**Supplementary Table 1: HER2 Biomarker Analyses**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient ID** | **Age (Year)** | **Sex** | **NGS Result** | **FISH Result (HER2/CEP17 ratio)** | **HER2 IHC Result** | **HER2 Mass Spectrometry (amol/mg)** | **Response by RECIST v1.1 or Modified PERCIST** | **T-DM1**  **Therapy Line** | **Prior Lines of Anti-HER2 Therapy** | **Prior Anti-HER2 Therapy** |
|  |  |
| 5 | 73 | F | *ERBB2* Exon 20  p.P780\_Y781insGSP | 1.6 (7.6/4.8) | 1+ | 0 | No | 2nd | 0 | NA |
| 8 | 70 | F | *ERBB2* Exon 17 p.V659E | 1.2 (2.4/2.0) | 2+equivocal | NA | No | 1st | 0 | NA |
| 10 | 66 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.1 (2.7/2.5) | 0 | NA | Yes | 5th | 2 | Neratinib + Temsirolimus; Trastuzumab + Gemcitabine |
| 11 | 69 | F | *ERBB2* Exon 19 p.L755P | NA | 0 | NA | No | 2nd | 0 | NA |
| 12 | 57 | F | *ERBB2* Exon 20 p.G776\_V777.VCV | NA | NA | NA | Yes | 1st | 0 | NA |
| 14 | 57 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.8 (8.1/4.5) | 2+ | 642 | No | 4th | 1 | Neratinib |
| 16 | 65 | F | *ERBB2* Exon 8 p.S310F | 1.8 (3.2/1.8) | 0 | 0 | No | 3rd | 1 | Afatinib + Bevacizumab |
| 17 | 58 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA, amplification equivocal | NA | NA | NA | No | 4th | 1 | Trastuzumab + Pertuzumab |
| 19 | 50 | F | *ERBB2* amplification (FC: 5.4), *EGFR* exon 21 L858R missense mutation | 10.7 (37.2/3.5) | 3+ | NA | Yes | 2nd | 0 | NA |
| 22 | 49 | M | *ERBB2* Exon 17 p.V659E | 1.1 (2.3/2.0) | 2+ | 688 | Yes | 3rd | 1 | Neratinib |
| 24 | 50 | F | *ERBB2* Exon 20 p.G776delinsVC | 1.6 (5.7/3.6) | 0 | NA | Yes | 3rd | 0 | NA |
| 27 | 74 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | NA | NA | NA | No | 3rd | 1 | Afatinib |
| 30 | 65 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1 (2.1/2.0) | 1+ | NA | Yes | 3rd | 0 | NA |
| 33 | 66 | F | *ERBB2* Exon 19 p.L755P | 1.5 (3.2/2.1) | 2+ | 434 | No | 2nd | 1 | Neratinib |
| 36 | 61 | F | *ERBB2* Exon 20 p.G778-779 insCPG | 1.6 (4.3/2.7) | 0 | NA | No | 5th | 2 | Neratinib;  Trastuzumab + Vinorelbine |
| 38 | 72 | F | *ERBB2* Exon 8 p.S310F, Exon 7 p.D227Y, *ERBB2* amplification (FC: 2.8) | 3.7 (9.0/2.4) | 2+ equivocal | 1,495 | Yes | 2nd | 0 | NA |
| 40 | 48 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.4 (4.5/3.3) | 1+ | 586 | Yes | 4th | 1 | Neratinib |
| 42 | 55 | F | *ERBB2* amplification  (FC: 6.3) | 4.0 (9.3/2.3) | 3+ | 1271 | Yes | 2nd | 0 | NA |
| 44 | 57 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.4 (2.7/2.0) | 0 | 396 | Yes | 2nd | 1 | Afatinib |
| 46 | 62 | F | *ERBB2* Exon 20 p.P780\_Y781insGSP | 1.8 (4.6/2.5) | 2+ | 507 | Yes | 3rd | 0 | NA |
| 47 | 64 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.6 (3.0/1.9) | 2+ | 425 | NA | 3rd | 1 | Trastuzumab + Paclitaxel |
| 48 | 60 | M | *ERBB2* Exon 20 p.P780\_Y781insGSP | 1.4 (5.7/4.0) | 2+ | NA | No | 2nd | 0 | NA |
| 49 | 47 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.9 (5.6/2.9) | 1+ | 548 | Yes | 2nd | 0 | NA |
| 51 | 72 | M | *ERBB2* Exon 8 p.S335C | 2.4 (4.8/2.0) | 2+ equivocal | 902 | No | 2nd | 0 | NA |
| 53 | 63 | M | *ERBB2* amplification  (FC: 3.8) | 3.4 (12.8/3.9) | 3+ | 6,862 | Yes | 2nd | 0 | NA |
