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eTable 1. Search terms used in Embase via Ovid.

|  |  |
| --- | --- |
| 1 | gefitinib.ti,ab,kw |
| 2 | erlotinib.ti,ab,kw |
| 3 | osimertinib.ti,ab,kw |
| 4 | AZD9291.ti,ab,kw |
| 5 | necitumumab.ti,ab,kw |
| 6 | afatinib.ti,ab,kw |
| 7 | lorlatinib.ti,ab,kw |
| 8 | brigatinib.ti,ab,kw |
| 9 | crizotinib.ti,ab,kw |
| 10 | dabrafenib.ti,ab,kw |
| 11 | trametinib.ti,ab,kw |
| 12 | nivolumab.ti,ab,kw |
| 13 | pembrolizumab.ti,ab,kw |
| 14 | tislelizumab.ti,ab,kw |
| 15 | sintilimab.ti,ab,kw |
| 16 | furmonertinib.ti,ab,kw |
| 17 | atezolizumab.ti,ab,kw |
| 18 | durvalumab.ti,ab,kw |
| 19 | ramucirumab.ti,ab,kw |
| 20 | bevacizumab.ti,ab,kw |
| 21 | dacomitinib.ti,ab,kw |
| 22 | capmatinib.ti,ab,kw |
| 23 | savolitinib.ti,ab,kw |
| 24 | selpercatinib.ti,ab,kw |
| 25 | pralsetinib.ti,ab,kw |
| 26 | BLU-66.ti,ab,kw |
| 27 | pralsetinib.ti,ab,kw |
| 28 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 |
| 29 | ‘clinical trial’.ti,ab,kw |
| 30 | ‘random\* control\* trial’.ti,ab,kw |
| 31 | 29 or 30 |
| 32 | 28 and 31 |
| 33 | safety.mp. |
| 34 | toxicit\*.mp. |
| 35 | adverse.mp. |
| 36 | 33 or 34 or 35 |
| 37 | 32 and 36 |
| 38 | lung.mp. |
| 39 | pulmonary.mp. |
| 42 | 38 or 39 |
| 43 | 37 and 40 |

Note: This strategy will be adapted to identify trials in other electronic databases.

