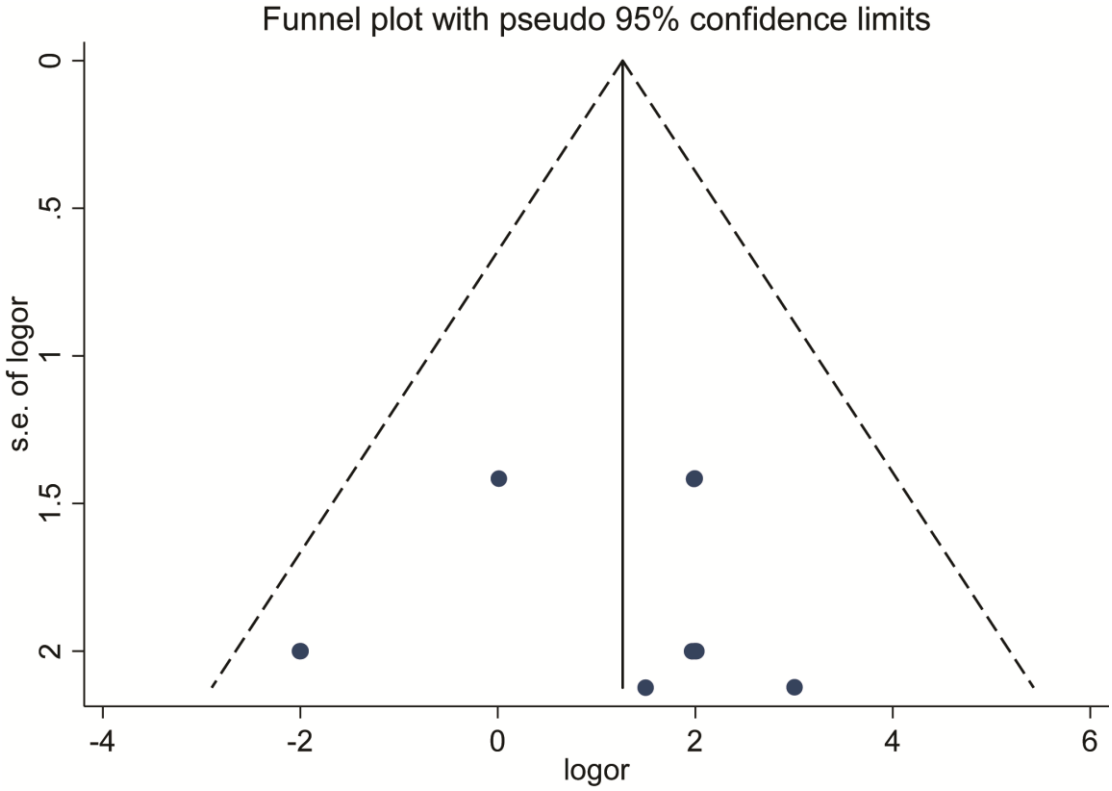
Supplementary Figure S16. Risk of all-grade type 1 diabetes following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



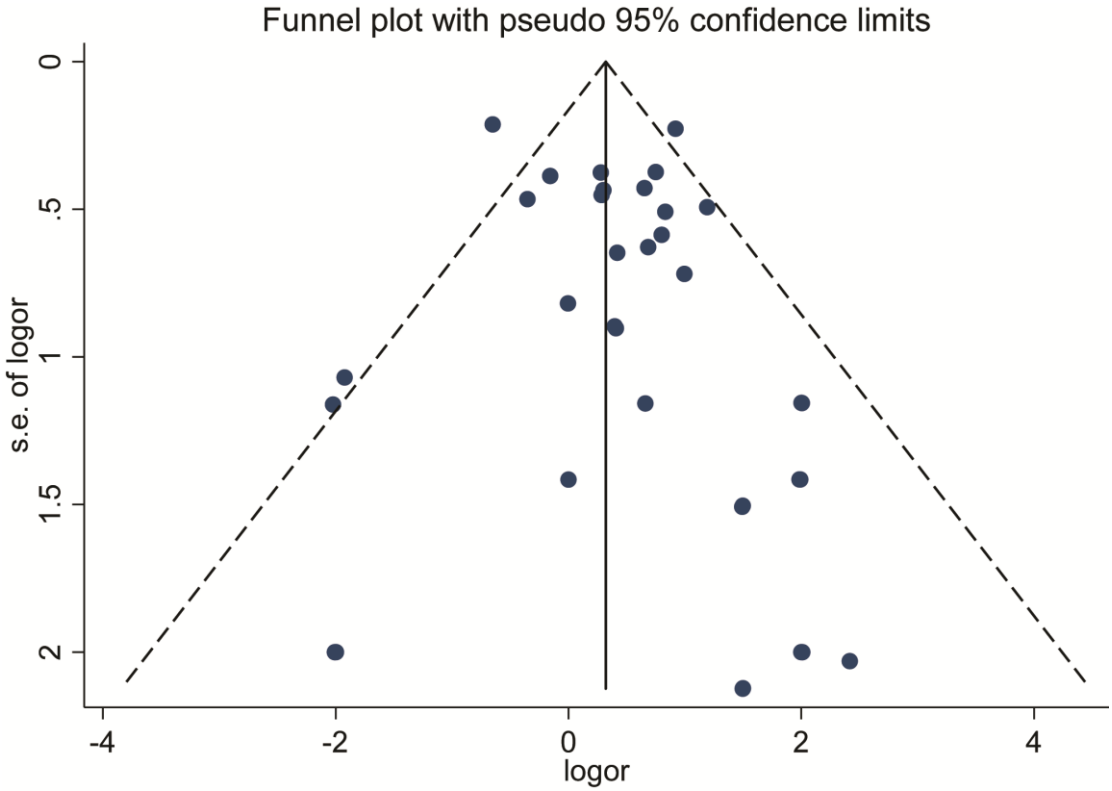
Supplementary Figure S17. Risk of serious-grade type 1 diabetes following the use of ICIs versus control treatment, stratified by the type of ICIs. (anti-PD-1 v anti-PD-L1 v anti-CTLA-4 v ICI combination)



