

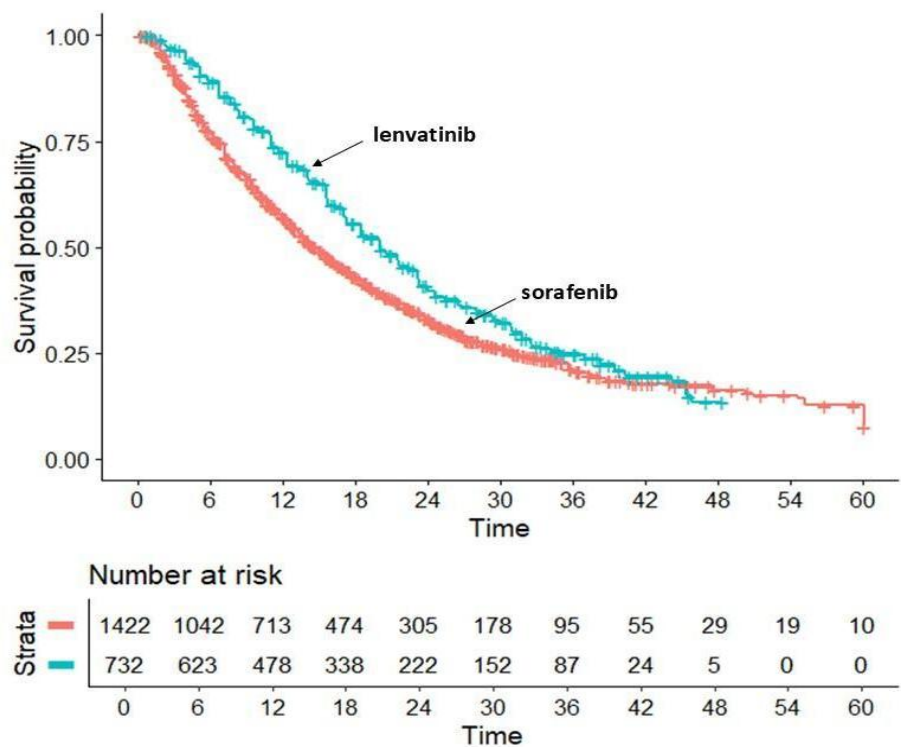
## Supplementary Table

| Trial<br>[Reference] | Treatments<br>under<br>Comparison                  | N. of Pts<br>(T vs C groups) | HR                                 |                                           |
|----------------------|----------------------------------------------------|------------------------------|------------------------------------|-------------------------------------------|
|                      |                                                    |                              | Reported in the<br>original trial) | Calculated from<br>reconstructed patients |
| IMbrave150<br>[3]    | Atezolizumab +<br>Bevacizumab<br>vs.<br>Sorafenib  | 336<br><br>165               | 0.66<br>(95% CI 0.52–0.85)         | 0.6502<br>(95% CI 0.5041–0.8386)          |
| HIMALAYA<br>[4]      | Tremelimumab<br>+ Durvalumab<br>vs.<br>Sorafenib   | 393<br><br>389               | 0.78<br>(95% CI 0.67–0.92)         | 0.7797<br>(95% CI 0.6614–0.9191)          |
| COSMIC-312<br>[6]    | Cabozantinib +<br>Atezolizumab<br>vs.<br>Sorafenib | 432<br><br>217               | 0.98<br>(95% CI 0.78–1.24)         | 1.011<br>(95% CI 0.8094–1.262)            |
| CARES-310<br>[7]     | Camrelizumab +<br>Rivoceranib<br>vs.<br>Sorafenib  | 272<br><br>271               | 0.64<br>(95% CI 0.49–0.80)         | 0.6678<br>(95% CI 0.5166– 0.8631)         |
| HEPATORCH<br>[8]     | Toripalimab +<br>Bevacizumab<br>vs.<br>Sorafenib   | 162<br><br>164               | 0.76<br>(95% CI 0.58–0.99)         | 0.7862<br>(95% CI 0.5992–1.032)           |
| APOLLO<br>[10]       | Anlotinib +<br>Penpulimab<br>vs.<br>Sorafenib      | 433<br><br>216               | 0.69<br>(95% CI 0.55–0.87)         | 0.7546<br>(95% CI 0.6104–0.9329)          |