eTable 2. General characteristics of studies included in meta-analysis.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Region** | **Registration** | **Population** | **Targeted therapy group** | | | | **Control Group** | | | | **Follow-up** | **Outcomes** |
| **Sample** | **Male** | **Age** | **Regimen** | **Sample** | **Male** | **Age** | **Regimen** |
| Ahn[1] | 2012 | Korea | NCT00409006 | Advanced NSCLC | 39 | 9 | 56 | pemetrexed plus cisplatin followed by gefitinib | 31 | 6 | 56 | pemetrexed plus cisplatin | 40m | ⑤/⑥ |
| Argiris[2] | 2017 | Greece | NCT00955305 | Advanced non-squamous NSCLC | 75 | 35 | - | CPB plus cixutumumab 6 mg/kg i.v. weekly | 78 | 38 | - | CPB (paclitaxel + carboplatin + bevacizumab) | 48m | ②/③ |
| Ciuleanu[3] | 2018 | Romania | NCT00981058 | Stage IV Squamous NSCLC | 261 | 211 | 62 | gemcitabine and cisplatin with necitumumab | 215 | 191 | 62 | gemcitabine and cisplatin | 39m | ⑪ |
| Ciuleanu[4] | 2013 | Romania | NCT00531960 | Advanced non-squamous NSCLC | 61 | 36 | 58 | bevacizumab plus chemotherapy (emcitabine/cisplatin or carboplatin/paclitaxel) | 63 | 37 | 61 | bevacizumab plus erlotinib | 13m | ② |
| Crinò[5] | 2008 | Italy | NCT00256711 | Advanced NSCLC | 97 | 75 | 74 | gefitinib (250 mg/d orally) | 99 | 73 | 74 | vinorelbine (30 mg/m2 infusion on days 1 and 8 of a 21-day cycle) | 20m | ⑥ |
| Doebele[6] | 2015 | USA | NCT01160744 | Nonsquamous advanced/metastatic NSCLC | 71 | 45 | - | pemetrexed and carboplatin (or cisplatin) plus pemetrexed and carboplatin (or cisplatin) | 69 | 36 | - | ramucirumab (10 mg/kg) plus pemetrexed and carboplatin (or cisplatin) | 20m | ② |
| Du[7] | 2013 | China | - | NSCLC | 36 | 19 | - | bevacizumab (300 mg) with cisplatin (30 mg) | 34 | 19 | - | cisplatin (30 mg) | 10m | ② |
| Ellis[8] | 2014 | Canada | NCT01000025 | Advanced or metastatic NSCLC | 480 | 244 | 63.5 | three previous lines of chemotherapy followed by oral dacomitinib 45 mg once-daily | 240 | 120 | 65.5 | three previous lines of chemotherapy followed by placebo | 32m | ①/④/⑥ |
| Gaafar[9] | 2011 | Egypt | NCT00091156 | Advanced NSCLC | 86 | 67 | 61 | four cycles of platinum-based chemotherapy followed by gefitinib 250 mg/d | 87 | 66 | 62 | four cycles of platinum-based chemotherapy followed by placebo | 60m | ⑤/⑥/⑦/⑨ |
| Garon[10] | 2014 | USA | NCT01168973 | Stage IV NSCLC | 628 | 419 | 62 | docetaxel 75 mg/m² and ramucirumab (10 mg/kg) | 625 | 415 | 61 | docetaxel 75 mg/m² and placebo | 36m | ①/②/④ |
| Goldman[11] | 2020 | USA | NCT02152631 | Stage IV NSCLC | 270 | 163 | 62 | platinum-based chemotherapy followed by 200 mg abemaciclib twice daily | 183 | 109 | 63 | platinum-based chemotherapy followed by 150 mg erlotinib once daily | 33m | ①/④/⑤ |
| Herbst[12] | 2018 | USA | NCT00946712 | Advanced NSCLC | 656 | 385 | 63 | cetuximab (250 mg/m² weekly) plus PCB | 657 | 359 | 63 | PCB (paclitaxel+carboplatin/carboplatin+ bevacizumab) | 60m | ②/⑤/⑥/⑦/⑧/⑪ |
| Johnson[13] | 2013 | USA | NCT00257608 | Advanced NSCLC | 373 | 196 | 64 | four cycles of chemotherapy and bevacizumab plus placebo | 370 | 193 | 64 | four cycles of chemotherapy and bevacizumab plus erlotinib (150 mg per day) | 24m | ①/②/④ |
| Karayama[14] | 2016 | Japan | - | Advanced NSCLC | 55 | 39 | 66 | Pemetrexed 500 mg/m2 | 55 | 35 | 65 | Pemetrexed 500 mg/m2 + bevacizumab 15 mg/kg | 24m | ② |
| Kenmotsu[15] | 2022 | Japan | NCT04181060 | Non-squamous NSCLC | 61 | 23 | 66 | osimertinib (80 mg daily) monotherapy | 61 | 24 | 67 | osimertinib (80 mg daily) plus bevacizumab (15 mg/kg every 3 weeks) | 36m | ②/③/④ |
| Lara[16] | 2016 | USA | - | Advanced NSCLC | 33 | 14 | 74.9 | 150 mg of erlotinib orally daily | 26 | 10 | 70.8 | four cycles of carboplatin and paclitaxel followed by 150 mg of erlotinib orally | 60m | ④ |
| Leighl[17] | 2017 | Canada | - | NSCLC | 44 | 14 | 61.5 | linsitinib 150 mg twice daily plus erlotinib 150 mg once daily | 44 | 12 | 57.5 | placebo plus erlotinib 150 mg once daily | 20m | ④ |
| Lynch[18] | 2009 | USA | - | Advanced NSCLC | 25 | 13 | 64 | erlotinib alone | 25 | 11 | 62 | erlotinib plus bortezomib | 20m | ⑥ |
| Miller[19] | 2012 | USA | NCT00656136 | Advanced metastatic NSCLC | 390 | 159 | 58 | chemotherapy followed by afatinib 50mg/d | 195 | 78 | 59 | chemotherapy followed by placebo | 24m | ⑥ |
| Nakagawa[20] | 2019 | Japa | NCT02411448 | Advanced NSCLC | 224 | 83 | 65 | oral erlotinib (150 mg/day) plus intravenous ramucirumab (10 mg/kg) | 225 | 83 | 64 | oral erlotinib (150 mg/day) plus placebo | 36m | ② |
| Niho[21] | 2012 | Japa | - | Advanced non-squamous NSCLC | 59 | 38 | 60 | carboplatin-paclitaxel | 121 | 77 | 61 | bevacizumab plus carboplatin-paclitaxel | 36m | ⑤ |
| Paz-Ares[22] | 2015 | Spain | NCT00982111 | Stage IV non-squamous NSCLC | 315 | 214 | 61 | 800mg necitumumab was continued after the end of chemotherapy | 318 | 210 | 60 | chemotherapy (pemetrexed +cisplatin) | 36m | ⑪ |
| Paz-Ares[23] | 2017 | Spain | NCT01168973 | Advanced NSCLC | 628 | - | - | ramucirumab (10 mg/kg) plus docetaxel (75 mg/m2) | 625 | - | - | placebo plus docetaxel | 36m | ①/②/④ |
| Pérol[24] | 2012 | France | - | Advanced NSCLC | 154 | 113 | 57.9 | four cycles of cisplatin-gemcitabine followed by gemcitabine 1250 mg/m2 | 155 | 113 | 26.4 | four cycles of cisplatin-gemcitabine followed by daily erlotinib 150 mg/day | 44m | ①/④ |
| Pujol[25] | 2015 | France | NCT00930891 | Extensive small-cell lung cancer | 37 | 26 | 60.1 | chemotherapy alone | 37 | 25 | 61.2 | chemotherapy plus bevacizumab 7.5mg/kg | 30m | ②/④ |
| Ramlau[26] | 2012 | Poland | NCT00532155 | Advanced or metastatic NSCLC | 456 | 305 | 59.6 | aflibercept 6 mg/kg combination with docetaxel 75 mg/m2 | 457 | 300 | 59.6 | placebo combination with docetaxel 75 mg/m2 | 36m | ② |
| Reck[27] | 2016 | Germany | NCT00981058 | Stage IV squamous NSCLC | 545 | 450 | 62 | necitumumab (800 mg) plus gemcitabine-cisplatin | 548 | 458 | 62 | gemcitabine-cisplatin | 32m | ④/⑪ |
| Reck[28] | 2009 | Germany | - | Non-squamous NSCLC | 696 | 223 | 57 | bevacizumab 7.5 mg/kg plus cisplatin/gemcitabine | 347 | 223 | 59 | placebo plus cisplatin/gemcitabine | 18m | ② |
| Sandler[29] | 2006 | USA | NCT00021060 | NSCLC | 417 | 210 | - | bevacizumab plus paclitaxel–carboplatin | 433 | 253 | - | paclitaxel–carboplatin | 42m | ②/⑤ |
| Scagliotti[30] | 2012 | Italy | - | Advanced NSCLC | 480 | 297 | 61 | previously treated with one to two chemotherapies followed by sunitinib 37.5 mg/d plus erlotinib 150 mg/d | 480 | 284 | 61 | previously treated with one to two chemotherapies followed by placebo plus erlotinib 150 mg/d | 30m | ④/⑤/⑥/⑦/⑧/⑨/⑩/⑪ |
| Schuler[31] | 2016 | Germany | NCT01121393 | NSCLC | 186 | 62 | 63 | afatinib 40 mg orally once daily | 97 | 30 | 60.5 | platinum-based chemotherapy | 45m | ⑤/⑥ |
| Sequist[32] | 2011 | USA | NCT00777309 | NSCLC | 84 | 51 | 64 | oral erlotinib (150 mg daily) plus oral tivantinib (360 mg twice daily) | 83 | 49 | 62 | erlotinib plus placebo | 20m | ④ |
| Seto[33] | 2014 | Japan | - | Non-squamous NSCLC | 75 | 30 | 67 | erlotinib 150 mg/day plus bevacizumab 15 mg/kg every 3 weeks | 77 | 26 | 67 | erlotinib 150 mg/day monotherapy | 28m | ② |
| Shaw[34] | 2017 | USA | NCT01828112 | NSCLC | 115 | 47 | 54 | oral ceritinib 750 mg per day fasted (in 21-day treatment cycles) | 116 | 55 | 54 | chemotherapy (intravenous pemetrexed 500 mg/m² or docetaxel 75 mg/m², every 21 days) | 24m | ④ |
| Shi[35] | 2017 | China | NCT01719536 | Advanced EGFR mutation-positive lung adenocarcinoma | 148 | 43 | 56 | oral icotinib | 137 | 42 | 56 | chemotherapy (cisplatin + pemetrexed) | 24m | ⑥ |
| Socinski[36] | 2010 | USA | NR | NSCLC | 30 | 16 | 65 | sunitinib plus BCP | 26 | 14 | 66 | BCP (bevacizumab plus carboplatin plus paclitaxel) | 12m | ⑤ |
| Spigel[37] | 2018 | USA | NR | Advanced NSCLC | 127 | 66 | 66 | erlotinib (150 mg by mouth daily) plus pazopanib (600 mg by mouth daily) | 65 | 38 | 67 | erlotinib (150 mg by mouth daily) plus placebo | 45m | ② |
| Spigel[38] | 2013 | USA | NCT00854308 | Advanced NSCLC | 69 | 40 | 64 | onartuzumab plus erlotinib | 68 | 42 | 63 | placebo plus erlotinib | 18m | ③ |
| Spigel[39] | 2017 | USA | NCT01769391 | Stage IV Squamous NSCLC | 110 | 87 | 66 | necitumumab plus chemotherapy (paclitaxel + carboplatin) | 57 | 44 | 65 | chemotherapy (paclitaxel + carboplatin) | 24m | ⑪ |
| Spigel[40] | 2017 | USA | NCT00609804 | Advanced NSCLC | 24 | 8 | 67 | erlotinib and sorafenib (400 mg orally twice daily) | 28 | 10 | 63 | sorafenib alone | 48m | ③/⑤/⑥ |
| Steendam[41] | 2021 | Netherlands | NCT0277500 | Relapsed non-squamous NSCLC | 22 | 11 | - | docetaxel 75 mg/m2 plus erlotinib 150 mg/day | 23 | 8 | - | docetaxel 75 mg/m2 intravenously on day 1 every 21 days | 12m | ①/④ |
| Stephenson[42] | 2014 | USA | NCT00732810 | NSCLC | 17 | 10 | 63.2 | intravenous (IV) dinaciclib (50 mg/m2) | 33 | 21 | 63.3 | oral erlotinib (150 mg) | 22m | ⑤ |
| Stinchcombe[43] | 2019 | USA | NCT01532089 | Advanced EGFR-Mutant NSCLC | 43 | 12 | 65 | erlotinib plus bevacizumab | 45 | 14 | 63 | erlotinib alone | 60m | ② |
| Tada[44] | 2022 | Japan | UMIN000006252 | Resected Stage II-IIIA NSCLC | 116 | 44 | 64 | gefitinib (250 mg once daily) | 116 | 45 | 64 | cisplatin (80 mg/m2) plus vinorelbine (25 mg/m2) | 108m | ④/⑤/⑥ |
| Takeda[45] | 2010 | Japan | UMINC000000035 | Advanced NSCLC | 298 | 191 | 63 | platinum-doublet chemotherapy | 300 | 192 | 62 | chemotherapy followed by gefitinib 250 mg orally once daily | 60m | ④ |
| Takeda[46] | 2016 | Japan | NCT01351415 | Advanced non-squamous NSCLC | 50 | 33 | 64.5 | bevacizumab plus docetaxel | 50 | 32 | 67 | docetaxel | 30m | ②/④ |
| Thatcher[47] | 2015 | UK | NCT00981058 | Stage IV squamous NSCLC | 545 | 450 | 62 | necitumumab plus chemotherapy (gemcitabine and cisplastin) | 548 | 458 | 62 | chemotherapy (gemcitabine and cisplastin) | 40m | ⑪ |
| von Pawel[48] | 2018 | Germany | NCT01366131 | Non-squamous NSCLC | 52 | - | - | placebo plus bevacizumab (15 mg/kg) and carboplatin/paclitaxel | 52 | - | - | parsatuzumab (600 mg) plus bevacizumab (15 mg/kg) and carboplatin/paclitaxel | 15m | ② |
| Wakelee[49] | 2017 | USA | NCT01496742 | Advanced non-Squamous NSCLC | 69 | 47 | 60 | onartuzumab plus paclitaxel/platinum/bevacizumab | 70 | 34 | 60.5 | placebo plus paclitaxel/platinum/bevacizumab | 16m | ⑤ |
| 59 | 33 | 66 | onartuzumab plus platinum/pemetrexed | 61 | 26 | 63 | placebo plus platinum/pemetrexed | 16m | ⑤/⑥ |
| Wakelee[50] | 2017 | USA | NCT00324805 | Resected NSCLC | 749 | 375 | 61 | chemotherapy alone | 752 | 371 | 61 | bevacizumab 15 mg/kg plus chemotherapy | 84m | ①/②/③/④/⑤/⑥/⑦/⑧/⑩/⑪ |
| Witta[51] | 2012 | USA | NR | Advanced NSCLC | 65 | 43 | 67 | erlotinib 150mg plus placebo | 67 | 39 | 66 | erlotinib 150 mg plus entinostat 10 mg | 30m | ⑥/⑩ |
| Wu[52] | 2018 | China | NCT01639001 | Advanced NSCLC | 104 | 50 | 48 | orally crizotinib 250 mg twice daily | 103 | 43 | 50 | chemotherapy (pemetrexed plus cisplatin or carboplatin) | 30m | ⑤ |
| Wu[53] | 2015 | China | NCT01342965 | NSCLC | 110 | 42 | 57.5 | oral erlotinib 150 mg once daily | 107 | 42 | 56 | chemotherapy (gemcitabine plus cisplatin) | 36m | ⑥ |
| Yoh[54] | 2016 | Japan | NCT01703091 | Stage IV NSCLC | 76 | 59 | 65.6 | ramucirumab 10 mg/kg followed by docetaxel | 81 | 62 | 64.9 | placebo followed by docetaxel | 30m | ①/②/④ |
| Yoshioka[55] | 2015 | Japan | NCT01377376 | Stage IIIB/IV non-squamous NSCLC | 153 | 102 | 63 | erlotinib plus placebo | 154 | 109 | 63 | erlotinib plus tivantinib | 28m | ⑩ |
| Zhong[56] | 2018 | China | NCT01405079 | Stage II-IIIA (N1-N2) EGFR-mutant NSCLC | 111 | 44 | 58 | geftinib (250 mg once daily) for 24 months | 111 | 45 | 60 | vinorelbine (25 mg/m²) plus cisplatin (75 mg/m²) | 60m | ⑥ |
| Zhou[57] | 2015 | China | NCT01364012 | Advanced or recurrent non-squamous NSCLC | 138 | 75 | 57 | bevacizumab 15 mg/kg plus carboplatin/paclitaxel | 138 | 77 | 56 | placebo plus carboplatin/paclitaxel | 36m | ② |

