

Overall bias

Up to 2 “unclear” and no “high risk”, the overall bias was considered “low”.

3 or more “unclear” and up to one “high risk”, the overall bias was considered “moderate”; and otherwise it was considered “high”.

Our final risk of bias assessments for all eligible trials is presented in the table below:

#### Assessment of objective outcome (mortality)

| <b>Trials</b>      | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias objective</b> |
|--------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|-------------------------------|
| ARCHER 1009, 2014  | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| ARQ 197-209, 2011  | unclear                    | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| ATTENTION, 2015    | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Bergqvist, 2014    | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Besse, 2014        | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | high risk                          | moderate risk                 |
| BeTa, 2011         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Bhatnagar, 2012    | unclear                    | unclear                       | NA                                             | NA                                    | unclear                        | unclear                            | high risk                     |
| Blumenschein, 2015 | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| BR21, 2005         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                      |
| CALGB 30704, 2014  | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| CheckMate017, 2015 | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| CheckMate057, 2015 | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Chen, 2011         | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| CTONG0806, 2014    | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Dai, 2013          | unclear                    | unclear                       | NA                                             | NA                                    | unclear                        | unclear                            | high risk                     |
| DATE, 2015         | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| DELTA, 2014        | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                      |
| Dittrich, 2014     | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| E1512, 2015        | low risk                   | low risk                      | low risk                                       | low risk                              | high risk                      | low risk                           | moderate risk                 |
| Esteban, 2003      | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Gerber, 2014       | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | unclear                            | high risk                     |
| GFPC 05-06, 2011   | unclear                    | unclear                       | low risk                                       | low risk                              | high risk                      | unclear                            | moderate risk                 |
| Groen, 2013        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Hainsworth, 2010   | unclear                    | unclear                       | NA                                             | NA                                    | low risk                       | low risk                           | high risk                     |
| Han, 2011          | unclear                    | unclear                       | NA                                             | NA                                    | unclear                        | unclear                            | high risk                     |

| <b>Trials</b>                     | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias objective</b> |
|-----------------------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|-------------------------------|
| HANSHIN Oncology Group 0110, 2015 | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Herbst, 2007                      | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Heymach, 2007                     | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| HORG, 2013                        | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | high risk                          | moderate risk                 |
| Hosomi, 2015                      | low risk                   | low risk                      | low risk                                       | low risk                              | high risk                      | low risk                           | moderate risk                 |
| ICOGN, 2013                       | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| INTEREST, 2008                    | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| ISEL, 2005                        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                      |
| ISTANA, 2010                      | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Janne, 2013                       | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| JMEI, 2004                        | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Jones, 2008                       | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Juan, 2014                        | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Kapoor, 2015                      | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | unclear                            | high risk                     |
| Katakami, 2014                    | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | low risk                           | moderate risk                 |
| KCSG-LU08-01, 2012                | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Kelly, 2012                       | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| KEYNOTE-010,2015                  | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Kim A, 2012                       | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Kim B, 2012                       | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Kim, 2015                         | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | high risk                          | moderate risk                 |
| Krzakowski, 2010                  | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Kuo, 2013                         | unclear                    | unclear                       | NA                                             | NA                                    | unclear                        | unclear                            | high risk                     |
| Lee, 2013                         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Levy, 2014                        | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Li, 2010                          | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | unclear                            | high risk                     |
| Li, 2012                          | unclear                    | unclear                       | NA                                             | NA                                    | high risk                      | unclear                            | high risk                     |
| Li, 2013                          | low risk                   | unclear                       | low risk                                       | low risk                              | high risk                      | low risk                           | moderate risk                 |
| Li, 2014                          | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Liu, 2015                         | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| LUME-COLUMBUS,2016                | unclear                    | unclear                       | NA                                             | NA                                    | high risk                      | high risk                          | high risk                     |