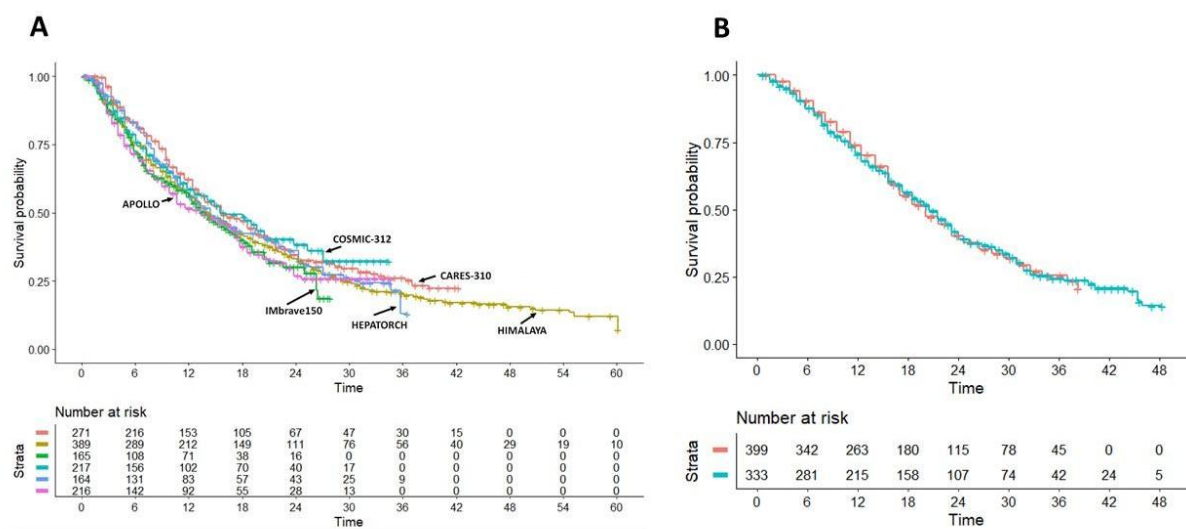
|                                                                                     |                                                               |                |                            |                                  |
|-------------------------------------------------------------------------------------|---------------------------------------------------------------|----------------|----------------------------|----------------------------------|
| LEAP-002<br>[9]                                                                     | Lenvatinib +<br>Pembrolizumab<br>vs<br>Lenvatinib             | 395<br><br>399 | 0.84<br>(95% CI 0.71-1.00) | 0.9031<br>(95% CI 0.7562-1.079)  |
| CheckMate<br>9DW<br>[5]                                                             | Nivolumab +<br>Ipilimumab<br>vs.<br>Sorafenib /<br>Lenvatinib | 335<br><br>333 | 0.79<br>(95% CI 0.65-0.96) | 0.804<br>(95% CI 0.6584- 0.9817) |
| Abbreviations: T, treatment; C, control; HR, hazard ratio; CI, confidence interval. |                                                               |                |                            |                                  |

*Table S1. Comparison between the values of HR reported in the original trials and those estimated from reconstructed patients. The Apollo trial [10] shows a small difference between the HR calculated from reconstructed patients and the original HR; in the remaining 7 cases, the two values are virtually identical.*

Supplementary Figures



Supplementary Figure 1: Indirect comparison of control arms of the 6 studies using sorafenib as standard of care (in red) vs the two studies using lenvatinib (in turquoise).



Supplementary Figure 2: Panel A: heterogeneity among the 6 control groups treated with sorafenib (trials: CARES-310, IMBRAVE-150, COSMIC-312, HIMALAYA). Panel B: heterogeneity between the 2 control groups treated with lenvatinib (CheckMate 9DW, LEAP-002). Endpoint: overall survival; time in months.