**Supplementary Table S1.** Patient baseline characteristics.

|  |  |  |  |
| --- | --- | --- | --- |
|   | HER2-positive |   | HER2-negative, ER-positive |
| Characteristic | Nº patients | % | Median  | Range |   | Nº patients | % | Median  | Range |
| Total number of patients | 78 |   |   |   |   | 72 |   |   |   |
| Age (years) |   |   | 49 | 25-75 |   |   |   | 54 | 30-78 |
| Length follow-up (months) |   |   | 30 | 6-107 |   |   |   | 41 | 6-156 |
| Menopausal status |   |   |   |   |   |   |   |   |   |
|  Pre | 44 | 57 |   |   |   | 20 | 28 |   |   |
|  Post | 34 | 43 |   |   |   | 52 | 72 |   |   |
| Tumor size |   |   |   |   |   |   |   |   |   |
|  T1 | 28 | 36 |   |   |   | 40 | 57 |   |   |
|  T2 | 33 | 42 |   |   |   | 25 | 35 |   |   |
|  T3 | 13 | 17 |   |   |   | 1 | 2 |   |   |
|  T4 | 4 | 5 |   |   |   | 4 | 6 |   |   |
| Not documented |   |   |   |   |   | 2 |   |   |   |
| Lymph node status |   |   |   |   |   |   |   |   |   |
|  N0 | 43 | 55 |   |   |   | 40 | 58 |   |   |
|  N1 | 24 | 31 |   |   |   | 15 | 22 |   |   |
|  N2  | 5 | 6 |   |   |   | 10 | 14 |   |   |
|  N3 | 6 | 8 |   |   |   | 4 | 6 |   |   |
| Not documented |   |   |   |   |   | 3 |   |   |   |
| Clinical stage |   |   |   |   |   |   |   |   |   |
|  I | 22 | 28 |   |   |   | 30 | 42 |   |   |
|  II | 36 | 46 |   |   |   | 32 | 44 |   |   |
|  III | 20 | 26 |   |   |   | 10 | 14 |   |   |
| Histological grade |   |   |   |   |   |   |   |   |   |
| 1 | 7 | 9 |   |   |   | 2 | 3 |   |   |
| 2 | 26 | 35 |   |   |   | 31 | 31 |   |   |
| 3 | 42 | 56 |   |   |   | 45 | 66 |   |   |
| Not documented | 3 |   |   |   |   | 4 |   |   |   |
| Estrogen receptor positive | 55 | 71 |   |   |   | 72 | 100 |   |   |
| Progesterone receptor positive | 47 | 60 |   |   |   | 75 | 92 |   |   |

**Supplementary Table S2.** Growth rate of TNFα-producing and control BT-474 tumors treated with trastuzumab

|  |  |  |  |
| --- | --- | --- | --- |
| Tumor | Growth rate ± SEM (mm3/day) | Mean Tumor Volume ± SEM (mm3) at day 11 | % inhibition |
| BT-474 C + IgG |  5.2 ± 1.6 | 134.4 ± 25.1 |  |
| BT-474 C + TZ |  -6.6 ± 1.1 |  7.9 ± 3.2\*\* | 94.1 |
| BT-474 T1 + IgG |  4.9 ± 1.1 |  91.2 ± 16.1 |   |
| BT-474 T1 + TZ |  6.1 ± 1.6 | 112.3 ± 27.3# | -23.1 |
| BT-474 T2 + IgG |  8.2 ± 2.5 | 195.1 ± 35.5 |   |
| BT-474 T2 + TZ |  5.6 ± 1.3 | 153.4 ± 11.0# |  21.4 |
|  |  |  |  |
| \*\*, *P* <0.01 vs. BT-474 C + IgG#, NS vs. IgG-treated |  |  |

**Supplementary Table S3:** Inhibition of JIMT-1 and KPL-4 growth by trastuzumab and etanercept.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Tumor | Treatment | Growth rate ± SEM (mm3/day) | Mean Tumor Volume ± SEM (mm3) # | % inhibition |
| JIMT-1 | IgG | 6.9 ± 0.8 | 217.6 ± 40.3 |  |
|  | Tz | 6.9 ± 0.9 | 219.7 ± 38.8 |  |
|  | Eta | 6.9 ± 0.7 | 217.7 ± 37.0 |  |
|  | Tz + Eta | 2.9 ± 0.2 | 99.9 ± 10.7\*\* | 54.1 |
|  |  |  |  |  |
| KPL-4 | IgG | 2.1 ± 0.3 | 100.7 ± 13.2 |  |
|  | Tz | 1.3 ± 0.4 | 93.5 ± 8.8 |  |
|  | Eta | 2.2 ± 0.3 | 109.8 ± 12.5 |  |
|   | Tz + Eta | -1.2 ± 0.3 | 33.2 ± 3.9\*\*\* | 67 |
|  |  |  |  |  |
| \*\*, *P*<0.01; \*\*\*, *P*<0.001 vs IgG |  |  |
| # JIMT-1 tumors, at day 28th and KPL-4 tumors, at day 21st |  |

**Supplementary Table S4.** Correlation between TNFand MUC4 expression

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **MUC4 -** | **MUC4 +** | **Total N (%)** | ***P*** |
|  **TNF -** | 6 | 2 | 8 (11) | 0.040 |
|  **TNF +** | 25 | 45 | 70 (89) |   |
| **Total N (%)** | 31 (40) | 47 (60) | 78 (100) |   |

**Supplementary Table S5.** Correlation between MUC4 expression and clinocopathological characteristics.

|  |  |  |
| --- | --- | --- |
| Clinicopathologicalcharacteristics | MUC4(n= 78)  | *P* |
|   |   | Negative (N, %) | Positive (N, %) |   |
| Overall population |   | 31 (39.7) | 47 (60.3) |   |
| Menopausal status | Pre | 14 (31.8) | 30 (68.2) | 0.104 |
|  | Post | 17 (50) | 17 (50) |  |
| Tumor size | I, II | 25 (41.0) | 39 (59.0) | 0.672 |
|   | II, IV | 6 (35.3) | 11 (64.7) |   |
| Lymphnode status | 0 | 15 (35.7) | 27 (64.3) | 0.373 |
|  | 1 to 3 | 16 (45.7) | 19 (54.3) |  |
| Clinical stage | I, II | 22 (37.9) | 36 (61.9) | 0.577 |
|   | III | 9 (45) | 11 (55) |   |
| Histological grade | 1.2 | 13 (44.8) | 16 (55.2) | 0.498 |
|  | 3 | 17 (37) | 29 (63) |  |
| Estrogen receptor | Negative | 12 (52.2) | 11 (47.8) | 0.147 |
|   | Positive | 19 (34.5) | 36 (65.5) |   |
| Progesterone receptor | Negative | 14 (45.2) | 17 (54.8) | 0.427 |
|   | Positive | 17 (36.2) | 30 (63.8) |   |