

**Evaluation of hyperprogressive disease with atezolizumab plus bevacizumab  
for hepatocellular carcinoma: a secondary analysis of the IMbrave150 trial**

**(Supplementary documents)**

**Authors:** Yuan Gao, Ann-Lii Cheng, Lee X Li, Natalie Parent, Ganessan  
Kichenadasse, Christos S Karapetis, Andrew Rowland, Ashley M Hopkins, Michael J  
Sorich

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**Supplementary Table 1. Demographic features of the included patient population**

| Characteristic                                                               | Overall<br>N = 408 <sup>1</sup> | Atezo+Bev<br>N = 272 <sup>1</sup> | Sorafenib<br>N = 136 <sup>1</sup> | p <sup>2</sup> |
|------------------------------------------------------------------------------|---------------------------------|-----------------------------------|-----------------------------------|----------------|
| Age (years)                                                                  | 66 (59, 72)                     | 66 (59, 72)                       | 67 (61, 72)                       | 0.3            |
| Sex                                                                          |                                 |                                   |                                   | 0.8            |
| Female                                                                       | 75 (18%)                        | 51 (19%)                          | 24 (18%)                          |                |
| Male                                                                         | 333 (82%)                       | 221 (81%)                         | 112 (82%)                         |                |
| Region                                                                       |                                 |                                   |                                   | 0.13           |
| Asia                                                                         | 198 (49%)                       | 122 (45%)                         | 76 (56%)                          |                |
| Europe                                                                       | 124 (30%)                       | 86 (32%)                          | 38 (28%)                          |                |
| North America                                                                | 77 (19%)                        | 56 (21%)                          | 21 (15%)                          |                |
| Oceania                                                                      | 9 (2%)                          | 8 (3%)                            | 1 (1%)                            |                |
| ECOG performance status score                                                |                                 |                                   |                                   | >0.9           |
| 0                                                                            | 265 (65%)                       | 177 (65%)                         | 88 (65%)                          |                |
| 1                                                                            | 143 (35%)                       | 95 (35%)                          | 48 (35%)                          |                |
| Child-Pugh classification                                                    |                                 |                                   |                                   | 0.7            |
| Grade A                                                                      | 405 (99%)                       | 269 (99%)                         | 136 (100%)                        |                |
| Grade B                                                                      | 1 (0.2%)                        | 1 (0.4%)                          | 0 (0%)                            |                |
| Missing                                                                      | 2 (0.5%)                        | 2 (0.7%)                          | 0 (0%)                            |                |
| Barcelona Clinic liver cancer stage                                          |                                 |                                   |                                   | 0.9            |
| A                                                                            | 11 (3%)                         | 7 (3%)                            | 4 (3.0%)                          |                |
| B                                                                            | 65 (16%)                        | 42 (15%)                          | 23 (17%)                          |                |
| C                                                                            | 332 (81%)                       | 223 (82%)                         | 109 (80%)                         |                |
| Presence of macrovascular invasion and/or extrahepatic spread at study entry | 301 (74%)                       | 205 (75%)                         | 96 (71%)                          | 0.3            |
| Varices                                                                      | 115 (28%)                       | 78 (29%)                          | 37 (27%)                          | 0.8            |
| Prior local therapy                                                          | 189 (46%)                       | 122 (45%)                         | 67 (49%)                          | 0.4            |
| Cause of hepatocellular carcinoma                                            |                                 |                                   |                                   | >0.9           |
| Hepatitis B                                                                  | 160 (39%)                       | 106 (39%)                         | 54 (40%)                          |                |
| Hepatitis C                                                                  | 100 (25%)                       | 68 (25%)                          | 32 (24%)                          |                |
| Non-viral                                                                    | 148 (36%)                       | 98 (36%)                          | 50 (37%)                          |                |
| Alcohol consumption                                                          |                                 |                                   |                                   | 0.4            |
| Current                                                                      | 69 (17%)                        | 46 (17%)                          | 23 (17%)                          |                |
| Never                                                                        | 132 (32%)                       | 82 (30%)                          | 50 (37%)                          |                |
| Previous                                                                     | 207 (51%)                       | 144 (53%)                         | 63 (46%)                          |                |
| Smoking history                                                              |                                 |                                   |                                   | 0.7            |
| Current                                                                      | 73 (18%)                        | 47 (17%)                          | 26 (19%)                          |                |
| Never                                                                        | 144 (35%)                       | 100 (37%)                         | 44 (32%)                          |                |
| Previous                                                                     | 191 (47%)                       | 125 (46%)                         | 66 (49%)                          |                |
| Metastatic sites                                                             |                                 |                                   |                                   | 0.2            |
| 0                                                                            | 216 (53%)                       | 140 (51%)                         | 76 (56%)                          |                |
| 1                                                                            | 159 (39%)                       | 114 (42%)                         | 45 (33%)                          |                |
| 2                                                                            | 31 (7.5%)                       | 17 (6%)                           | 14 (10%)                          |                |
| 3                                                                            | 2 (0.5%)                        | 1 (5%)                            | 1 (1%)                            |                |

