**SUPPLEMENTAL MATERIAL – FIGURES LEGEND**

**Figure S1.** Study workflow.

**Figure S2.** Optimal cut-offs of semi-quantitative parameters to predict responder vs non-responder patients at 12 months defined using the receiver operating characteristic (ROC) curve.



**Figure S3.** Optimal cut-offs of semi-quantitative parameters to predict PFS and OS defined using the receiver operating characteristic (ROC) curve.



**SUPPLEMENTAL MATERIAL – TABLE LEGEND**

**Table S1.** Semi-quantitative parameters extrapolated for each district from the PET images.

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters** mean ± SD (range) | **Entire cohort** **(44/44)** | **Target therapy cohort (28/44)** | **Immunotherapy cohort (16/44)** |
| *Soft tissue MTV (mL)**Soft tissue TLG**Soft tissue SUVmax\** | 5.3 ± 15.3 (0.0 - 77.5)25.8 ± 75.4 (0.0 – 336.4)2.9 ± 6.2 (0.0 - 25.6) | 3.0 ± 9.5 (0.0 - 49.4) \*\*19.1 ± 66.3 (0.0 – 336.4)3.1 ± 6.0 (0.0 – 25.6) | 9.3 ± 21.9 (0.0 – 77.5) \*\*37.7 ± 90.3 (0.0 – 269.5)2.6 ± 6.6 (0.0 – 24.5) |
| *Lymph nodes MTV (mL)**Lymph nodes TLG**Lymph nodes SUVmax\** | 19.2 ± 49.9 (0.0 – 304.4)133.9 ± 289.3 (0.0 – 1634.5)12.1 ± 17.2 (0.0 – 82.3) | 25.2 ± 61.2 (0.0 – 304.4)166.8 ± 337.6 (0.0 – 1634.5)14.2 ± 20.1 (0.0 – 82.3) | 8.8 ± 14.3 (0.0 – 49.7)76.3 ± 171.1 (0.0 – 682.9)8.4 ± 9.9 (0.0 – 28.7) |
| *Soft tissue +LFN MTV (mL)**Soft tissue + LFN TLG**Soft tissue + LFN SUVmax\** | 24.6 ± 53.8 (0.0 – 304.4)159.8 ± 308.3 (0.0 – 1634.5)12.6 ± 17.1 (0.0 – 82.3) | 28.2 ± 64.8 (0.0 – 304.4)185.9 ± 361.5 (0.0 – 1634.5)14.8 ± 19.9 (0.0 – 82.3) | 18.2 ± 25.6 (0.0 – 79.0)114.1 ± 183.8 (0.0 – 682.9)8.8 ± 10.1 (0.0 – 28.7) |
| *Lung MTV (mL)**Lung TLG**Lung SUVmax\** | 2.0 ± 3.7 (0.0 – 16.1)10.2 ± 25.5 (0.0 – 143.4)2.9 ± 4.9 (0.0 – 18.4) | 0.7 ± 2.5 (0.0 – 12.4) \*\*1.9 ± 7.2 (0.0 – 36.2) \*\*0.7 ± 2.0 (0.0 – 9.5) \*\* | 4.2 ± 4.3 (0.0 – 16.1) \*\*24.6 ± 37.8 (0.0 – 143.4) \*\*6.6 ± 6.2 (0.0 – 18.4) \*\* |
| *Liver MTV (mL)**Liver TLG**Liver SUVmax\** | 0.7 ± 2.9 (0.0 – 16.76)5.0 ± 25.5 (0.0 – 166.0)1.5 ± 8.9 (0.0 – 59.2) | 0.9 ± 3.6 (0.0 – 16.7)7.2 ± 31.8 (0.0 – 166.0)2.2 ± 11.1 (0.0 – 59.2) | 0.2 ± 1.1 (0.0 – 4.6)1.2 ± 5.1 (0.0 – 20.7)0.3 ± 1.5 (0.0 – 6.3) |
| *Bone MTV (mL)**Bone TLG**Bone SUVmax\** | 3.3 ± 10.4 (0.0 – 49.1)12.7 ± 40.9 (0.0 – 236.5)2.2 ± 9.5 (0.0 -61.9) | 4.0 ± 12.1 (0.0 – 49.1)15.9 ± 49.1 (0.0 – 236.5)3.0 ± 11.8 (0.0 – 61.9) | 2.2 ± 6.5 (0.0 – 24.4)7.2 ± 19.9 (0.0 – 66.0)0.8 ± 2.6 (0.0 – 9.8) |
| *Other MTV (mL)**Other TLG**Other SUVmax\** | 1.9 ± 6.9 (0.0 – 42.7)12.8 ± 45.3 (0.0 – 253.6)2.2 ± 7.5 (0.0 – 40.3) | 1.4 ± 3.6 (0.0 – 15.1)10.8 ± 32.2 (0.0 – 131.0)2.9 ± 9.1 (0.0 – 40.3) | 2.7 ± 10.6 (0.0 – 42.7)16.1 ± 63.3 (0.0 – 253.6)1.0 ± 3.0 (0.0 – 253.6) |
| *Whole body MTV (mL)**Whole body TLG**Whole body SUVmax\** | 32.7 ± 59.9 (0.8 – 329.5)198.4 ± 326.2 (1.5 – 1732.9)15.5 ± 16.0 (1.2 – 82.3) | 35.5 ± 72.0 (0.8 – 329.5)218.4 ± 384.4 (1.5 – 1732.9)16.4 ± 19.4 (1.7 – 82.3) | 27.7 ± 30.6 (1.5 – 103.5)163.4 ± 192.5 (5.2 – 682.9)14.0 ± 7.3 (1.2 – 28.7) |
| NOTE: LFN = lymph nodes; MTV = metabolic tumor volume, SUVmax= maximum standardize uptake value, TLG = total lesion glycolysis.\* Corresponds to the highest SUVmax found in each district. \*\* The only statistically different means to Levine's test (*p<0.05*), comparing the means of the two sub-cohorts (target therapy vs immunotherapy). |