[illegible]

| <b>Trials</b>                                   | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias objective</b> |
|-------------------------------------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|-------------------------------|
| Sun, 2013                                       | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| TAILOR, 2013                                    | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| TALISMAN, 2015                                  | low risk                   | low risk                      | low risk                                       | low risk                              | high risk                      | low risk                           | moderate risk                 |
| TAX 317, 2000                                   | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| TITAN, 2012                                     | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| TORI L-03, 2013                                 | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | low risk                           | moderate risk                 |
| ULTIMATE-IFCT1103,2016                          | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | unclear                            | high risk                     |
| V15-32, 2008                                    | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Wen, 2016                                       | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| Witta, 2012                                     | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                      |
| WJOG 5108L, 2016                                | unclear                    | low risk                      | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                      |
| ZEAL, 2011                                      | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| ZEST, 2011                                      | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| Zhang, 2015                                     | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | moderate risk                 |
| ZODIAC, 2010                                    | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                      |
| <i>East Asia S-1 Trial in Lung Cancer, 2017</i> | <i>unclear</i>             | <i>unclear</i>                | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>low risk</i>                    | <i>low risk</i>               |
| <i>Fandi, 2018</i>                              | <i>unclear</i>             | <i>unclear</i>                | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>unclear</i>                     | <i>moderate risk</i>          |
| <i>SELECT-2, 2017</i>                           | <i>unclear</i>             | <i>low risk</i>               | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>low risk</i>                    | <i>low risk</i>               |
| <i>Wu, 2017</i>                                 | <i>unclear</i>             | <i>unclear</i>                | <i>low risk</i>                                | <i>low risk</i>                       | <i>unclear</i>                 | <i>unclear</i>                     | <i>moderate risk</i>          |
| <i>Yu, 2018</i>                                 | <i>unclear</i>             | <i>unclear</i>                | <i>unclear</i>                                 | <i>unclear</i>                        | NA                             | NA                                 | high risk                     |
| <i>JAVELIN, 2018</i>                            | <i>low risk</i>            | <i>low risk</i>               | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>low risk</i>                    | <i>low risk</i>               |
| <i>ABOUND 2L+, 2018</i>                         | <i>low risk</i>            | <i>unclear</i>                | <i>low risk</i>                                | <i>low risk</i>                       | high risk                      | high risk                          | high risk                     |

\*Studies in *Italic* are the new studies added in 2018 update

**Assessment of subjective outcomes (progression free survival, objective response rate, serious adverse events)**

| <b>Trials</b>                     | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias subjective</b> |
|-----------------------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|--------------------------------|
| ARCHER 1009, 2014                 | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| ARQ 197-209, 2011                 | unclear                    | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| ATTENTION, 2015                   | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Bergqvist, 2014                   | low risk                   | low risk                      | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Besse, 2014                       | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | high risk                          | high risk                      |
| BeTa, 2011                        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Bhatnagar, 2012                   | unclear                    | unclear                       | unclear                                        | unclear                               | unclear                        | unclear                            | high risk                      |
| Blumenschein, 2015                | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| BR21, 2005                        | low risk                   | low risk                      | low risk                                       | unclear                               | low risk                       | unclear                            | low risk                       |
| CALGB 30704, 2014                 | low risk                   | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| CheckMate017, 2015                | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| CheckMate057, 2015                | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Chen, 2011                        | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| CTONG0806, 2014                   | low risk                   | unclear                       | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Dai, 2013                         | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| DATE, 2015                        | low risk                   | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| DELTA, 2014                       | low risk                   | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Dittrich, 2014                    | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| E1512, 2015                       | low risk                   | low risk                      | high risk                                      | high risk                             | high risk                      | low risk                           | high risk                      |
| Esteban, 2003                     | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Gerber, 2014                      | unclear                    | unclear                       | high risk                                      | low risk                              | unclear                        | unclear                            | high risk                      |
| GFPC 05-06, 2011                  | unclear                    | unclear                       | high risk                                      | low risk                              | high risk                      | unclear                            | high risk                      |
| Groen, 2013                       | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Hainsworth, 2010                  | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Han, 2011                         | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| HANSHIN Oncology Group 0110, 2015 | unclear                    | unclear                       | high risk                                      | low risk                              | low risk                       | unclear                            | moderate risk                  |
| Herbst, 2007                      | unclear                    | unclear                       | unclear                                        | high risk                             | low risk                       | unclear                            | high risk                      |
| Heymach, 2007                     | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| HORG, 2013                        | low risk                   | unclear                       | high risk                                      | low risk                              | low risk                       | high risk                          | high risk                      |