Outcomes: ①AKI; ②proteinuria; ③urinary tract infection; ④blood creatinine increased; ⑤hyponatraemia; ⑥hypokalaemia; ⑦hyperkalaemia; ⑧hypocalcaemia; ⑨hypercalcaemia; ⑩hypophosphatemia; ⑪hypomagnesaemia.

Abbreviations: NSCLC, non-small cell lung cancer.

eTable 3. Test results of the consistency in the network analysis for acute kidney injury.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Treatments | Direct Coef. | Std. Err. | Indirect Coef. | Std. Err. | Difference Coef. | Std. Err. | P>|z| | tau |
| Chemo vs EGFR+chemo | -0.7230 | 0.6543 | -1.5848 | 194.2210 | 0.8618 | 194.2221 | 0.9960 | 0.0000 |
| Chemo vs VEGF+chemo | 0.0109 | 0.2434 | -1.0995 | 489.3731 | 1.1104 | 489.3731 | 0.9980 | 0.0000 |
| EGFR+chemo vs EGFR+chemo | 2.0196 | 1.0491 | 0.2960 | 386.8185 | 1.7236 | 386.8223 | 0.9960 | 0.0000 |
| VEGF+chemo vs VEGF+EGFR+chemo | 1.6122 | 1.5510 | -0.6097 | 989.7853 | 2.2218 | 989.7881 | 0.9980 | 0.0000 |

Note: The targeted therapies were categorized based on the targeted molecules.

Abbreviations: chemo, chemotherapy.

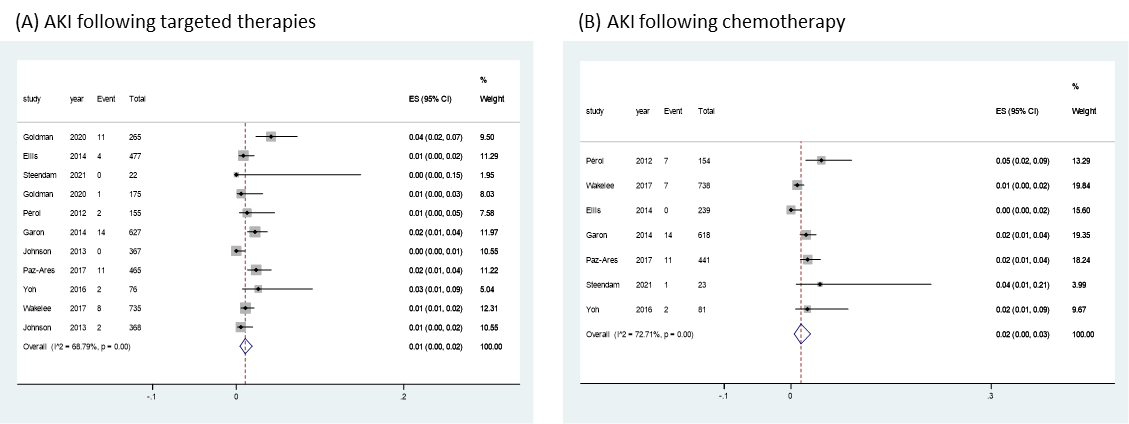
eTable 4. Test results of the consistency in the network analysis for proteinuria.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Treatments | Direct Coef. | Std. Err. | Indirect Coef. | Std. Err. | Difference Coef. | Std. Err. | P>|z| | tau |
| Chemo vs VEGF+chemo | 1.4314 | 0.1873 | 1.9280 | 1.5234 | -0.4966 | 1.5372 | 0.7470 | 0.2669 |
| Chemo vs VEGF+EGFR+chemo | 2.3447 | 1.4834 | 1.8448 | 0.4075 | 0.4999 | 1.5384 | 0.7450 | 0.2668 |
| EGFR vs VEGF+EGFR | 1.8650 | 0.3032 | 4.6712 | 87.9225 | -2.8062 | 87.9224 | 0.9750 | 0.2619 |
| VEGF+chemo vs VEGF+EGFR | 0.6931 | 0.9233 | -0.7597 | 43.4572 | 1.4528 | 43.4671 | 0.9730 | 0.2619 |
| VEGF+chemo vs VEGF+EGFR+chemo | 0.4134 | 0.3520 | 0.9130 | 1.4951 | -0.4996 | 1.5383 | 0.7450 | 0.2668 |

Note: The targeted therapies were categorized based on the targeted molecules.

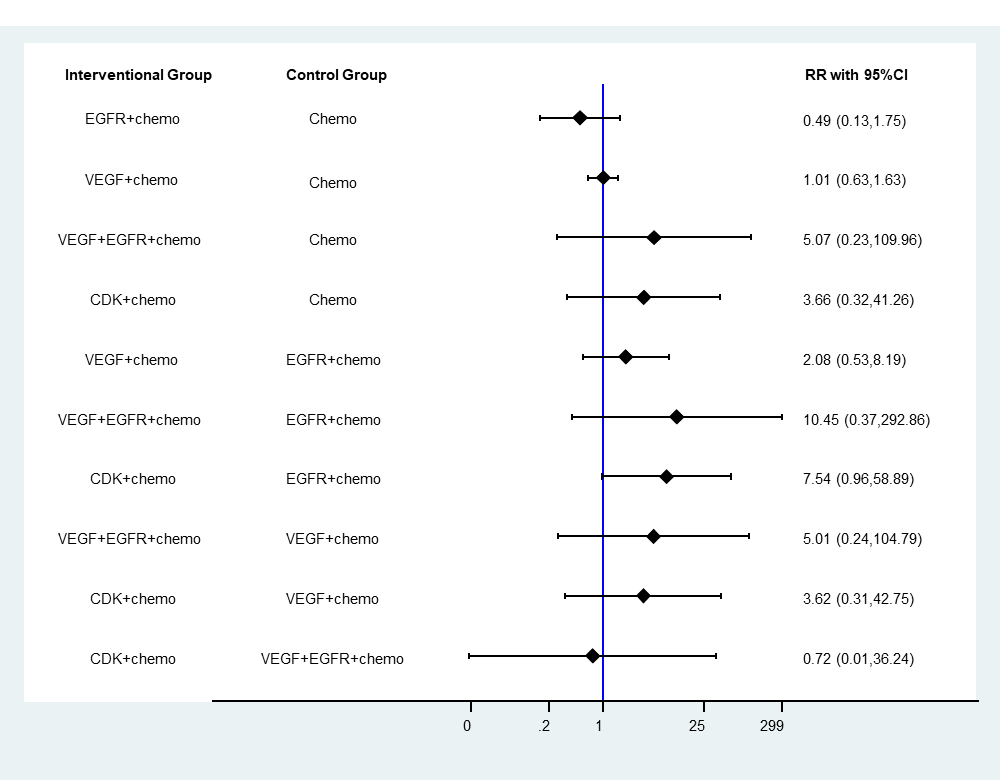
Abbreviations: chemo, chemotherapy.

eFigure 1. Pooled incidence of AKI following regimens containing targeted therapy and chemotherapy alone.



Note: The pooled incidence of AKI following targeted therapy (A) and chemotherapy alone (B) form the included studies that had reported the occurrence of AKI.

