

ID1 and ID4 are Biomarkers of Tumor Aggressiveness and Poor Outcome in Immunophenotypes of Breast Cancer

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Table S1. Correlation between *ID2* and *ID3* mRNA expression and clinical-pathological variables.

| | Patients (n = 297) | <i>ID2</i> <2 (214) % (n) | <i>ID2</i> ≥2 (83) % (n) | OR (CI95) | <i>p</i> * | <i>ID3</i> <2 (236) % (n) | <i>ID3</i> ≥2 (61) % (n) | OR (CI95) | <i>p</i> * |
|---------------------------|-----------------------|------------------------------|-----------------------------|---------------|------------|------------------------------|-----------------------------|---------------|------------|
| Age | | | | | | | | | |
| ≥50 | 188 | 62.1% (133) | 66.3% (55) | 1.2 (0.7–2.0) | ns | 63.9% (146) | 68.9% (42) | 1.4 (0.8–2.5) | ns |
| <50 | 109 | 37.9% (81) | 33.7% (28) | 1 | | 38.1% (90) | 31.1% (19) | 1 | |
| Size | | | | | | | | | |
| ≥20 | 162 | 55.4% (118) | 53.0% (44) | 0.9 (0.6–1.5) | ns | 54.9% (129) | 54.1% (33) | 1.0 (0.6–1.7) | ns |
| <20 | 134 | 44.6% (95) | 47.0% (39) | 1 | | 54.1% (106) | 45.9% (28) | 1 | |
| NA | 1 | | | | | ns | | ns | |
| Histological Grade | | | | | | | | | |
| 1 | 30 | 10.3% (22) | 9.6% (8) | 1 | | 10.6% (25) | 8.2% (5) | 1 | |
| 2 | 89 | 31.3% (67) | 26.5% (22) | 0.9 (0.4–2.3) | ns | 30.1% (71) | 29.5% (18) | 1.3 (0.4–3.8) | ns |
| 3 | 178 | 58.4% (125) | 63.9% (53) | 1.2 (0.5–2.8) | ns | 59.3% (140) | 62.3% (38) | 1.4 (0.5–3.8) | ns |
| Necrosis | | | | | | | | | |
| Present | 100 | 36.5% (77) | 27.7% (23) | 0.7 (0.4–1.2) | ns (0.097) | 35.5% (83) | 28.3% (17) | 0.7 (0.4–1.3) | ns |
| Absent | 194 | 63.5% (134) | 72.3% (60) | 1 | | 64.5% (151) | 71.7% (43) | 1 | |
| NA | 3 | | | | | | | | |
| Vascular Invasion | | | | | | | | | |
| Present | 107 | 38.2% (81) | 31.3% (26) | 0.7 (0.4–1.3) | ns | 36.6% (86) | 35.0% (21) | 0.9 (0.5–1.7) | ns |
| Absent | 188 | 61.8% (131) | 68.7% (57) | 1 | | 63.4% (149) | 65.0% (39) | 1 | |
| NA | 2 | | | | | | | | |

Lymph Nodes

| | | | | | | | | | |
|----------|-----|-------------|------------|---------------|----|-------------|------------|---------------|----|
| Positive | 117 | 40.2% (86) | 37.3% (31) | 0.9 (0.5–1.5) | ns | 37.7% (89) | 45.9% (28) | 1.4 (0.8–2.5) | ns |
| Negative | 180 | 59.8% (128) | 62.7% (52) | 1 | | 62.3% (147) | 54.1% (33) | 1 | |

NA: not available; ns: not significant (p>0.05). * Chi Square Test.

Table S2. Correlations between clinical-pathological variables and OS (Kaplan-Meier method; log-rank test).

| | Patients (n) | Survival % | p * |
|------------------|---------------------|-------------------|------------|
| Phenotype | | | |
| Luminal A-like | 55 | 90.2 | |
| Luminal B/HER2- | 54 | 91.5 | |
| Luminal B/HER2+ | 40 | 83.3 | 0.027 |
| HER2-enriched | 27 | 65.9 | |
| TNBL | 82 | 83.7 | |

* Log-rank test.