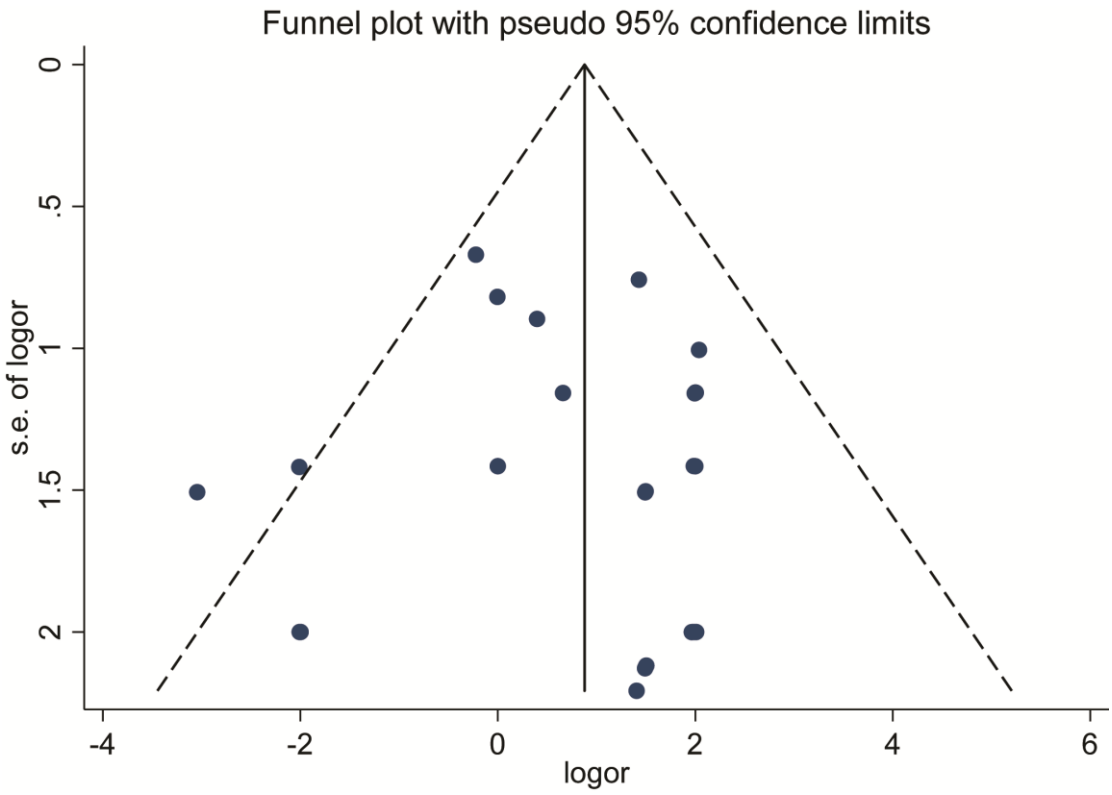
Supplementary Figure S18. Funnel plot of meta-analysis for diabetes mellitus