| <b>Trials</b>      | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias subjective</b> |
|--------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|--------------------------------|
| Hosomi, 2015       | low risk                   | low risk                      | low risk                                       | low risk                              | high risk                      | low risk                           | moderate risk                  |
| ICOGN, 2013        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| INTEREST, 2008     | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| ISEL, 2005         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                       |
| ISTANA, 2010       | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Janne, 2013        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| JMEI, 2004         | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Jones, 2008        | low risk                   | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Juan, 2014         | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Kapoor, 2015       | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| Katakami, 2014     | unclear                    | unclear                       | high risk                                      | unclear                               | unclear                        | low risk                           | high risk                      |
| KCSG-LU08-01, 2012 | low risk                   | unclear                       | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Kelly, 2012        | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| KEYNOTE-010,2015   | low risk                   | low risk                      | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Kim A, 2012        | low risk                   | low risk                      | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Kim B, 2012        | low risk                   | low risk                      | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Kim, 2015          | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | high risk                          | high risk                      |
| Krzakowski, 2010   | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Kuo, 2013          | unclear                    | unclear                       | high risk                                      | low risk                              | unclear                        | unclear                            | high risk                      |
| Lee, 2013          | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Levy, 2014         | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Li, 2010           | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| Li, 2012           | unclear                    | unclear                       | high risk                                      | high risk                             | high risk                      | unclear                            | high risk                      |
| Li, 2013           | low risk                   | unclear                       | high risk                                      | high risk                             | high risk                      | low risk                           | high risk                      |
| Li, 2014           | low risk                   | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Liu, 2015          | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| LUME-COLUMBUS,2016 | unclear                    | unclear                       | low risk                                       | low risk                              | high risk                      | high risk                          | high risk                      |
| LUME-LUNG 1, 2014  | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| LUME-LUNG 2, 2013  | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Lux-Lung 8, 2015   | low risk                   | low risk                      | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Maitland, 2014     | unclear                    | unclear                       | high risk                                      | high risk                             | high risk                      | low risk                           | high risk                      |

| <b>Trials</b>        | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias subjective</b> |
|----------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|--------------------------------|
| Marangolo, 2000      | unclear                    | unclear                       | unclear                                        | unclear                               | unclear                        | unclear                            | high risk                      |
| MARQUEE, 2013        | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| MARVEL, 2013         | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| METLung, 2014        | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | low risk                           | moderate risk                  |
| Moran, 2014          | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Natale, 2009         | unclear                    | unclear                       | unclear                                        | unclear                               | low risk                       | high risk                          | high risk                      |
| NCCTG N0626, 2011    | unclear                    | unclear                       | high risk                                      | high risk                             | high risk                      | unclear                            | high risk                      |
| NCIC CTG BR.26, 2014 | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| NVALT-10, 2013       | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| OAK,2016             | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Paz-Ares, 2008       | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| POPLAR, 2016         | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| PROSE, 2014          | low risk                   | low risk                      | high risk                                      | high risk                             | high risk                      | low risk                           | high risk                      |
| Ramalingam, 2011     | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Ramalingam, 2012     | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Ramlau, 2006         | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Ramlau, 2012         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| REVEL, 2014          | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Sbar, 2010           | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | unclear                            | high risk                      |
| Scagliotti, 2012     | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Scagliotti, 2014     | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| Schiller, 2010       | low risk                   | unclear                       | high risk                                      | unclear                               | low risk                       | low risk                           | moderate risk                  |
| SELECT 1,2017        | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| SIGN, 2006           | unclear                    | low risk                      | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Spigel, 2011         | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Spigel, 2012         | unclear                    | unclear                       | low risk                                       | low risk                              | unclear                        | low risk                           | moderate risk                  |
| Spigel, 2013         | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Sun, 2013            | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| TAILOR, 2013         | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| TALISMAN, 2015       | low risk                   | low risk                      | high risk                                      | high risk                             | high risk                      | low risk                           | high risk                      |
| TAX 317, 2000        | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |