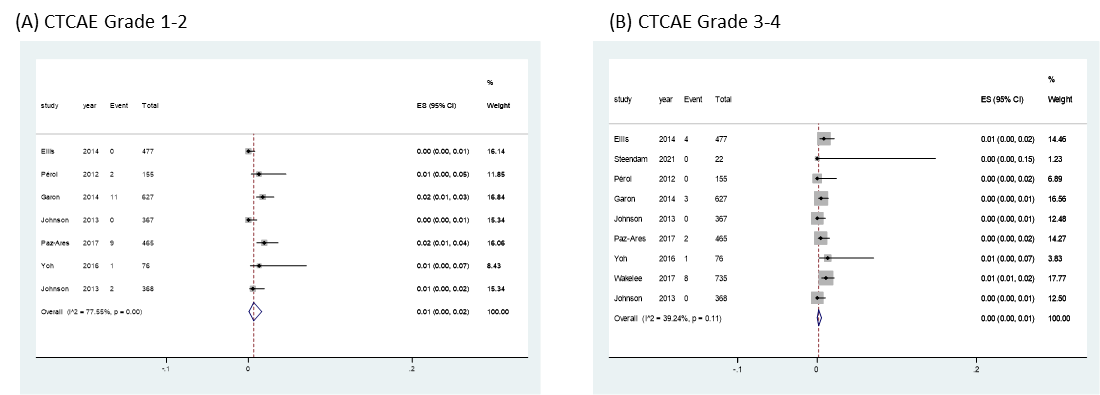
eFigure 2. Forest plots of direct comparisons of the risk of AKI following different treatments in lung cancer.



Note: The targeted therapies were categorized based on the targeted molecules.

Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; VEGF, vascular endothelial growth factor.

eFigure 3. Pooled incidence of AKI following targeted treatments in lung cancer based on CTCAE grade.



eFigure 4. Pooled incidence of increased serum creatinine following regimens containing targeted therapy and chemotherapy alone.



Note: The targeted therapies were categorized based on the targeted molecules.

Abbreviations: chemo, chemotherapy.

eFigure 5. Pooled incidence of increased serum creatinine following chemotherapy alone and different categories of targeted therapies.



Note: The targeted therapies were categorized based on the targeted molecules.

Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; IGF-R, insulin-like growth factor receptor; VEGF, vascular endothelial growth factor.

eFigure 6. Pooled incidence of increased serum creatinine (CTCAE grade 1-2) following targeted treatments in lung cancer.



Note: The targeted therapies were categorized based on the targeted molecules.

eFigure 7. Pooled incidence of increased serum creatinine (CTCAE grade 3-4) following targeted treatments in lung cancer.

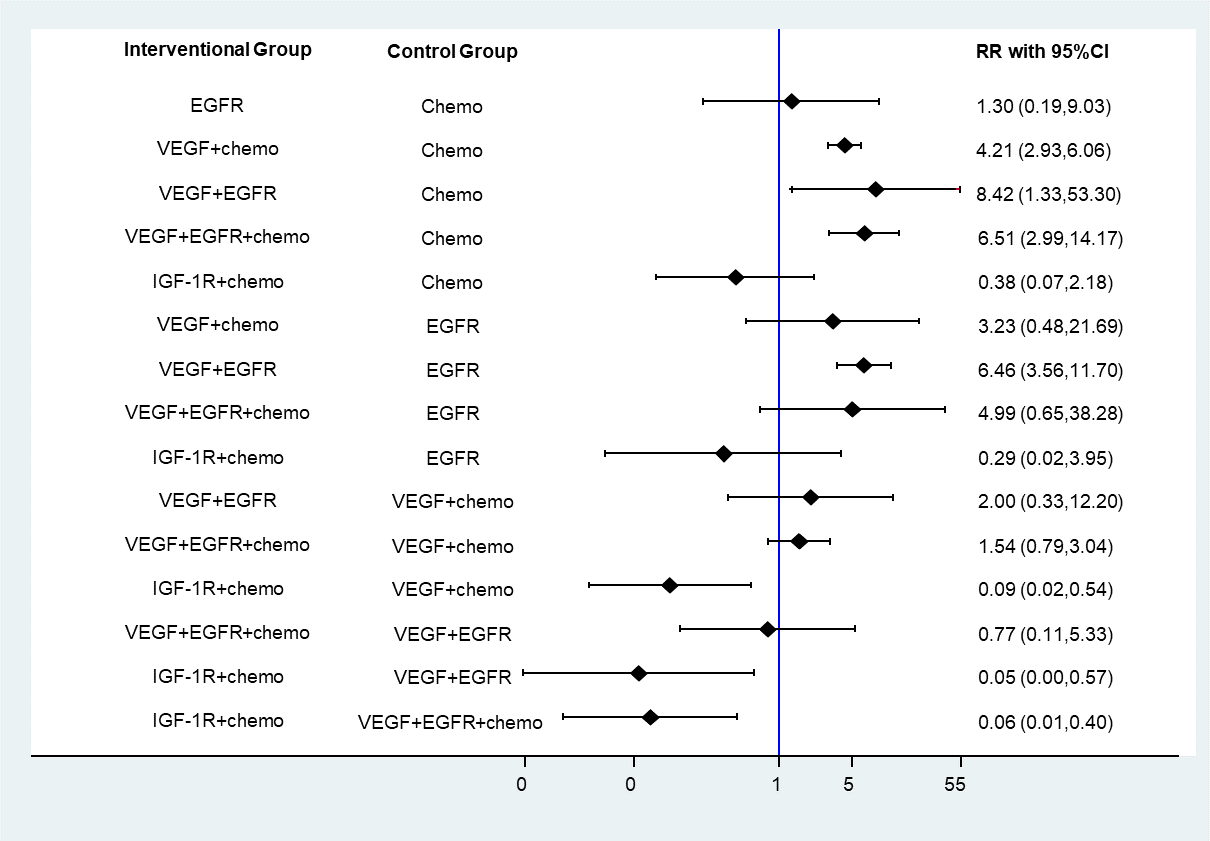


Note: The targeted therapies were categorized based on the targeted molecules.

eFigure 8. Pooled incidence of proteinuria following regimens containing targeted therapy.



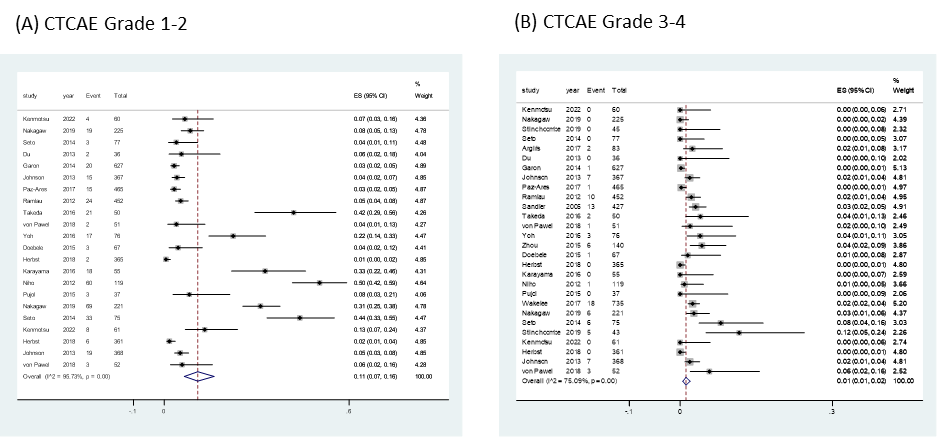
eFigure 9. Forest plots of direct comparisons of proteinuria for all treatments in lung cancer.