<sup>1</sup> Median (IQR); n (%)

<sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

<sup>3</sup> Atezo+Bev: Atezolizumab plus bevacizumab

**Supplementary Table 2. Baseline information on biomarkers by treatment group**

| Predictors               | Total population                |                                                |                                   |                | TF HPD                         |                                               |                                  |                |
|--------------------------|---------------------------------|------------------------------------------------|-----------------------------------|----------------|--------------------------------|-----------------------------------------------|----------------------------------|----------------|
|                          | Overall<br>N = 408 <sup>1</sup> | Atezo+Bev <sup>3</sup><br>N = 272 <sup>1</sup> | Sorafenib<br>N = 136 <sup>1</sup> | p <sup>2</sup> | Overall<br>N = 55 <sup>1</sup> | Atezo+Bev <sup>3</sup><br>N = 23 <sup>1</sup> | Sorafenib<br>N = 32 <sup>1</sup> | p <sup>2</sup> |
| PLR                      | 129 (95, 192)                   | 130 (97, 197)                                  | 128 (91, 184)                     | 0.4            | 169 (113, 288)                 | 182 (149, 294)                                | 154 (93, 237)                    | 0.08           |
| CRP <sub>mg/L</sub>      | 5.00 (2.00, 18.00)              | 5.00 (2.00, 18.00)                             | 5.00 (2.00, 1.00)                 | 0.8            | 8.00 (3.00, 36.00)             | 12.00 (3.00, 29.00)                           | 7.00 (3.00, 41.00)               | 0.70           |
| LMR                      | 2.58 (1.79, 3.60)               | 2.85 (1.78, 3.61)                              | 2.56 (1.82, 3.57)                 | 0.9            | 2.19 (1.47, 3.13)              | 2.06 (1.38, 2.32)                             | 2.33 (1.76, 3.43)                | 0.09           |
| NLR                      | 2.82 (1.96, 4.20)               | 2.92 (1.98, 4.20)                              | 1.60 (1.95, 4.18)                 | 0.5            | 3.58 (2.30, 5.97)              | 4.08 (2.69, 6.66)                             | 3.11 (2.20, 5.47)                | 0.12           |
| log(AFP) <sub>ug/L</sub> | 3.99 (1.79, 7.42)               | 3.66 (1.78, 7.68)                              | 4.73 (1.89, 7.37)                 | 0.6            | 6.40 (3.50, 9.30)              | 8.60 (5.20, 9.50)                             | 5.90 (2.90, 7.90)                | 0.08           |
| ALBI                     |                                 |                                                |                                   |                |                                |                                               |                                  |                |
| Grade 1                  | 209 (51%)                       | 143 (53%)                                      | 66 (49%)                          | 0.4            | 23 (42%)                       | 15 (47%)                                      | 8 (35%)                          | 0.4            |
| Grade 2                  | 199 (49%)                       | 129 (47%)                                      | 70 (51%)                          |                | 32 (58%)                       | 17 (53%)                                      | 15 (65%)                         |                |