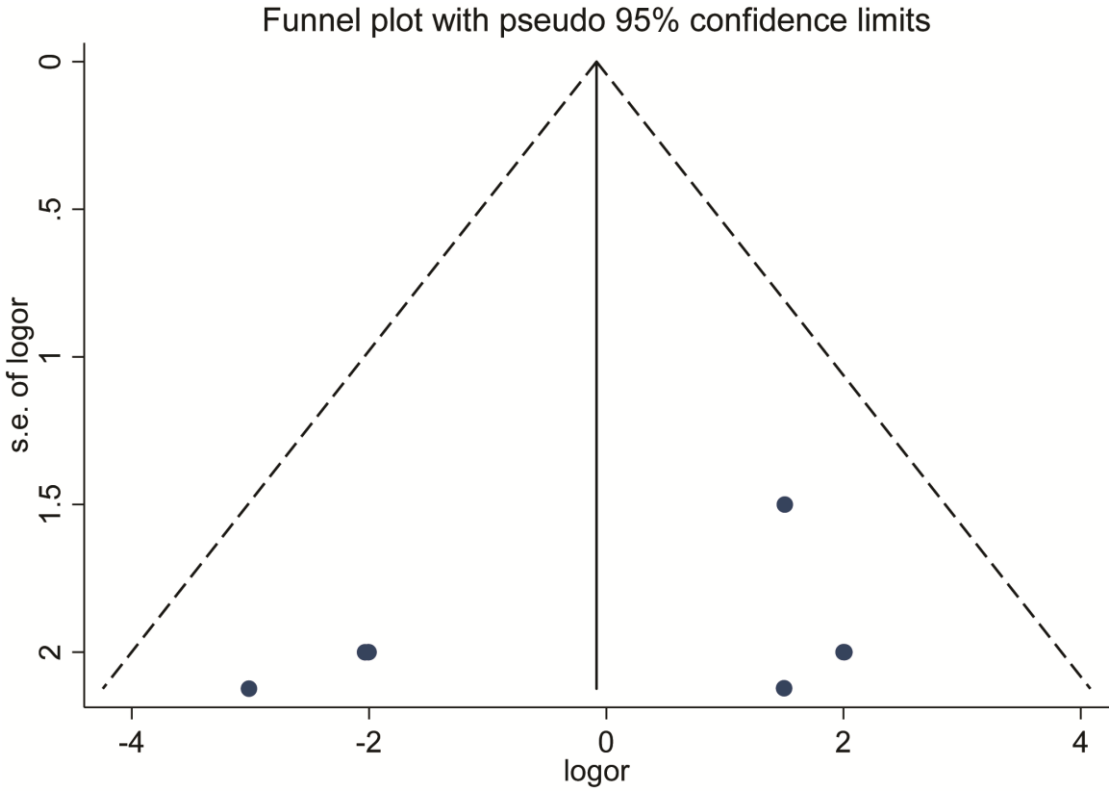
Supplementary Figure S19. Funnel plot of meta-analysis for all-grade hyperglycemia



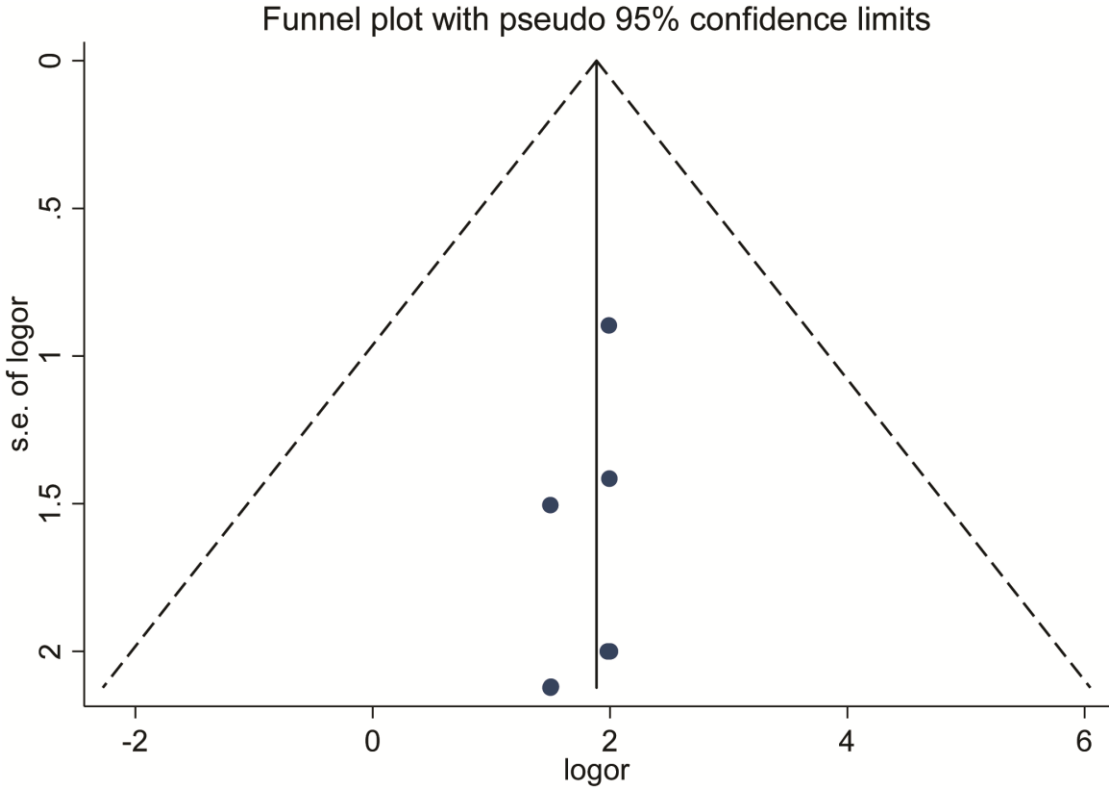
Supplementary Figure S20. Funnel plot of meta-analysis for serious-grade hyperglycemia