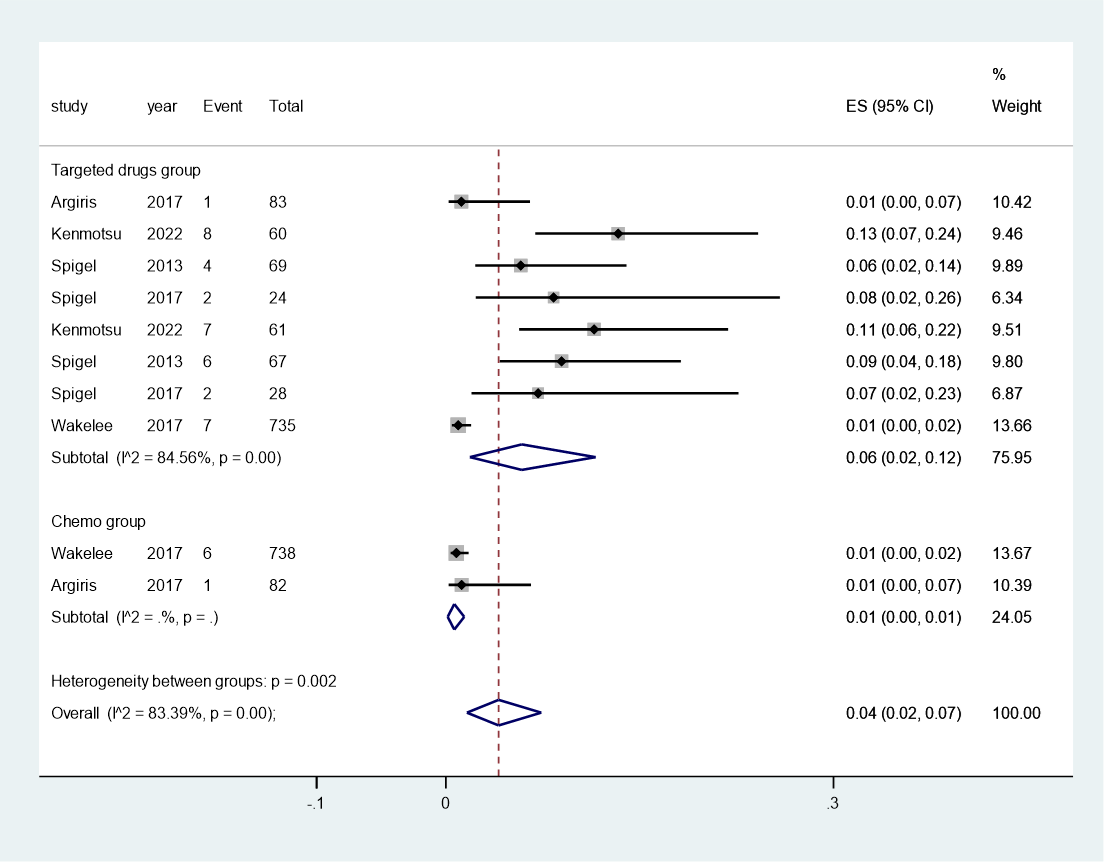
Note: The targeted therapies were categorized based on the targeted molecules.

Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; IGF-R, insulin-like growth factor receptor; VEGF, vascular endothelial growth factor.

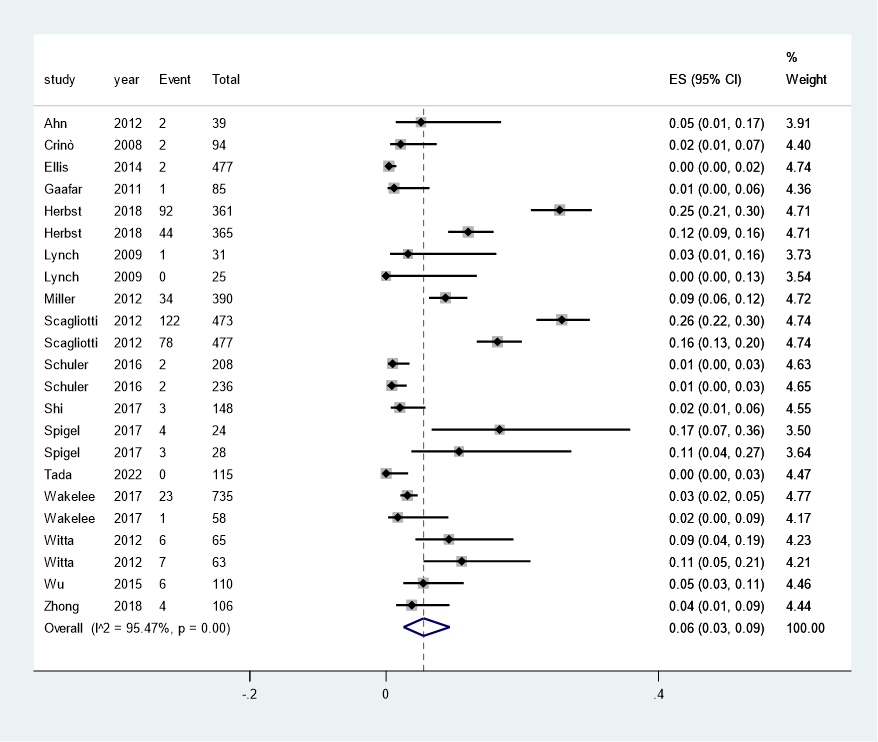
eFigure 10. Pooled incidence of proteinuria following targeted treatments in lung cancer based on CTCAE grade.



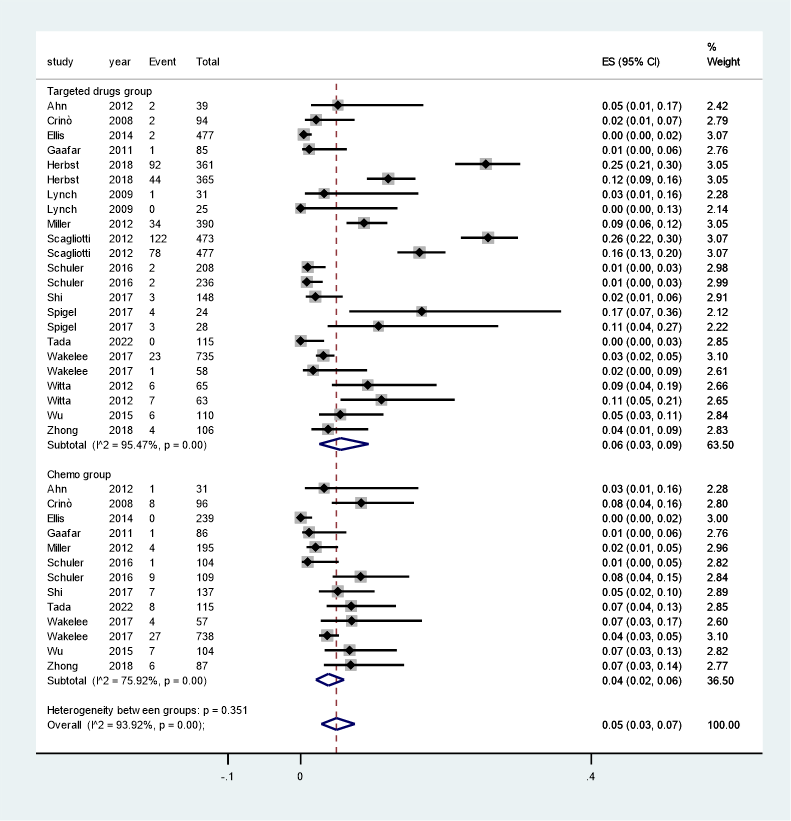
eFigure 11. Pooled incidence of UTI following targeted treatments and chemotherapy alone in lung cancer.



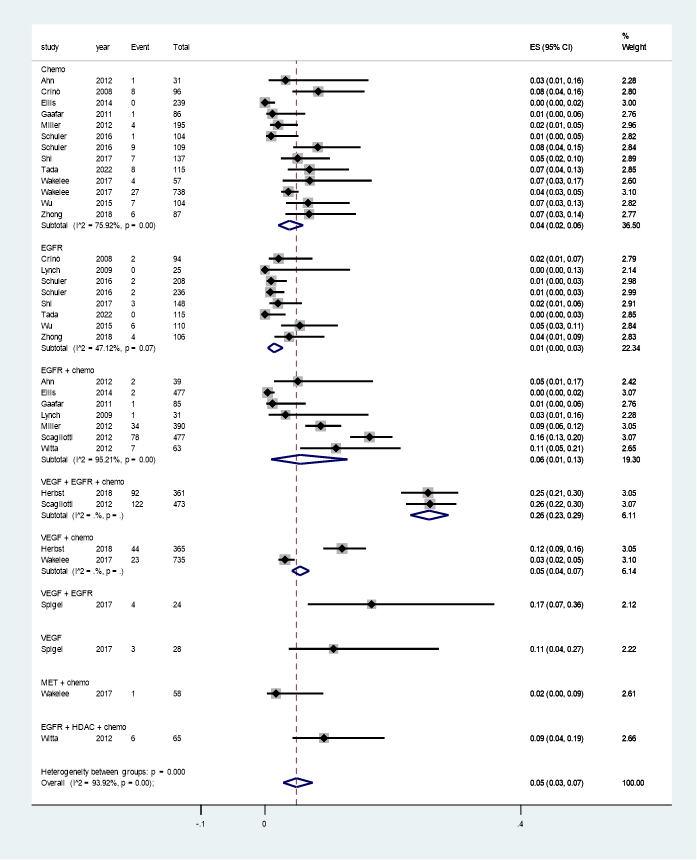
eFigure 12. Pooled incidence of hypokalemia following targeted treatments in lung cancer.



eFigure 13. Pooled incidence of hypokalemia following targeted treatments and chemotherapy alone in lung cancer.

