**Online Supplementary Table 1. Risk of bias**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Sequence Generation | Allocation Concealment | Performance Bias | Detection Bias | Attrition Bias | Other Bias |
| Overall Survival | Progression-Free Survival/Serious adverse events |
| Gross-Goupil 2018(8) | Low | Low | Low | Low | Low | Low | Low |
| Chamie 2017(9) | Low | Low | Low | Low | Low | Low | Low |
| Passalacqua 2014(10) | Low | Low | High | Low | Unclear | Low | Low |
| Aitchison 2014(11) | Low | Low | High | Low | Unclear | High | Low |
| Messing 2003(12) | Unclear | Low | High | Low | Unclear | Unclear | Low |
| Pizzocaro 2001(13) | Unclear | Unclear | High | Low | Unclear | Low | Low |
| Hinotsu 2013(14) | Unclear | Unclear | High | Low | Unclear | Low | Low |
| Motzer 2017(15) | Unclear | Unclear | Low | Low | Unclear | High | Unclear |
| Choueiri 2021(16) | Low | Low | Low | Low | Low | Low | Low |
| Haas 2016(17) | Low | Low | Low | Low | Low | High | Low |
| Ravaud 2016(19) | Low | Low | Low | Low | Low | High | Low |
| Margulis 2009(20) | Unclear | Unclear | High | Low | Unclear | Unclear | Unclear |
| Eisen 2020(18) | Low | Low | Low | Low | Low | Low | Low |

**Online Supplementary Table 2.** OS all treatment comparisons, hazard ratio [confidence intervals]

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Axitinib** | 0.97 [0.57; 1.67] | 0.96 [0.52; 1.78] | 1.04 [0.50; 2.19] | 0.85 [0.45; 1.61] | 1.12 [0.63; 1.99] | 0.80 [0.44; 1.46] | 0.94 [0.53; 1.66] | 1.04 [0.59; 1.85] |
| 1.03 [0.60; 1.76] | **Control** | 0.99 [0.74; 1.32] | 1.07 [0.64; 1.79] | 0.87 [0.61; 1.24] | 1.15 [0.92; 1.42] | 0.82 [0.62; 1.08] | 0.96 [0.80; 1.16] | 1.07 [0.87; 1.31] |
| 1.04 [0.56; 1.91] | 1.01 [0.76; 1.35] | G**irentuximab** | 1.08 [0.60; 1.95] | 0.88 [0.56; 1.38] | 1.16 [0.81; 1.66] | 0.83 [0.56; 1.23] | 0.97 [0.69; 1.38] | 1.08 [0.76; 1.54] |
| 0.96 [0.46; 2.02] | 0.93 [0.56; 1.56] | 0.93 [0.51; 1.67] | **IL-2+Interferon** | 0.81 [0.44; 1.52] | 1.07 [0.61; 1.87] | 0.77 [0.43; 1.37] | 0.90 [0.52; 1.56] | 1.00 [0.57; 1.73] |
| 1.18 [0.62; 2.24] | 1.15 [0.81; 1.63] | 1.14 [0.72; 1.79] | 1.23 [0.66; 2.29] | **IL-2+Interferon+5-FU** | 1.32 [0.87; 1.99] | 0.94 [0.60; 1.47] | 1.11 [0.74; 1.65] | 1.23 [0.82; 1.84] |
| 0.89 [0.50; 1.60] | 0.87 [0.70; 1.08] | 0.86 [0.60; 1.24] | 0.93 [0.53; 1.63] | 0.76 [0.50; 1.15] | **Interferon-alpha** | 0.72 [0.50; 1.01] | 0.84 [0.63; 1.12] | 0.93 [0.69; 1.25] |
| 1.25 [0.69; 2.29] | 1.22 [0.93; 1.60] | 1.21 [0.81; 1.80] | 1.30 [0.73; 2.34] | 1.06 [0.68; 1.65] | 1.40 [0.99; 1.98] | **Pazopanib** | 1.18 [0.84; 1.64] | 1.30 [0.92; 1.83] |
| 1.06 [0.60; 1.88] | 1.04 [0.86; 1.25] | 1.03 [0.73; 1.45] | 1.11 [0.64; 1.92] | 0.90 [0.61; 1.34] | 1.19 [0.89; 1.58] | 0.85 [0.61; 1.18] | **Sorafenib** | 1.11 [0.84; 1.46] |
| 0.96 [0.54; 1.71] | 0.94 [0.76; 1.15] | 0.93 [0.65; 1.32] | 1.00 [0.58; 1.75] | 0.82 [0.54; 1.22] | 1.08 [0.80; 1.45] | 0.77 [0.55; 1.08] | 0.90 [0.68; 1.20] | **Sunitinib** |

**Online Supplementary Figure 1.** PRISMA flow chart



**Online Supplementary Figure 2.** Forest plot for severe adverse events versus observation