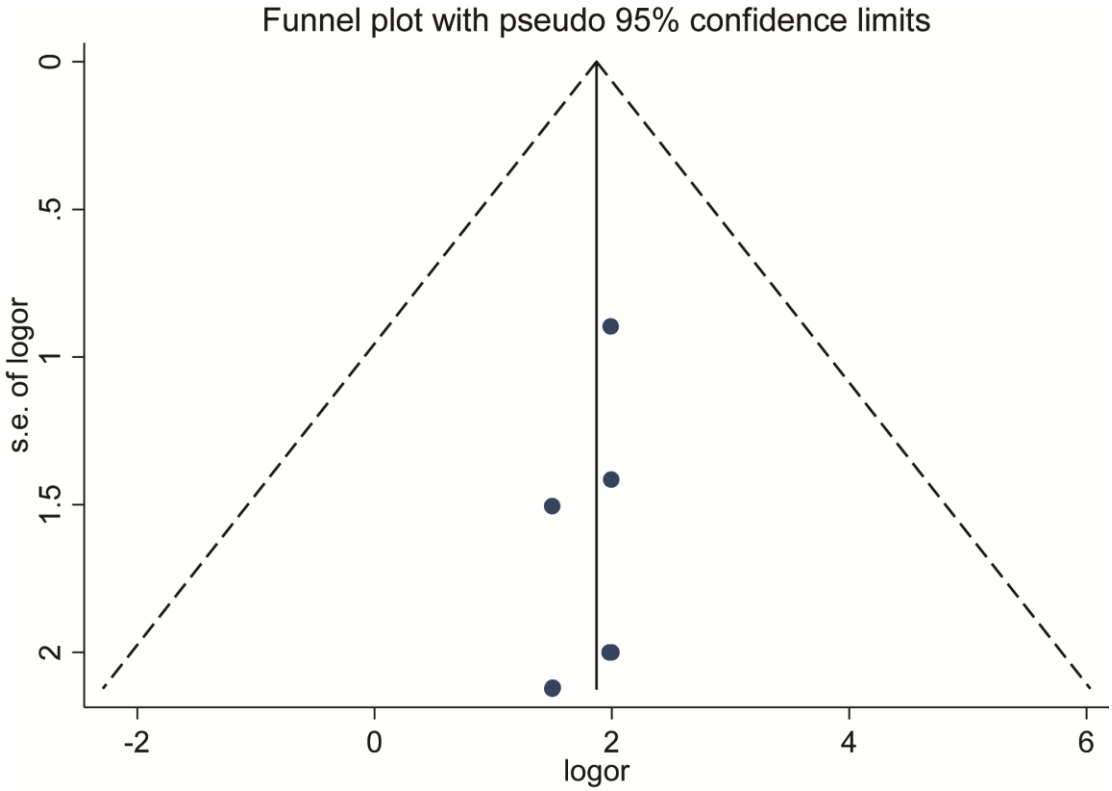
Supplementary Figure S21. Funnel plot of meta-analysis for type 2 diabetes



Supplementary Figure S22. Funnel plot of meta-analysis for all-grade type 1 diabetes



Supplementary Figure S23. Funnel plot of meta-analysis for serious-grade type 1 diabetes



Reference:

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Chih-Hsin Yang, J., Shepherd, F.A., Kim, D.W., Lee, G.W., Lee, J.S., Chang, G.C., et al. (2019). Osimertinib Plus Durvalumab versus Osimertinib Monotherapy in EGFR T790M-Positive NSCLC following Previous EGFR TKI Therapy: CAURAL Brief Report. *J Thorac Oncol* 14(5)**,** 933-939. doi: 10.1016/j.jtho.2019.02.001.

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Eggermont, A.M., Chiarion-Sileni, V., Grob, J.J., Dummer, R., Wolchok, J.D., Schmidt, H., et al. (2015). Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial. *Lancet Oncol* 16(5)**,** 522-530. doi: 10.1016/S1470-2045(15)70122-1.

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