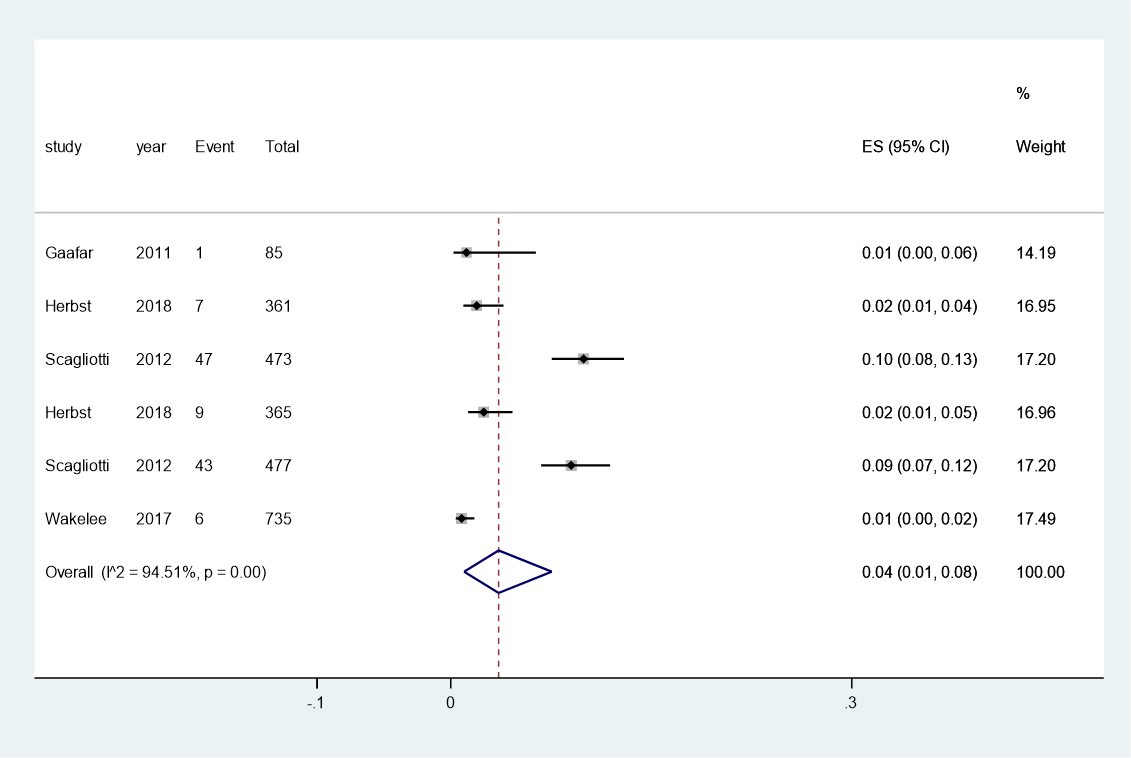


eFigure 14. Pooled incidence of hypokalemia following different categories of targeted treatments and chemotherapy alone in lung cancer.

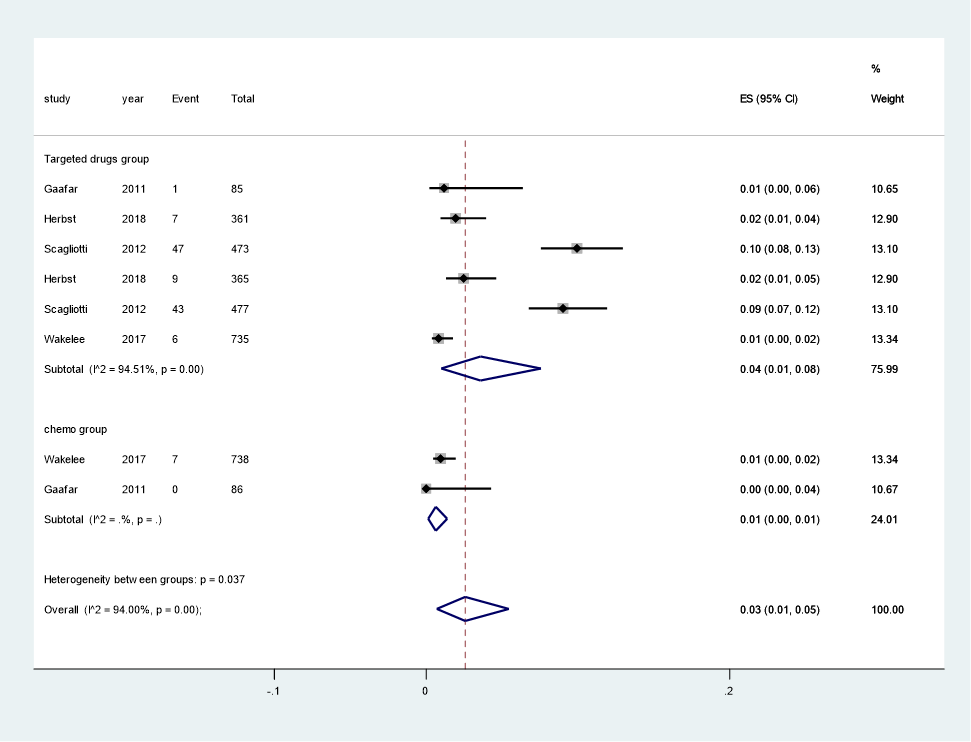


Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; HDAC, histone deacetylase; Met, hepatocyte growth factor receptor; VEGF, vascular endothelial growth factor.

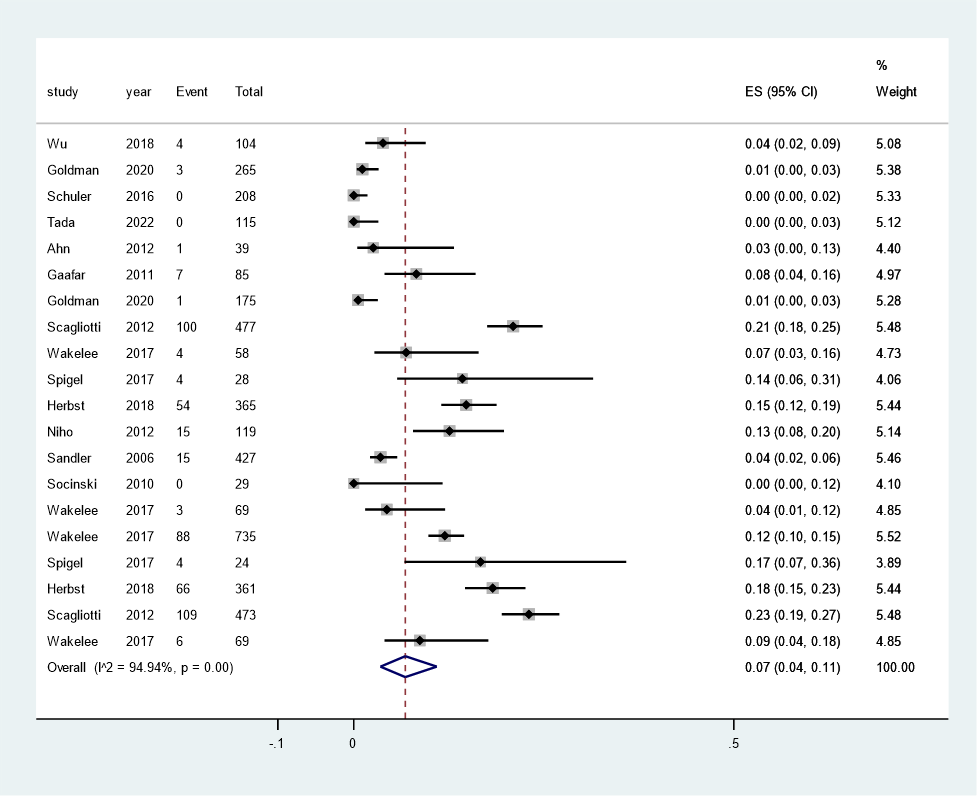
eFigure 15. Pooled incidence of hyperkalemia following targeted treatments in lung cancer.



