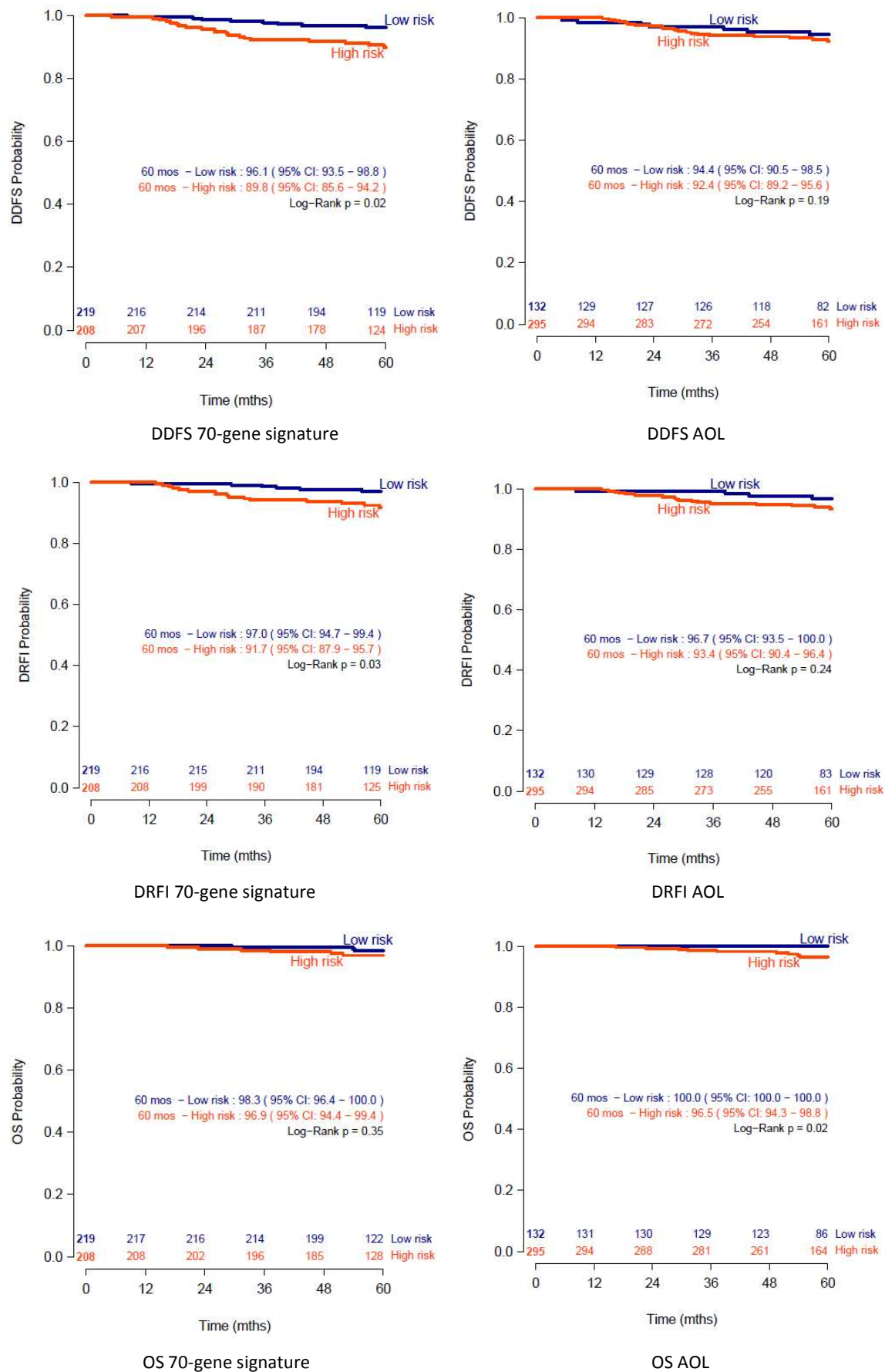


Supplementary figure 1. Kaplan-Meier plots for DDFS, DRFI and OS by 70-gene signature or AOL



Supplementary table 1. Clinico-pathological characteristics by 70-gene signature result