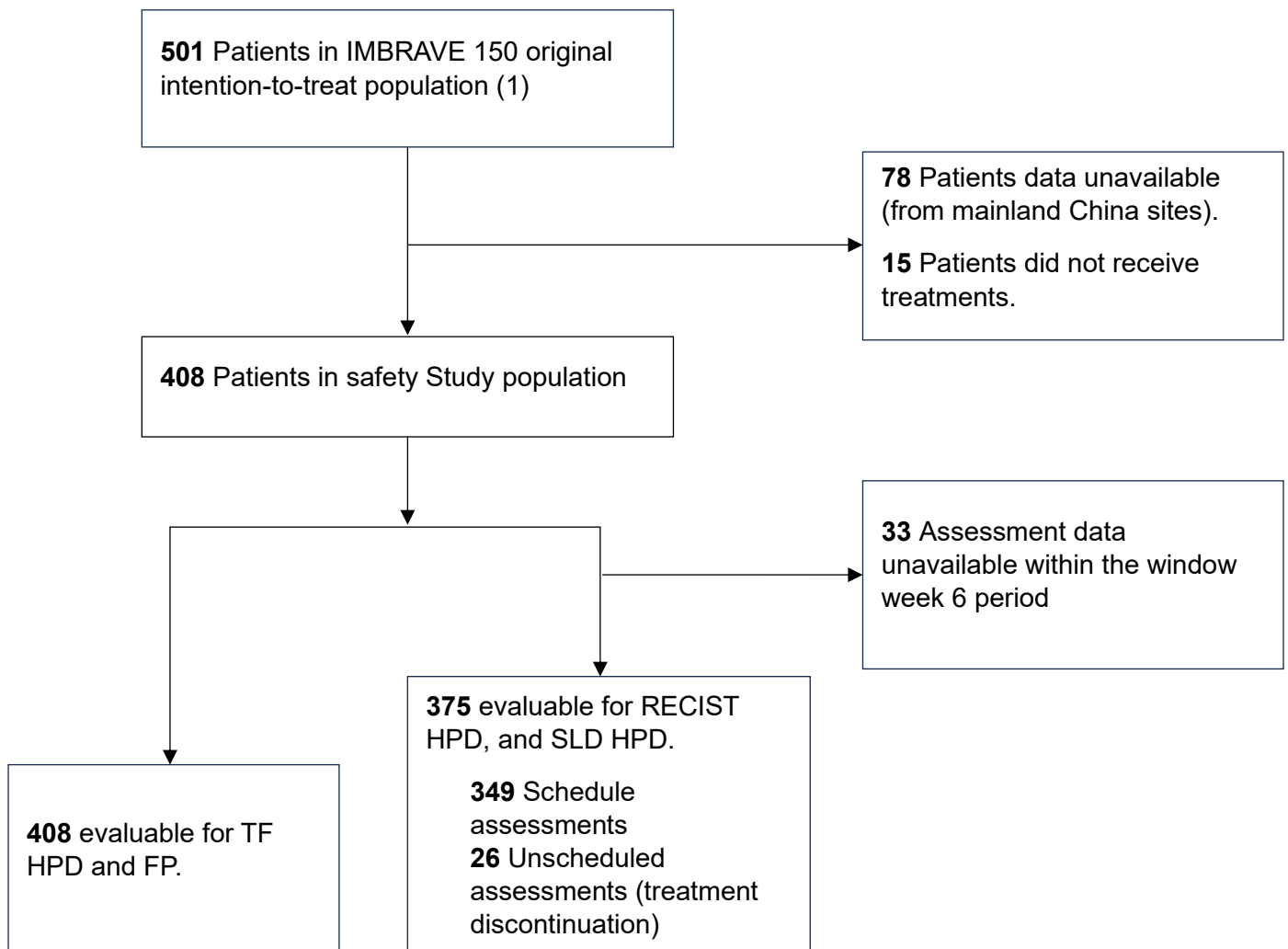
AFP = alpha-fetoprotein; ALBI = Albumin-Bilirubin Grade; CRP = c-reactive protein; LMR = lymphocyte to monocyte ratio; NLR = Neutrophil-to-lymphocyte ratio; PLR = platelet to lymphocyte ratio

<sup>1</sup> Median (IQR); n (%)

<sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

<sup>3</sup> Atezo+Bev: Atezolizumab plus bevacizumab

### Supplementary Figure 1. Inclusion and exclusion criteria for the study population



1. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim T-Y, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. New England Journal of Medicine. 2020;382(20):1894-905

**Supplementary Figure 2. Percent change of log(NLR) and log(AFP) from baseline to TF HPD onset/week 8 assessment**