**Table S2.** Semi-quantitative parameters extrapolated for each district from the PET images associated to early and late response assessment results.

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters**  | **Entire cohort****(44/44)** | **Target therapy cohort****(28/44)** | **Immunotherapy cohort****(16/44)** |
| **At 3 months** | *Responders**(mean)* | *Non responders (mean)* | *p value* | *Responders**(mean)* | *Non responders (mean)* | *p value* | *Responders**(mean)* | *Non responders (mean)* | *p value* |
| *Soft tissue MTV (mL)**Soft tissue TLG**Soft tissue SUVmax\** | 5.222.82.4 | 5.845.26.2 | 0.8810.7260.628 | 3.220.12.4 | 0.46.612.8 | 0.9360.6400.476 | 9.628.82.5 | 8.664.62.9 | 0.9350.8620.862 |
| *Lymph nodes MTV (mL)**Lymph nodes TLG**Lymph nodes SUVmax\** | 21.9149.411.6 | 2.936.015.6 | 0.2450.4310.777 | 26.9173.112.7 | 3.386.134.7 | 0.3810.6980.894 | 11.098.29.3 | 2.611.06.0 | 1.0000.8620.862 |
| *Soft tissue +LFN MTV (mL)**Soft tissue + LFN TLG**Soft tissue + LFN SUVmax\** | 27.1172.312.0 | .8781.316.5 | 0.2590.5140.881 | 30.1193.213.3 | 3.792.634.7 | 0.2960.5820.963 | 20.6127.09.4 | 11.275.77.4 | 1.0000.9531.000 |
| *Lung MTV (mL)**Lung TLG**Lung SUVmax\** | 1.99.62.5 | 2.814.55.4 | 0.4930.4510.431 | 0.92.10.8 | 0.00.00.0 | 0.6980.6980.698 | 4.225.66.2 | 4.221.88.1 | 0.6840.6840.684 |
| *Liver MTV (mL)**Liver TLG**Liver SUVmax\** | 0.75.31.7 | 0.83.51.1 | 0.7010.7010.677 | 1.07.82.4 | 0.00.00.0 | 0.8940.8940.894 | 0.00.00.0 | 1.25.21.6 | 0.5210.5210.521 |
| *Bone MTV (mL)**Bone TLG**Bone SUVmax\** | 2.36.82.0 | 10.150.43.7 | 0.3740.3560.356 | 2.58.12.8 | 24.6118.36.2 | 0.3390.3390.381 | 2.04.10.4 | 2.816.52.5 | 0.6840.5990.599 |
| *Other MTV (mL)**Other TLG**Other SUVmax\** | 2.014.02.4 | 1.25.01.2 | 1.0000.9870.987 | 1.310.62.9 | 3.615.03.5 | 0.5290.4760.476 | 3.621.51.4 | 0.00.00.0 | 0.6840.6840.684 |
| *Whole body MTV (mL)**Whole body TLG**Whole body SUVmax\** | 34.2205.414.6 | 23.6154.722.1 | 0.9870.5820.289 | 35.9217.914.6 | 32.0225.940.9 | 0.6400.2960.222 | 30.5178.314.5 | 19.4119.112.7 | 0.5990.6840.862 |
|  |  |  |  |  |  |  |  |  |  |
