

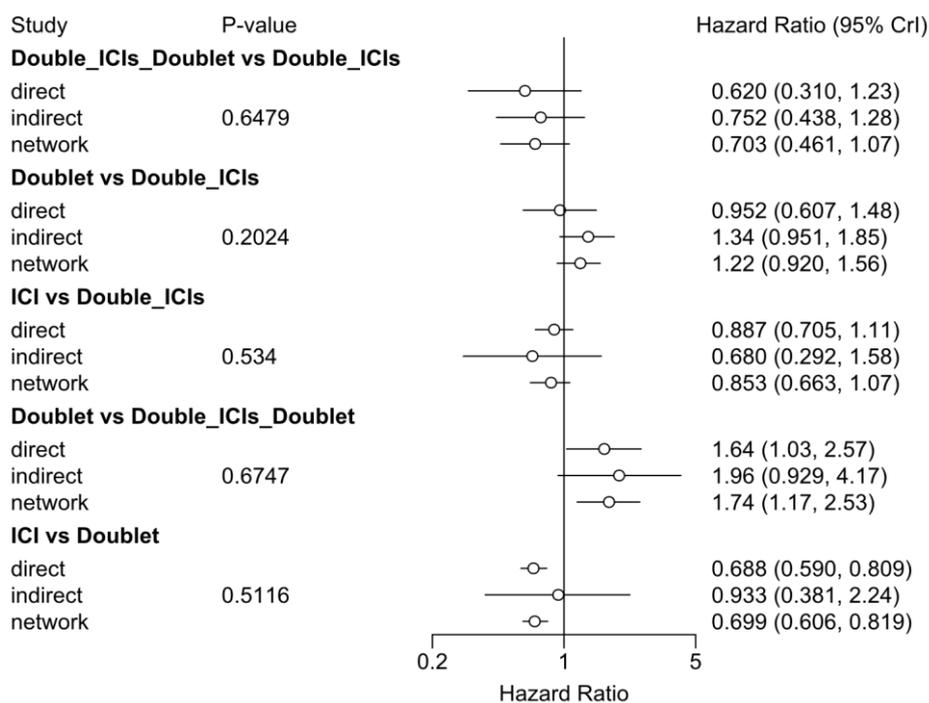
(A)

|   | Camel | DCTGBR34 | CheckMate028 | CheckMate27Part1 | CheckMateLA | EMPOWERLung1 | Impower10 | Impower130 | Impower131 | Impower132 | Impower150 | KEYNOTE24 | KEYNOTE42 | KEYNOTE189 | KEYNOTE47 | KEYNOTE666 | MYSTIC | ORIENT11 | ORIENT12 | RATIONALE304 | RATIONALE307 | TASUK52 |   |
|---|-------|----------|--------------|------------------|-------------|--------------|-----------|------------|------------|------------|------------|-----------|-----------|------------|-----------|------------|--------|----------|----------|--------------|--------------|---------|---|
| Random sequence generation (selection bias)               | +     | +        | +            | +                | +           | +            | +         | +          | ?          | ?          | ?          | +         | +         | +          | +         | +          | +      | +        | +        | +            | +            | +       | ? |
| Allocation concealment (selection bias)                   | +     | +        | +            | +                | +           | +            | +         | +          | ?          | ?          | ?          | +         | +         | +          | +         | +          | +      | +        | +        | +            | +            | +       | + |
| Blinding of participants and personnel (performance bias) | -     | -        | -            | -                | -           | -            | +         | -          | -          | -          | -          | -         | +         | +          | +         | +          | +      | +        | +        | -            | -            | -       | + |
| Blinding of outcome assessment (detection bias)           | +     | ?        | +            | +                | +           | +            | +         | +          | -          | -          | -          | +         | +         | +          | +         | +          | +      | +        | +        | +            | ?            | ?       | + |
| Incomplete outcome data (attrition bias)                  | +     | +        | +            | ?                | +           | ?            | +         | +          | +          | +          | +          | +         | +         | +          | +         | +          | +      | +        | +        | +            | +            | +       | + |
| Selective reporting (reporting bias)                      | +     | +        | +            | +                | +           | +            | +         | +          | +          | +          | +          | +         | +         | +          | +         | +          | +      | +        | +        | +            | +            | +       | + |
| Other bias  | +     | +        | +            | ?                | +           | ?            | +         | +          | +          | +          | ?          | +         | ?         | +          | +         | +          | +      | +        | +        | +            | +            | +       | + |

(B)

Figure S1. Graphic (A) and tabular representation (B) of risk of bias in all studies included.