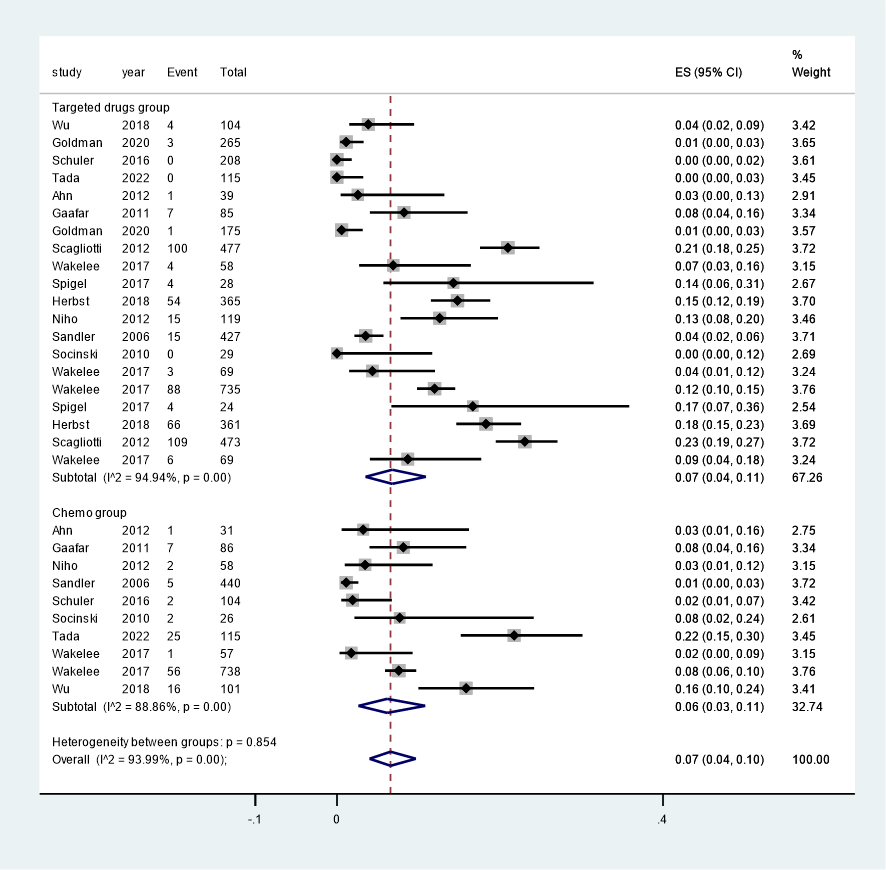
eFigure 16. Pooled incidence of hyperkalemia following targeted treatments and chemotherapy alone in lung cancer.



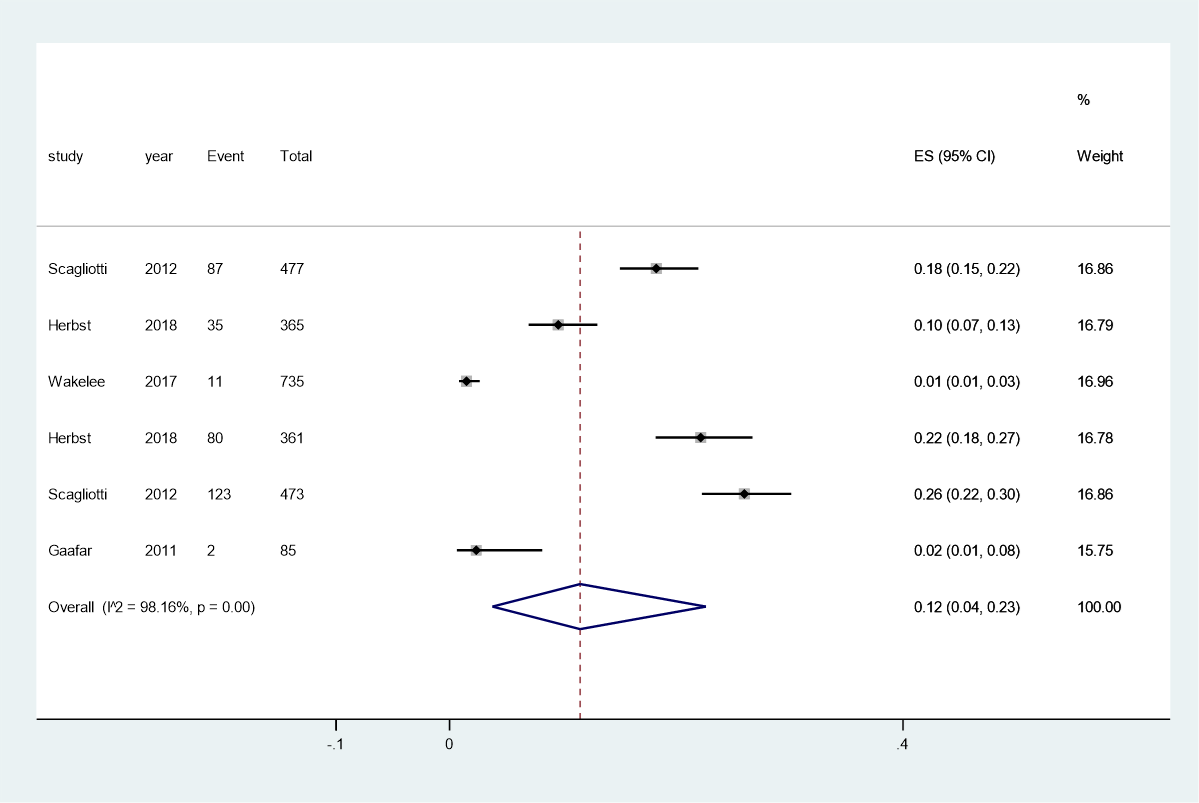
eFigure 17. Pooled incidence of hyponatremia following targeted treatments in lung cancer.



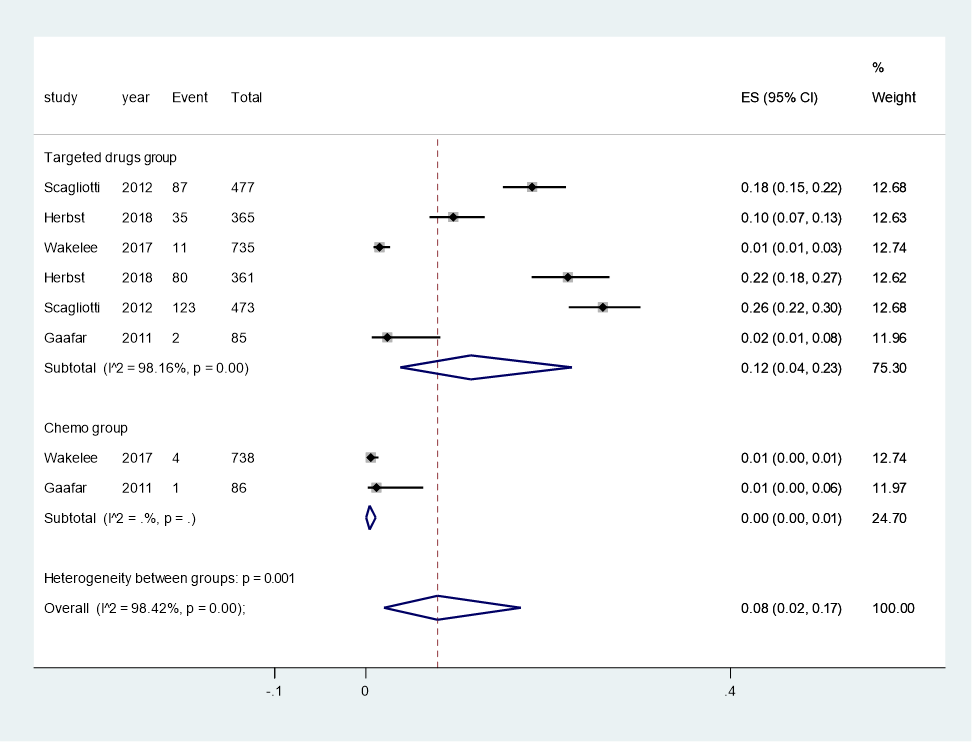
eFigure 18. Pooled incidence of hyponatremia following targeted treatments and chemotherapy alone in lung cancer.



eFigure 19. Pooled incidence of hypocalcemia following targeted treatments in lung cancer.



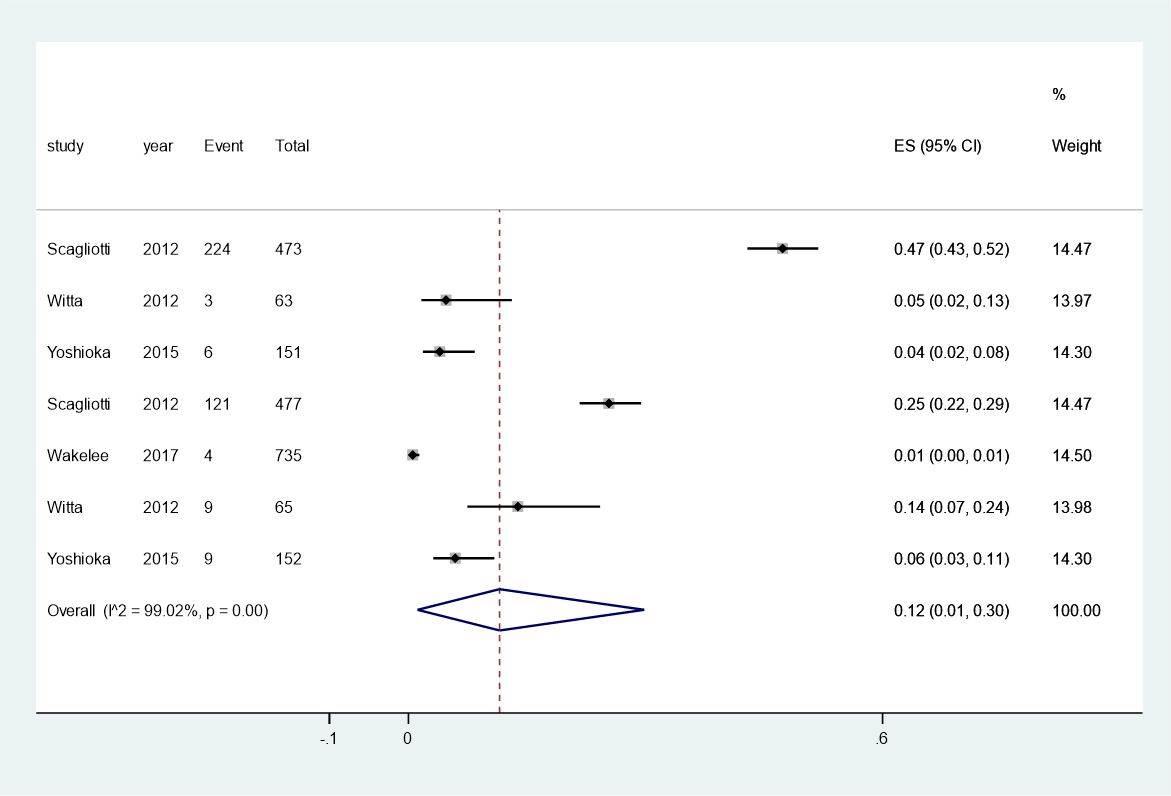
eFigure 20. Pooled incidence of hypocalcemia following targeted treatments and chemotherapy alone in lung cancer.



