

Supplementary table 3: ICI cohort

| Patient | Biopsy or resectate | No. Of ROIs | Area covered by tissue [mm <sup>2</sup> ] | Sex | Age [years] | Etiology | Immunotype        | BCLC stage | Child Pugh score | ECOG at baseline | Therapy regimen | Drug(s)                               | Line | Best Response (RECIST v1.1) | Response=1 | PFS [months] | OS [months] | Censored [0=yes] | Cirrhosis [1=yes] | AFP [ng/dl] |
|---------|---------------------|-------------|---|-----|-------------|----------|-------------------|------------|------------------|------------------|-----------------|---------------------------------------|------|-----------------------------|------------|--------------|-------------|------------------|-------------------|-------------|
| ICI_01  | B                   | 1           | 1.676402                                  | f   | 81          | HCV      | Enriched          | 2          | 5                | 0                | ICB_combo       | Nivolumab + ipilimumab                | 2    | PR                          | 1          | 1.809210526  | 9.733333333 | 1                | 1                 | 41891       |
| ICI_02  | B                   | 3           | 1.676402                                  | f   | 78          | HCV      | Depleted          | 3          | 5                | 1                | ICB_TKI_combo   | Nivolumab + ipilimumab + cabozantinib | 2    | SD                          | 0          | 4.078947368  | 21.3        | 1                | 1                 | 5.4         |
| ICI_03  | B                   | 1           | 0.501016                                  | m   | 59          | ALD      | Depleted          | 3          | 5                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 5.493421053  | 8.366666667 | 1                | 1                 | 2218        |
| ICI_04  | B                   | 1           | 1.4802                                    | m   | 57          | NA       | Compartmentalized | 3          | 5                | 0                | ICB_mono        | Tislelizumab                          | 3    | SD                          | 0          | 2.664473684  | 12.06666667 | 1                | 0                 | 38          |
| ICI_05  | B                   | 2           | 1.914995                                  | m   | 61          | ALD      | Enriched          | 2          | 12               | 0                | ICB_mono        | Nivolumab                             | 1    | PD                          | 0          | 1.233333333  | 1.533333333 | 1                | 1                 | 385         |
| ICI_06  | B                   | 1           | 1.208461                                  | m   | 79          | ALD      | Compartmentalized | 3          | 5                | 1                | ICB_TKI_combo   | Capmatinib + spartalizumab            | 2    | SD                          | 0          | 2.730263158  | 16.66666667 | 0                | 1                 | 106         |
| ICI_07  | B                   | 1           | 1.441754                                  | m   | 57          | HCV      | Compartmentalized | 4          | 11               | 2                | ICB_mono        | Nivolumab                             | 2    | PD                          | 0          | 2.2          | 2.9         | 1                | 1                 | 64.7        |
| ICI_08  | B                   | 2           | 1.908018                                  | m   | 71          | HCV      | NA                | 2          | 6                | 0                | ICB_mono        | Pembrolizumab                         | 2    | PD                          | 0          | 1.4          | 26.6        | 0                | 1                 | 5.4         |
| ICI_09  | B                   | 2           | 1.895166                                  | m   | 56          | NA       | Depleted          | 3          | 8                | 1                | ICB_mono        | Nivolumab                             | 2    | SD                          | 0          | 1.133333333  | 1.733333333 | 1                | 0                 | 50000       |
| ICI_10  | B                   | 2           | 1.871471                                  | m   | 66          | HCV      | Enriched          | 3          | 5                | 1                | ICB_mono        | Nivolumab                             | 2    | PR                          | 1          | 39.36666667  | 39.36666667 | 0                | 1                 | 5630        |
| ICI_11  | B                   | 1           | 1.473947                                  | m   | 57          | HCV      | Compartmentalized | 3          | 7                | 1                | ICB_mono        | Nivolumab                             | 2    | PD                          | 0          | 0.86         | 0.86666667  | 1                | 1                 | 2279        |
| ICI_12  | B                   | 2           | 1.620788                                  | m   | 68          | SLD      | Depleted          | 4          | 10               | 2                | ICB_mono        | Nivolumab                             | 2    | PR                          | 1          | 3.07         | 4.26666667  | 1                | 1                 | 24.8        |