| | | 70-gene signature | 70-gene signature | Total |
|---------------------------|----------------|-----------------------|------------------------|--------------|
| | | Low Risk (219) | High Risk (208) | |
| Age | <35 | 7 (3%) | 19 (9%) | 26 (6%) |
| | 36-40 | 14 (6%) | 27 (13%) | 41 (10%) |
| | 41-45 | 37 (17%) | 47 (23%) | 84 (20%) |
| | 46-50 | 86 (39%) | 55 (26%) | 141 (33%) |
| | 51-55 | 56 (26%) | 44 (21%) | 100 (23%) |
| | >55 | 19 (9%) | 16 (8%) | 35 (8%) |
| pT (TNM) | pT1 (<20mm) | 177 (81%) | 124 (60%) | 301 (70%) |
| | pT2 (>20-50mm) | 42 (19%) | 83 (40%) | 125 (29%) |
| | pT3 (>50mm) | 0 (0%) | 1 (0.5%) | 1 (0.2%) |
| Histological grade | Good | 72 (33%) | 15 (7%) | 87 (20%) |
| | Intermediate | 131 (60%) | 73 (35%) | 204 (48%) |
| | Poor | 16 (7%) | 120 (58%) | 136 (32%) |
| Histological type | Ductal | 162 (74%) | 183 (88%) | 345 (81%) |
| | Lobular | 38 (17%) | 9 (4%) | 47 (11%) |
| | Other | 16 (7%) | 15 (7%) | 31 (7%) |
| | Unknown | 3 (1%) | 1 (0.5%) | 4 (1%) |
| ER status | Negative | 3 (1%) | 82 (39%) | 85 (20%) |
| | Positive | 216 (99%) | 126 (61%) | 342 (80%) |
| PgR status | Negative | 33 (15%) | 100 (48%) | 133 (31%) |
| | Positive | 186 (85%) | 107 (51.5%) | 293 (68.6%) |
| | Unknown | 0 (0%) | 1 (0.5%) | 1 (0.2%) |
| HER2 status | Negative | 197 (90%) | 161 (77%) | 358 (84%) |
| | Positive | 9 (4%) | 39 (19%) | 48 (11%) |
| | Unknown | 13 (6%) | 8 (4%) | 21 (5%) |
| CBO 2004 | Low Risk | 167 (76%) | 76 (37%) | 243 (57%) |
| | High Risk | 52 (24%) | 132 (63%) | 184 (43%) |
| Adjuvant! Online | Low Risk | 95 (43%) | 37 (18%) | 132 (31%) |
| | High Risk | 124 (57%) | 171 (82%) | 295 (69%) |
| Chemotherapy | None | 186 (85%) | 39 (19%) | 225 (53%) |
| | FEC/FAC* | 25 (11%) | 108 (52%) | 133 (31%) |
| | AC** | 7 (3,5%) | 26 (12%) | 33 (8%) |
| | TAC*** | 0 (0%) | 20 (10%) | 20 (5%) |
| | AC-Paclitaxel | 1 (0,5%) | 15 (7%) | 16 (4%) |

*Chemotherapy regimen consisting of fluorouracil, cyclophosphamide and either adriamycine or epirubicine

** Adriamycine and cyclophosphamide

*** Docetaxel, adriamycine and cyclophosphamide

Supplementary table 2. Characteristics of patients with one or more events

| Type of Event | IHC subtype | 70-gene signature | 70-gene signature |
|--|---------------------------------|-------------------|-------------------|
| | | low risk | high risk |
| Locoregional event | ER+HER2- | 4 [‡] | 3 |
| | ER+HER2+ | 0 | 0 |
| | ER-HER2- | 0 | 1 |
| | ER-HER2+ | 0 | 1 |
| | ER+HER2 unknown | 0 | 1 |
| | Median age at diagnosis (range) | 42 (27-46) | 49 (33-59) |
| Distant metastasis event | ER+HER2- | 6* | 5 |
| | ER+HER2+ | 1* | 2 [#] |
| | ER-HER2- | 0 | 8 |
| | ER-HER2+ | 0 | 2 |
| | Median age at diagnosis (range) | 46 (39-57) | 50 (34-59) |
| | Breast cancer-specific death | ER+HER2- | 2 |
| ER+HER2+ | | 0 | 0 |
| ER-HER2- | | 0 | 4 |
| ER-HER2+ | | 0 | 1 |
| Median age at diagnosis (range) | | ND (46-51) | 51 (45-59) |
| Death due to other causes | | | 2 [†] |
| Contralateral breast cancer ^Δ | | 10 [‡] | 4 |
| Second primary tumor | | 2 | 7 |

IHC = immunohistochemistry

[‡]One patient first developed an ipsilateral axillary recurrence, 10 months later followed by a contralateral breast cancer.

*Of these 7 70-gene signature[®]low risk cases, 4 cases were also low risk according to AOL. Of the three AOL high risk cases, only one did not receive any form of AST. This case developed a recurrence at 82 months of follow-up.

[#]One case was AOL low risk and 70-gene signature high risk. No AST was administered. She had a recurrence at 5 months of follow-up.

[†]One patient died due to a cardiac cause. This patient had only received adjuvant radiotherapy of the breast. She had no signs of breast cancer recurrence. She had had an ER+HER2- breast cancer at the age of 57. The second patient died of right-sided primary lung cancer, proven by histology and ER negative immunohistochemistry, two years after the primary diagnosis of invasive lobular breast cancer, ER+HER2-. She had only received adjuvant radiotherapy on the right breast after breast conserving therapy. She had stopped smoking one year before the diagnosis of breast cancer.

^ΔOut of patients with low risk 70-gene signature, only one had received AST. Of 4 high risk 70-gene signature patients, 3 had received AST. One AML (no adjuvant chemotherapy) and one lung cancer in the 70-gene signature low risk group. Four lung cancers, 2 colorectal cancers and 1 carcinoid in the 70-gene signature high risk group.

Supplementary table 3. Kaplan-Meier risk estimations for DRFI using different AOL cut-offs

| AOL cut-off 10-years OS | AOL | Number of patients | 5-years DRFI (%) (95% CI) |
|--------------------------------|------------|---------------------------|----------------------------------|
| 85% | Low | 253 (59.3%) | 97 (95.1-99.5) |
| | High | 174 (40.7%) | 90 (85.8-94.9) |
| 90% | Low | 132 (30.9%) | 97 (93.5-100) |
| | High | 295 (69.1%) | 93 (90.4-96.4) |
| 88% (ER+) / 92% (ER-) | Low | 194 (45.4%) | 98 (88.0-95.0) |
| | High | 233 (54.6%) | 92 (96.0-100) |
| 95% | Low | 19 (4.4%) | 100 (100-100) |
| | High | 408 (95.6%) | 94 (91.8-96.6) |