| **Parameters**  | **Entire cohort****(44/44)** | **Target therapy cohort****(28/44)** | **Immunotherapy cohort****(16/44)** |
| **At 12 months** | *Responders**(mean)* | *Non responders (mean)* | *p value* | *Responders**(mean)* | *Non responders (mean)* | *p value* | *Responders**(mean)* | *Non responders (mean)* | *p value* |
| *Soft tissue MTV (mL)**Soft tissue TLG**Soft tissue SUVmax\** | 4.616.83.1 | 7.854.73.0 | 0.9450.9240.945 | 1.69.63.4 | 7.449.03.0 | 0.9350.8930.935 | 9.628.82.5 | 8.664.62.9 | 0.9530.8620.862 |
| *Lymph nodes MTV (mL)**Lymph nodes TLG**Lymph nodes SUVmax\** | 9.486.311.3 | 48.7279.515.0 | 0.4330.3010.651 | 8.579.212.4 | 75.1432.920.1 | 0.1790.1040.431 | 11.098.29.3 | 2.611.06.0 | 1.0000.8620.862 |
| *Soft tissue +LFN MTV (mL)**Soft tissue + LFN TLG**Soft tissue + LFN SUVmax\** | 14.0103.111.7 | 56.6334.215.5 | 0.5010.2760.573 | 10.188.813.1 | 82.5481.920.2 | 0.2400.1620.464 | 20.6127.09.4 | 11.275.77.4 | 1.0000.9531.000 |
| *Lung MTV (mL)**Lung TLG**Lung SUVmax\** | 1.69.72.5 | 2.89.43.6 | 0.4500.5190.555 | 0.10.20.2 | 2.02.41.0 | 0.4310.4310.464 | 4.225.66.2 | 4.221.88.1 | 0.6840.6840.684 |
| *Liver MTV (mL)**Liver TLG**Liver SUVmax\** | 0.51.10.1 | 1.317.06.0 | 0.4830.4660.450 | 0.81.80.2 | 1.423.78.5 | 0.7660.7250.725 | 0.00.00.0 | 1.25.21.6 | 0.5210.5210.521 |
| *Bone MTV (mL)**Bone TLG**Bone SUVmax\** | **0.8****1.5****0.1** | **11.3****46.5****8.7** | **0.037\*****0.034\*****0.034\*** | **0.0****0.0****0.0** | **16.2****63.7****12.3** | **0.026\*****0.026\*****0.026\*** | 2.04.10.4 | 2.816.52.5 | 0.6840.5990.599 |
| *Other MTV (mL)**Other TLG**Other SUVmax\** | 2.316.62.9 | 0.93.00.8 | 0.9670.9670.967 | 1.513.63.7 | 1.44.81.2 | 0.7250.6850.685 | 3.621.51.4 | 0.00.00.0 | 0.6840.6840.684 |
| *Whole body MTV (mL)**Whole body TLG**Whole body SUVmax\** | 19.3129.014.7 | 73.2410.218.6 | 0.1170.0820.433 | **12.6****99.4**14.9 | **104.0****576.5**22.0 | **0.013\*****0.022\***0.314 | 30.5178.314.5 | 19.4119.112.7 | 0.5990.6840.862 |
| NOTE: LFN = lymph nodes; MTV = metabolic tumor volume, SUVmax= maximum standardize uptake value, TLG = total lesion glycolysis.\* The only statistically different means to Mann-Whitney test (*p<0.05*). |