Table S3. Correlations between clinical-pathological variables and DFS (Kaplan-Meier method; log-rank test).

| | Patients (n) | Survival % | p * |
|------------------|---------------------|-------------------|------------|
| Phenotype | | | |
| Luminal A-like | 54 | 88.5 | |
| Luminal B/HER2- | 52 | 88.1 | |
| Luminal B/HER2+ | 38 | 79.2 | <0.001 |
| HER2-enriched | 24 | 58.5 | |
| TNBL | 85 | 86.7 | |

* Log-rank test.

Table S4. Antibodies and conditions for immunohistochemistry.

| Antibody | Vendor | Clone | Dilution |
|-----------------|---------------|--------------|-----------------|
| ER | Dako/Agilent | ER- α | 1:50 |
| PR | Dako/Agilent | PgR636 | 1:50 |
| HER2 | Dak/Agilent o | HercepTest™ | NA |
| p53 | Dako/Agilent | DO7 | 1:50 |
| Ki67 | Dako/Agilent | MIB-I | 1:100 |

| | | | |
|-------|--------------|--------------|-------|
| Bcl2 | Neomarkers | Bcl2/100/D5 | 1:50 |
| CK5/6 | Dako/Agilent | D5/16B4 | 1:100 |
| EGFR | Dako/Agilent | Pharmaco Dx™ | NA |

NA: Not available. Dako/Agilent Technol (Santa Clara, CA); NeoMarkers Inc (Fremont, CA, USA).