| ICI_13  | B                   | 2           | 1.904014                                  | m   | 65          | SLD      | Compartmentalized | 3          | 7                | 1                | ICB_mono        | Nivolumab                             | 1    | PD                          | 0          | 4.26666667   | 4.86666667  | 1                | 1                 | 66          |
| ICI_14  | B                   | 2           | 1.438137                                  | m   | 73          | ALD      | Compartmentalized | 2          | 5                | 0                | ICB_mono        | Pembrolizumab                         | 1    | SD                          | 0          | 9.01         | 34.77       | 0                | 1                 | 2           |
| ICI_15  | B                   | 3           | 1.029179                                  | m   | 69          | HBV      | Depleted          | 2          | 6                | 0                | ICB_combo       | Tremelimumab + durvalumab             | 1    | SD                          | 0          | 5.526315789  | 10.46666667 | 1                | 1                 | 4.1         |
| ICI_16  | B                   | 2           | 1.799427                                  | m   | 74          | NA       | NA                | 2          | 6                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 8.289473684  | 14.96666667 | 1                | 0                 | 6984        |
| ICI_17  | B                   | 2           | 1.683957                                  | m   | 79          | ALD      | Compartmentalized | 3          | 5                | 1                | ICB_TKI_combo   | Capmatinib + spartalizumab            | 2    | SD                          | 0          | 2.730263158  | 16.66666667 | 0                | 1                 | 106         |
| ICI_18  | B                   | 2           | 2.188534                                  | f   | 71          | HCV      | Enriched          | 3          | 5                | 1                | ICB_TKI_combo   | Capmatinib + spartalizumab            | 2    | SD                          | 0          | 31.84210526  | 34.53333333 | 0                | 0                 | 15616       |
| ICI_19  | B                   | 2           | 2.153869                                  | f   | 71          | HCV      | Enriched          | 3          | 5                | 1                | ICB_TKI_combo   | Capmatinib + spartalizumab            | 2    | SD                          | 0          | 31.84210526  | 34.53333333 | 0                | 0                 | 15616       |
| ICI_20  | B                   | 1           | 2.172107                                  | f   | 63          | NA       | Compartmentalized | 3          | 5                | 1                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 3.684210526  | 18.46666667 | 0                | 0                 | 3.5         |
| ICI_21  | B                   | 2           | 2.003066                                  | m   | 71          | ALD      | Compartmentalized | 3          | 6                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | PR                          | 1          | 25           | 35.4        | 1                | 1                 | 14949       |
| ICI_22  | B                   | 1           | 1.911489                                  | f   | 63          | NA       | Depleted          | 3          | 5                | 1                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 3.684210526  | 18.46666667 | 0                | 0                 | 3.5         |
| ICI_23  | B                   | 1           | 2.098004                                  | m   | 74          | NA       | Enriched          | 2          | 6                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 8.289473684  | 14.96666667 | 1                | 0                 | 6984        |
| ICI_24  | B                   | 2           | 1.596961                                  | m   | 79          | SLD      | Depleted          | 3          | 5                | 1                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 3.618421053  | 8.8         | 0                | 0                 | 2.6         |
| ICI_25  | B                   | 2           | 1.95248                                   | m   | 64          | HCV      | Enriched          | 3          | 5                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | PR                          | 1          | 13.65131579  | 23.16666667 | 1                | 0                 | 92.4        |
| ICI_26  | B                   | 1           | 1.406807                                  | m   | 71          | HCV      | Compartmentalized | 3          | 6                | 1                | ICB_TKI_combo   | Spartalizumab + sorafenib             | 1    | SD                          | 0          | 6.644736842  | 9.633333333 | 1                | 0                 | NA          |
| ICI_27  | B                   | 3           | 1.320579                                  | m   | 75          | ALD      | Depleted          | 2          | 5                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 5.493421053  | 9.5         | 1                | 1                 | 3.2         |
| ICI_28  | B                   | 2           | 1.464742                                  | m   | 78          | ALD      | Depleted          | 3          | 5                | 0                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 3.453947368  | 8.266666667 | 1                | 0                 | NA          |