(A)



(B)

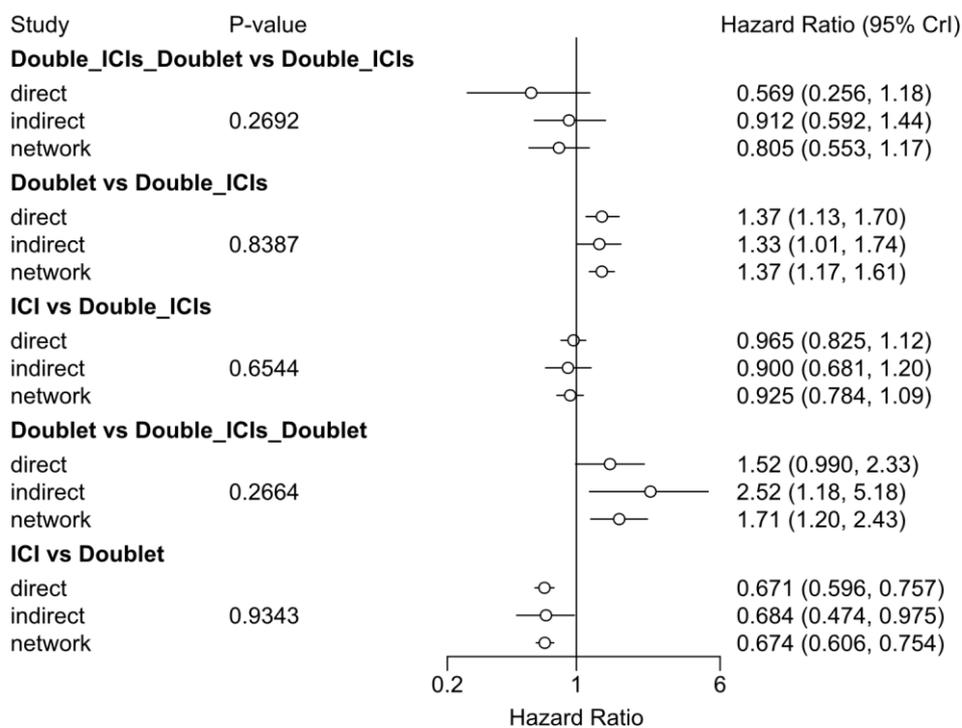


Figure S2. Node splitting analysis for PFS (A) and OS (B).

**Table S1.** Detailed characteristics of the 22 studies included in the Bayesian network meta-analysis.

| Study [ref]        | Trial Design           | Mutations                       | PD-L1 Criteria | PD-L1 Detection | Intervention Arm   | Control Arm   |
|--------------------|------------------------|---------------------------------|----------------|-----------------|--|---|
| KEYNOTE-024 [13]   | Phase III Open-label   | Without EGFR or ALK alterations | $\geq 50\%$    | 22C3 pharmDx    | Pembrolizumab 200mg Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5-6 or Cisplatin 75mg/m <sup>2</sup> Q3W<br>Gemcitabine 1250mg/m <sup>2</sup> D1,8 + Carboplatin AUC5-6 or Cisplatin 75mg/m <sup>2</sup> Q3W<br>Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5-6 Q3W |
| KEYNOTE-042 [15]   | Phase III Open-label   | Without EGFR or ALK alterations | $\geq 1\%$     | 22C3 pharmDx    | Pembrolizumab 200mg Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5-6 Q3W<br>Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5-6 Q3W  |
| KEYNOTE-189 [29]   | Phase III Double-blind | Without EGFR or ALK alterations | All comers     | 22C3 pharmDx    | Pembrolizumab 200mg Q3W + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W   |
| KEYNOTE-407 [16]   | Phase III Double-blind | Unselected                      | All comers     | 22C3 pharmDx    | Pembrolizumab 200mg Q3W + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W   | Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W  |
| KEYNOTE-598 [43]   | Phase III Double-blind | Without EGFR or ALK alterations | $\geq 50\%$    | 22C3 pharmDx    | Pembrolizumab 200mg Q3W + ipilimumab 1mg/kg Q6W  | Pembrolizumab 200mg Q3W   |
| IMpower110 [21]    | Phase III Open-label   | Without EGFR or ALK alterations | $\geq 1\%$     | SP142           | Atezolizumab 1200mg Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W<br>Gemcitabine 1000mg/m <sup>2</sup> D1,8 + Carboplatin AUC5 Q3W<br>Gemcitabine 1250mg/m <sup>2</sup> D1,8 + Cisplatin 75mg/m <sup>2</sup> Q3W                    |
| IMpower130 [19]    | Phase III Open-label   | Without EGFR or ALK alterations | All comers     | SP142           | Atezolizumab 1200mg + nab-Paclitaxel 100mg/m <sup>2</sup> + Carboplatin AUC6 Q3W   | nab-Paclitaxel 100mg/m <sup>2</sup> + Carboplatin AUC6 Q3W  |
| IMpower131 [20]    | Phase III Open-label   | Unselected                      | All comers     | SP142           | Atezolizumab 1200mg + nab-Paclitaxel 100mg/m <sup>2</sup> + Carboplatin AUC6 Q3W   | nab-Paclitaxel 100mg/m <sup>2</sup> + Carboplatin AUC6 Q3W  |
| IMpower132 [22]    | Phase III Open-label   | Without EGFR or ALK alterations | All comers     | SP142           | Atezolizumab 1200mg + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W   |
| IMpower150 [30]    | Phase III Open-label   | Without EGFR or ALK alterations | All comers     | SP142           | 1. Atezolizumab 1200mg + Bevacizumab 15mg/kg + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W<br>2. Atezolizumab 1200mg + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W | Bevacizumab 15mg/kg + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W  |
| CheckMate 026 [17] | Phase III Open-label   | Without EGFR or ALK alterations | $\geq 1\%$     | 28-8 PharmDx    | Nivolumab 3mg/kg Q2W   | Gemcitabine 1250mg/m <sup>2</sup> D1,8 + Cisplatin 75mg/m <sup>2</sup> Q3W  |