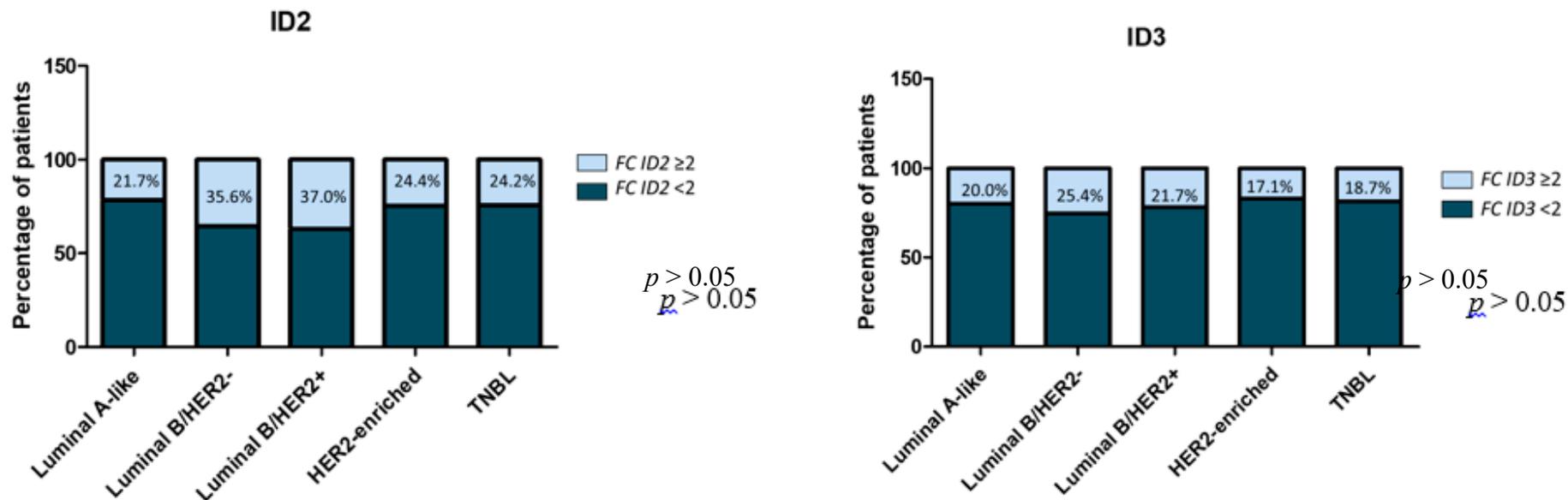
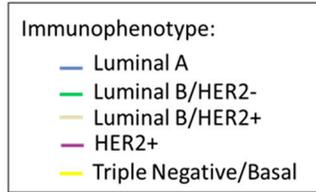
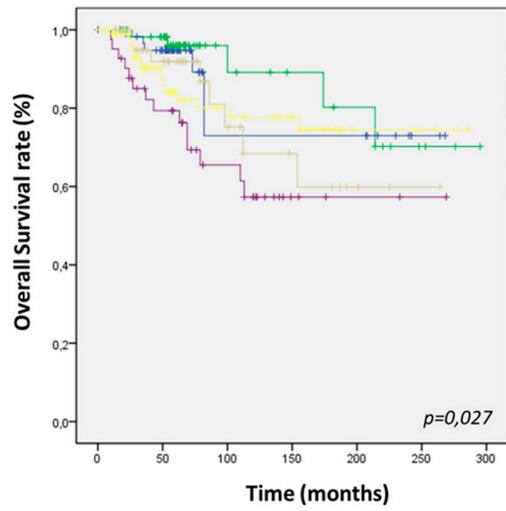
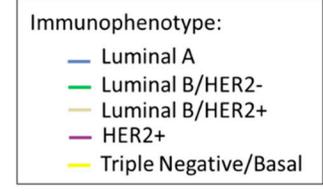
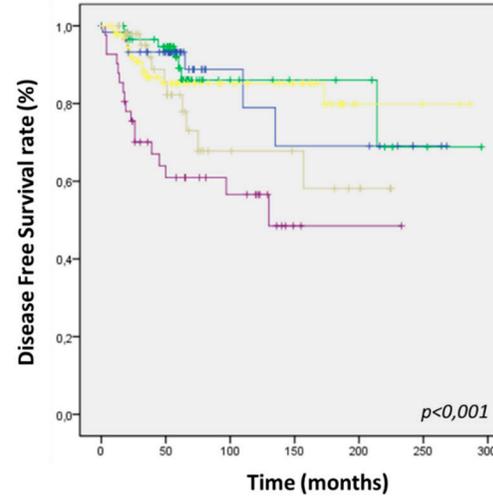


Figure S1. Percentage of samples overexpressing ID2 (A) and ID3 (B) in each BC immunophenotype.