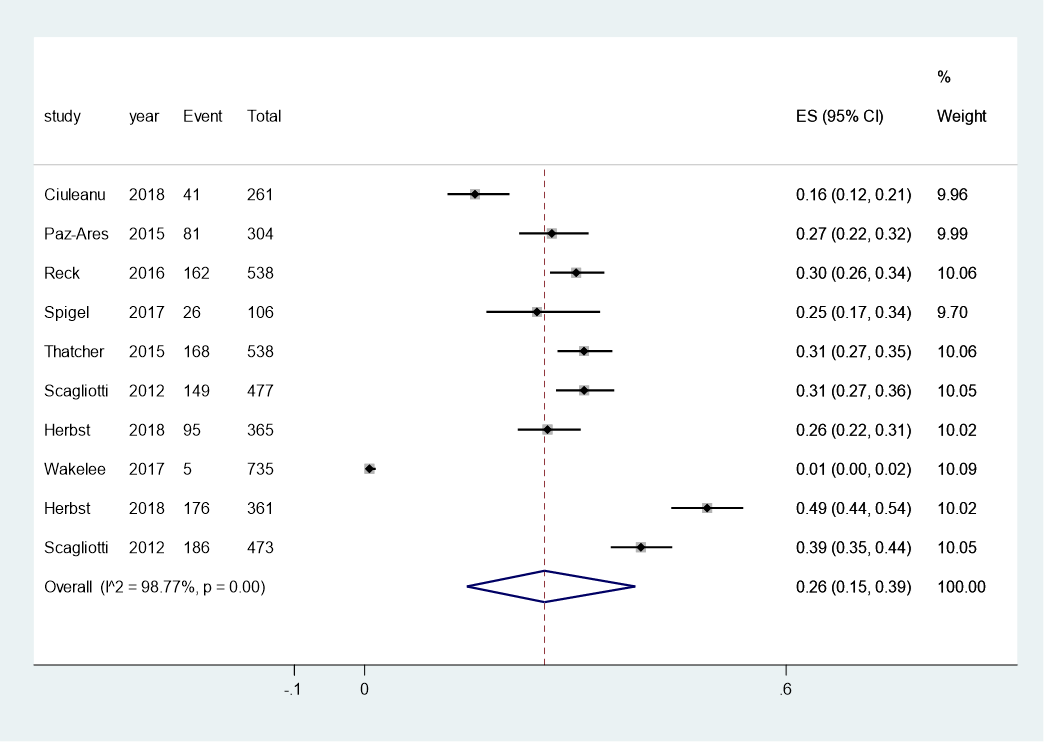
eFigure 21. Pooled incidence of hypercalcemia following targeted treatments in lung cancer.



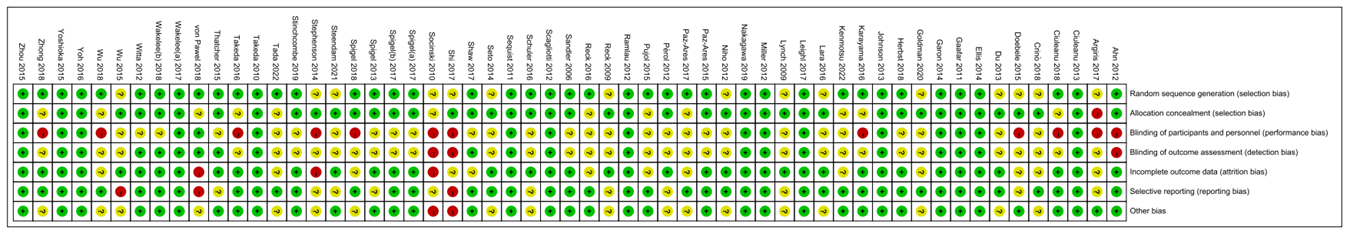
eFigure 22. Pooled incidence of hypophosphatemia following targeted treatments in lung cancer.



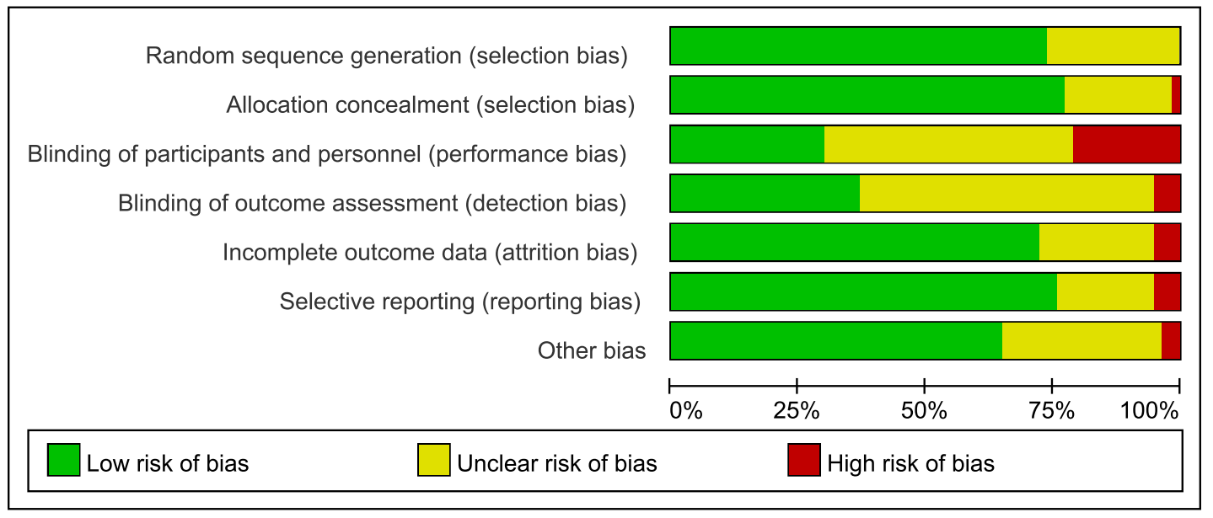
eFigure 23. Pooled incidence of hypomagnesemia following targeted treatments in lung cancer.



eFigure 24. Risk of bias assessment of individual studies using the 7-item Cochrane criteria.



eFigure 25. Summary graph of the risk of bias assessment of included studies using the Cochrane criteria.



eFigure 26. Comparison adjusted funnel plot for direct comparisons of AKI following targeted therapies in lung cancer.



Note: The treatments are as follows: A: Chemo; B: EGFR + chemo; C: VEGF + chemo; D: VEGF + EGFR + chemo; E: CDK + chemo.

Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; VEGF, vascular endothelial growth factor.

eFigure 27. Funnel plot for increased serum Cr following targeted therapies in lung cancer.



eFigure 28. Comparison adjusted funnel plot for direct comparisons of proteinuria following targeted therapies in lung cancer.



Note: The treatments are as follows: A: chemo; B: EGFR; C: VEGF+chemo; D: VEGF+EGFR; E: VEGF+EGFR+chemo; F: IGF-1R+chemo.

Abbreviations: CDK, cyclin dependent kinase; chemo, chemotherapy; EGFR, epidermal growth factor receptor; IGF-R, insulin-like growth factor receptor; VEGF, vascular endothelial growth factor.

eFigure 29. Funnel plot for UTI following targeted therapies in lung cancer.



eFigure 30. Funnel plot for electrolyte disorders following targeted therapies in lung cancer.



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