| <b>Trials</b>                                   | <b>Sequence generation</b> | <b>Allocation concealment</b> | <b>Blinding of patients and care providers</b> | <b>Blinding of outcomes assessors</b> | <b>Incomplete outcome data</b> | <b>Selective outcome reporting</b> | <b>Overall bias subjective</b> |
|-------------------------------------------------|----------------------------|-------------------------------|------------------------------------------------|---------------------------------------|--------------------------------|------------------------------------|--------------------------------|
| TITAN, 2012                                     | low risk                   | low risk                      | high risk                                      | high risk                             | low risk                       | low risk                           | high risk                      |
| TORI L-03, 2013                                 | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | low risk                           | high risk                      |
| ULTIMATE-IFCT1103,2016                          | unclear                    | unclear                       | high risk                                      | high risk                             | unclear                        | unclear                            | high risk                      |
| V15-32, 2008                                    | unclear                    | unclear                       | high risk                                      | low risk                              | low risk                       | low risk                           | moderate risk                  |
| Wen, 2016                                       | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| Witta, 2012                                     | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | unclear                            | low risk                       |
| WJOG 5108L, 2016                                | unclear                    | low risk                      | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| ZEAL, 2011                                      | low risk                   | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| ZEST, 2011                                      | unclear                    | unclear                       | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| Zhang, 2015                                     | unclear                    | unclear                       | high risk                                      | high risk                             | low risk                       | unclear                            | high risk                      |
| ZODIAC, 2010                                    | low risk                   | low risk                      | low risk                                       | low risk                              | low risk                       | low risk                           | low risk                       |
| <i>East Asia S-1 Trial in Lung Cancer, 2017</i> | <i>unclear</i>             | <i>unclear</i>                | <i>high risk</i>                               | <i>high risk</i>                      | <i>low risk</i>                | <i>low risk</i>                    | <i>high risk</i>               |
| <i>Fandi, 2018</i>                              | <i>unclear</i>             | <i>unclear</i>                | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>unclear</i>                     | <i>moderate risk</i>           |
| <i>SELECT-2, 2017</i>                           | <i>unclear</i>             | <i>low risk</i>               | <i>low risk</i>                                | <i>low risk</i>                       | <i>low risk</i>                | <i>low risk</i>                    | <i>low risk</i>                |
| <i>Wu, 2017</i>                                 | <i>unclear</i>             | <i>unclear</i>                | <i>high risk</i>                               | <i>high risk</i>                      | <i>unclear</i>                 | <i>unclear</i>                     | <i>high risk</i>               |
| <i>Yu, 2018</i>                                 | <i>unclear</i>             | <i>unclear</i>                | <i>unclear</i>                                 | <i>unclear</i>                        | <i>NA</i>                      | <i>NA</i>                          | <i>high risk</i>               |
| <i>JAVELIN, 2018</i>                            | <i>low risk</i>            | <i>low risk</i>               | <i>high risk</i>                               | <i>low risk</i>                       | <i>low risk</i>                | <i>low risk</i>                    | <i>moderate risk</i>           |
| <i>ABOUND 2L+, 2018</i>                         | <i>low risk</i>            | <i>unclear</i>                | <i>high risk</i>                               | <i>high risk</i>                      | <i>high risk</i>               | <i>high risk</i>                   | <i>high risk</i>               |

\* *Studies in Italic* are the new studies added in 2018 update