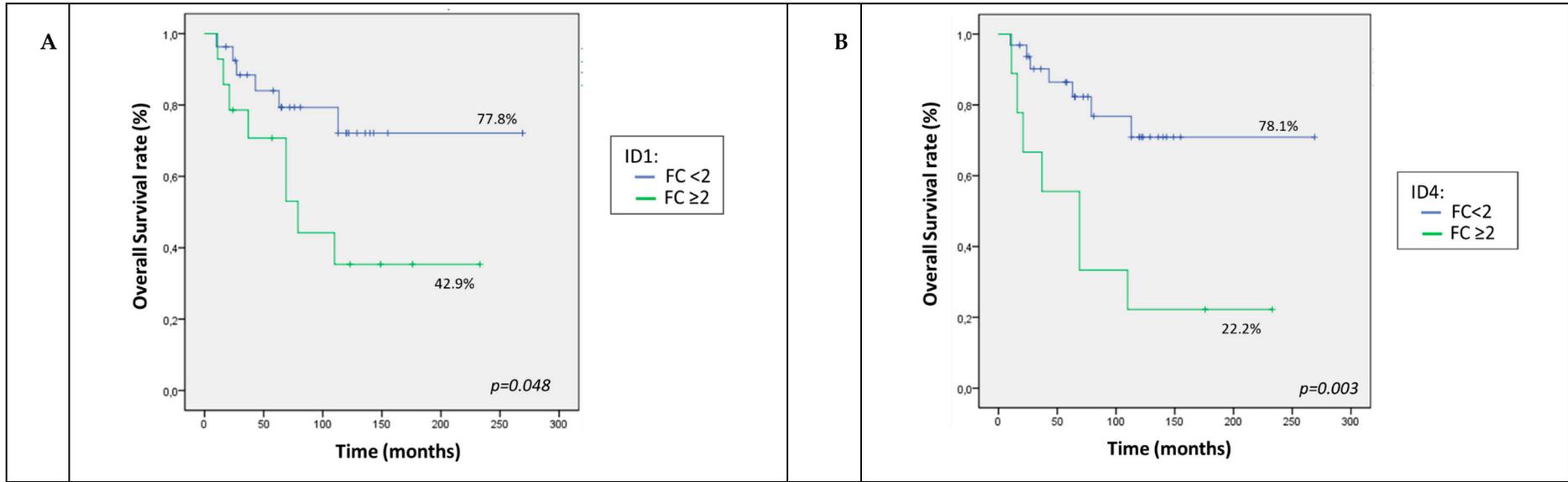


A



B

Figure S2. Kaplan-Meier plot for OS (A) and DFS (B) rates (%) for all patients classified according to breast cancer immunophenotypes.



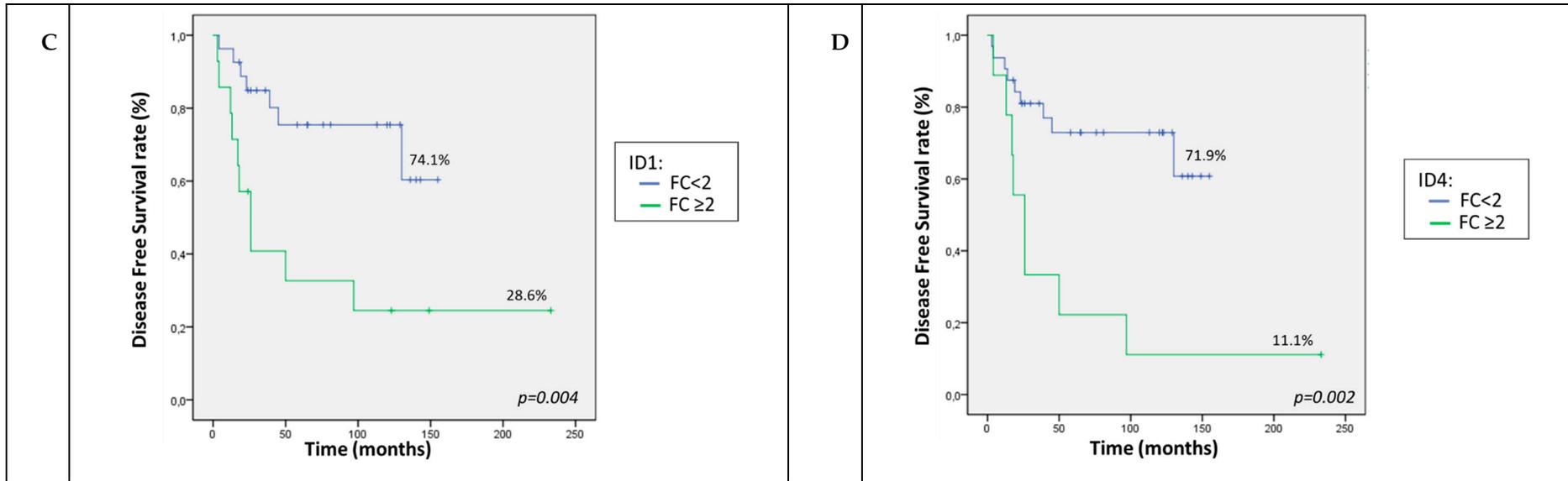


Figure S3. Kaplan-Meier plot for OS (A,B) and DFS (C,D) rates (%) for patients with HER2-enriched tumors classified according to ID1 (A,C) or ID4 (B,D) mRNA expression.