| ICI_29  | B                   | 2           | 1.673855                                  | f   | 71          | HBV      | Depleted          | 3          | 5                | 0                | ICB_TKI_combo   | Nivolumab + avadomide                 | 2    | SD                          | 0          | 3.914473684  | 8.566666667 | 1                | 1                 | 16          |
| ICI_30  | B                   | 4           | 1.778687                                  | m   | 59          | ALD      | Depleted          | 3          | 5                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 5.493421053  | 8.366666667 | 1                | 1                 | 2218        |
| ICI_31  | B                   | 1           | 1.568587                                  | f   | 79          | HCV      | Compartmentalized | 2          | 5                | 0                | ICB_TKI_combo   | Spartalizumab + sorafenib             | 1    | SD                          | 0          | 2.828947368  | 18.93333333 | 0                | 1                 | NA          |
| ICI_33  | B                   | 2           | 1.940899                                  | m   | 65          | HCV      | Compartmentalized | 3          | 6                | 0                | ICB_mono        | Durvalumab                            | 1    | PD                          | 0          | 1.677631579  | 5.666666667 | 1                | 1                 | 16.9        |
| ICI_35  | B                   | 1           | 1.25594                                   | m   | 74          | HCV      | Enriched          | 3          | 5                | 1                | ICB_TKI_combo   | Capmatinib + spartalizumab            | 2    | SD                          | 0          | 7.894736842  | 10.76666667 | 1                | 1                 | 50000       |
| ICI_37  | B                   | 3           | 2.046403                                  | m   | 70          | ALD      | Enriched          | 3          | 5                | 0                | ICB_combo       | Tremelimumab + durvalumab             | 1    | SD                          | 0          | 3.486842105  | 8.866666667 | 1                | 0                 | 69.4        |
| ICI_38  | B                   | 2           | 1.009866                                  | m   | 78          | ALD      | Depleted          | 3          | 5                | 0                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 3.453947368  | 8.266666667 | 1                | 0                 | NA          |
| ICI_39  | B                   | 1           | 1.507454                                  | m   | 73          | ALD      | Enriched          | 3          | 6                | 0                | ICB_mono        | Spartalizumab                         | 2    | SD                          | 0          | 2.664473684  | 3.366666667 | 1                | 0                 | 143         |
| ICI_32  | R                   | 3           | 3.422029                                  | m   | 74          | SLD      | Compartmentalized | 3          | 6                | 1                | ICB_mono        | Nivolumab                             | 2    | PD                          | 0          | 1.9          | 22.16666667 | 0                | 1                 | 132.4       |
| ICI_34  | R                   | 3           | 2.978783                                  | f   | 72          | NA       | Depleted          | 3          | 6                | 0                | ICB_mono        | Nivolumab                             | 2    | PD                          | 0          | 2.233333333  | 2.9         | 1                | 0                 | 51.3        |
| ICI_36  | R                   | 3           | 2.939962                                  | m   | 73          | HCV      | Depleted          | 3          | 8                | 1                | ICB_mono        | Nivolumab                             | 2    | PD                          | 0          | 2.833333333  | 3.433333333 | 1                | 1                 | 183.3       |
| ICI_40  | R                   | 3           | 4.297503                                  | f   | 79          | HCV      | Depleted          | 2          | 5                | 0                | ICB_TKI_combo   | Spartalizumab + sorafenib             | 1    | SD                          | 0          | 2.828947368  | 18.93333333 | 0                | 1                 | NA          |
| ICI_41  | R                   | 4           | 5.732468                                  | m   | 65          | HBV      | Depleted          | 3          | 5                | 0                | ICB_TKI_combo   | Nivolumab + cabozantinib              | 2    | SD                          | 0          | 2.697368421  | 15.46666667 | 1                | 0                 | 1.7         |
| ICI_42  | R                   | 3           | 4.30366                                   | m   | 77          | NA       | Depleted          | 2          | 5                | 0                | ICB_combo       | Tremelimumab + durvalumab             | 1    | PD                          | 0          | 1.776315789  | 3.1         | 1                | 0                 | 1.9         |