| 55 | 47 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA, *ERBB2* amplification equivocal | 2.5 (6.1/2.4) | 0 | NA | No | 2nd | 0 | NA |
| 58 | 54 | M | *ERBB2* Exon 19 p.L755P | 2.2 (4.6/2,1) | 0 | 523 | Yes | 2nd | 0 | NA |
| 60 | 57 | F | *ERBB2* Exon 20 p.P780\_Y781insGSP | 2.4 (5.7/2.3) | 2+ | NA | No | 2nd | 0 | NA |
| 69 | 42 | F | *ERBB2* amplification (FC: 1.6), *ERBB2*-*SHC1* fusion | 2.0 (4.5/2.2) | 0 | 896 | No | 3rd | 0 | NA |
| 70 | 79 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.7 (4.6/2.7) | 0 | 351.8 | No | 2nd | 0 | NA |
| 71 | 74 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 2.5 (6.4/2.5) | 3+ | 1085 | Yes | 4th | 0 | NA |
| 74 | 66 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 2.1 (5.2/2.5) | 2+ | 371 | Yes | 2nd | 0 | NA |
| 75 | 71 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | NA | 2+ | NA | Yes | 2nd | 0 | NA |
| 81 | 51 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | NA | NA | NA | Yes | 2nd | 0 | NA |
| 84 | 46 | F | *ERBB2* Exon 19 p.L755P | NA | NA | NA | Yes | 3rd | 0 | NA |
| 86 | 69 | F | *ERBB2* Exon 8 p.S310F | NA | NA | NA | No | 2nd | 0 | NA |
| 90 | 66 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | NA | NA | NA | No | 2nd | 0 | NA |
| 92 | 61 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.2 (2.4/2.1) | 2+ | 193 | Yes | 1st | 0 | NA |
| 93 | 57 | F | *ERBB2* amplification (FC: 2.3), *EGFR* exon 19 S752\_I759del | 5.1 (12.4/2.4) | 3+ | 15,176 | No | 6th | 2 | Afatinib + Cetuximab; Trastuzumab + Paclitaxel |
| 96 | 70 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | 2.5 (5.0/2.0) | NA | NA | No | 2nd | 0 | NA |
| 97 | 69 | M | *ERBB2* Exon 20 p.A775\_G776insYVMA | NA | NA | NA | Yes | 3rd | 0 | NA |
| 98 | 84 | F | *ERBB2* Exon 20 p.A775\_G776insYVMA | 1.5 (4.3/2.9) | 3+ | 606 | No | 1st | 0 | NA |
| 101 | 59 | F | *ERBB2* Exon 20 p.G778\_P780dup, *ERBB2* amplification  (FC: 3.7) | NA | NA | NA | Yes | 1st | 0 | NA |
| 102 | 76 | F | *ERBB2* amplification  (FC: unknown) | 8.2 (29.2/3.6) | 3+ | NA | Yes | 3rd | 0 | NA |
| 113 | 77 | F | *ERBB2* amplification  (FC: 11.4), *MET* exon 14 splicing mutation | NA | NA | NA | Yes | 3rd | 0 | NA |
| 114 | 78 | F | *ERBB2* amplification  (FC: 4.0), *EGFR* exon 21 L858R missense mutation | 2.3 (8.2/3.6) | focally strongly positive | NA | No | 7th | 1 | Afatinib |
| 115 | 25 | F | *ERBB2* amplification (FC: 8.2), *EGFR* exon 19 E746\_A750del, *MET* amplification FC: 2.2 | 6.2 (21.1/3.4) | 3+ | NA | No | 2nd | 0 | NA |
| 116 | 71 | F | *ERBB2* amplification (FC: 3.8), *EGFR* I740\_K745dup in-frame insertion | 4.8 (14/2.9) | 3+ | NA | Yes | 2nd | 0 | NA |
| 117 | 73 | M | *ERBB2* amplification (FC: 2.2), *EGFR* exon 18 E709K and *EGFR* exon 18 G719A mutation | 2.1 (11.2/5.3) | 2+ | NA | No | 4th | 1 | Afatinib |

Abbreviations: *ERBB*2, erb-b2 receptor tyrosine kinase 2; HER2, human epidermal growth factor receptor 2; *EGFR*, epidermal growth factor receptor; F, female; M, male; NGS, next generation sequencing; FISH, fluorescent in situ hybridization; IHC, immunohistochemistry; PET/CT, positron emission tomography/computed tomography; NA, not available; FC, fold change.