|                                 |                           |                                    |            |                 |  |  |
|---------------------------------|---------------------------|------------------------------------|------------|-----------------|--|--|
|                                 |                           |                                    |            |                 |  | Gemcitabine 1000mg/m <sup>2</sup> D1,8 + Carboplatin AUC5 Q3W<br>Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W<br>Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W   |
| <b>CheckMate 9LA</b><br>[26]    | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | 28-8<br>PharmDx | Nivolumab 350mg Q3W + Ipilimumab 1mg/kg Q6W + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W                          | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W  |
| <b>CheckMate 227</b><br>[25,41] | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | 28-8<br>PharmDx | 1. Nivolumab 3mg/kg Q2W + Ipilimumab 1mg/kg Q6W<br>2. Nivolumab 240mg Q2W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W<br>Gemcitabine 1250mg/m <sup>2</sup> D1,8 + Cisplatin 75mg/m <sup>2</sup> Q3W<br>Gemcitabine 1000mg/m <sup>2</sup> D1,8 + Carboplatin AUC5 Q3W   |
| <b>MYSTIC</b><br>[27]           | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | SP263           | 1. Durvalumab 20mg/kg + Tremelimumab 1mg/kg Q4W<br>2. Durvalumab 20mg/kg Q4W   | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W  |
| <b>CamEL</b><br>[23]            | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | 22C3<br>pharmDx | Camrelizumab 200mg + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 Q3W  | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 Q3W   |
| <b>CCTG BR 34</b><br>[42]       | Phase II<br>Open-label    | Without EGFR or<br>ALK alterations | All comers | SP263           | Durvalumab 1500mg Q4W + Tremelimumab 75mg Q4W + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC6 or Cisplatin 75mg/m <sup>2</sup> Q3W                        | Durvalumab 1500mg + Tremelimumab 75mg Q4W  |
| <b>RATIONALE 304</b><br>[33]    | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | SP263           | Tislelizumab 200mg + Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W   | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W  |
| <b>RATIONALE 307</b><br>[32]    | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | All comers | SP263           | Tislelizumab 200mg + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5 Q3W<br>Tislelizumab 200mg + nab-Paclitaxel 100mg/m <sup>2</sup> + Carboplatin AUC5 Q3W | Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5 Q3W   |
| <b>ORIENT-11</b><br>[31]        | Phase III<br>Double-blind | Without EGFR or<br>ALK alterations | All comers | 22C3<br>pharmDx | Sintilimab 200mg + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W   | Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W  |
| <b>ORIENT-12</b><br>[34]        | Phase III<br>Double-blind | Without EGFR or<br>ALK alterations | All comers | 22C3<br>pharmDx | Sintilimab 200mg + Gemcitabine 1000mg/m <sup>2</sup> D1,8 + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W  | Gemcitabine 1000mg/m <sup>2</sup> D1,8 + Carboplatin AUC5 or Cisplatin 75mg/m <sup>2</sup> Q3W   |
| <b>EMPOWER-Lung 1</b><br>[24]   | Phase III<br>Open-label   | Without EGFR or<br>ALK alterations | ≥ 50 %     | 22C3<br>pharmDx | Cemiplimab 350mg Q3W   | Pemetrexed 500mg/m <sup>2</sup> + Carboplatin AUC5-6 or Cisplatin 75mg/m <sup>2</sup> Q3W + Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC5-6 or Cisplatin 75mg/m <sup>2</sup> Q3W<br>Gemcitabine 1250mg/m <sup>2</sup> D1,8 + Carboplatin AUC5-6 or Cisplatin 100mg/m <sup>2</sup> Q3W |

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|--------------------------|---------------------------|------------------------------------|------------|-----------------|---|---|
| <b>TASUKI-52</b><br>[28] | Phase III<br>Double-blind | Without EGFR or<br>ALK alterations | All comers | 28-8<br>PharmDx | Nivolumab 360mg + Bevacizumab 15mg/kg +<br>Paclitaxel 200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W | Bevacizumab 15mg/kg + Paclitaxel<br>200mg/m <sup>2</sup> + Carboplatin AUC6 Q3W |
|--------------------------|---------------------------|------------------------------------|------------|-----------------|---|---|

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