

Supplementary Information

Phase III study of long-term prognosis of estrogen receptor-positive early breast cancer treated with neoadjuvant endocrine therapy with/without adjuvant chemotherapy

Hiroji Iwata¹, Yutaka Yamamoto², Takehiko Sakai³, Yoshie Hasegawa⁴, Rikiya Nakamura⁵, Hiromitsu Akabane⁶, Shoichiro Ohtani⁷, Masahiro Kashiwaba⁸, Naruto Taira⁹, Tatsuya Toyama¹⁰, Tomomi Fujisawa¹¹, Norikazu Masuda¹², Yukiko Shibahara^{13,#}, Hironobu Sasano¹³, Takuhiro Yamaguchi¹³

¹Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan

²Kumamoto University Hospital, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan

³Cancer Institute Hospital of Japanese Foundation for Cancer Research, 38-31 Ariake, Koto, Tokyo 135-8550, Japan

⁴Hachinohe City Hospital, 3-1-1 Tamukai, Hachinohe 031-8555, Japan

⁵Chiba Cancer Center, 666-2 Nitona-cho, Chuo-ku, Chiba 260-8717, Japan

⁶Hokkaido P.W.F.A.C. Asahikawa-Kosei General Hospital, 1-24-111 Asahikawa 078-8211, Japan

⁷Hiroshima City Hiroshima Citizens Hospital, 7-33 Motomachi, Naka-ku, Hiroshima 730-8518, Japan

⁸Adachi Breast Clinic, 98 Kamigamo Matsumoto-cho, Kita-ku, Kyoto 603-8052, Japan ⁹Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama 701-0192, Japan

¹⁰Nagoya City University Graduate School of Medical Sciences, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467-8601, Japan

¹¹Gunma Prefectural Cancer Center, 617-1 Takahayashinishi-cho, Ota, Gunma 373-8550, Japan

¹²Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

¹³Tohoku University School of Medicine, 2-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8575, Japan

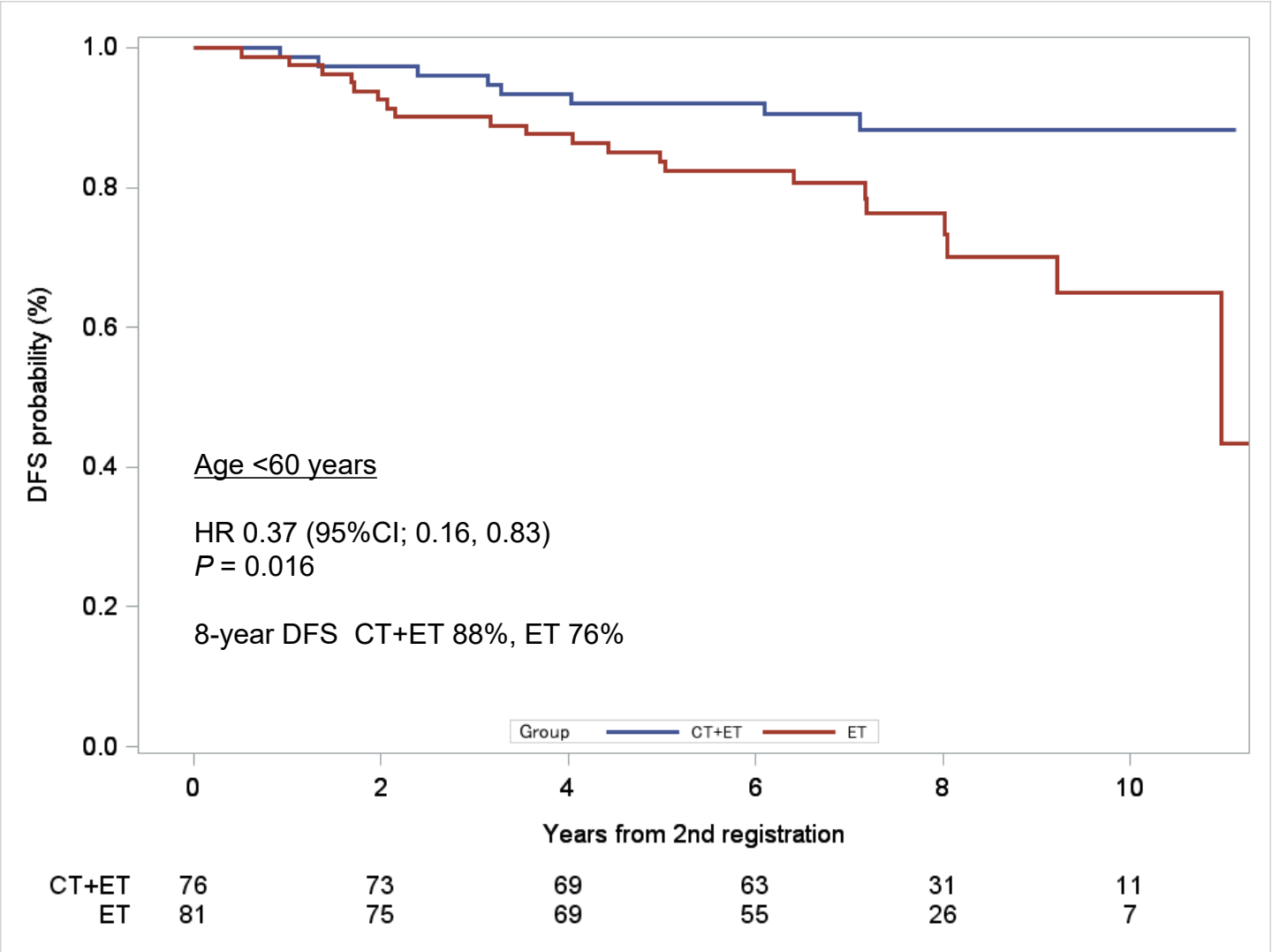
[#]Current affiliation:

Kitasato University, 1-15-1 Kitazato, Minami-ku, Sagami-hara, Kanagawa 252-0373, Japan

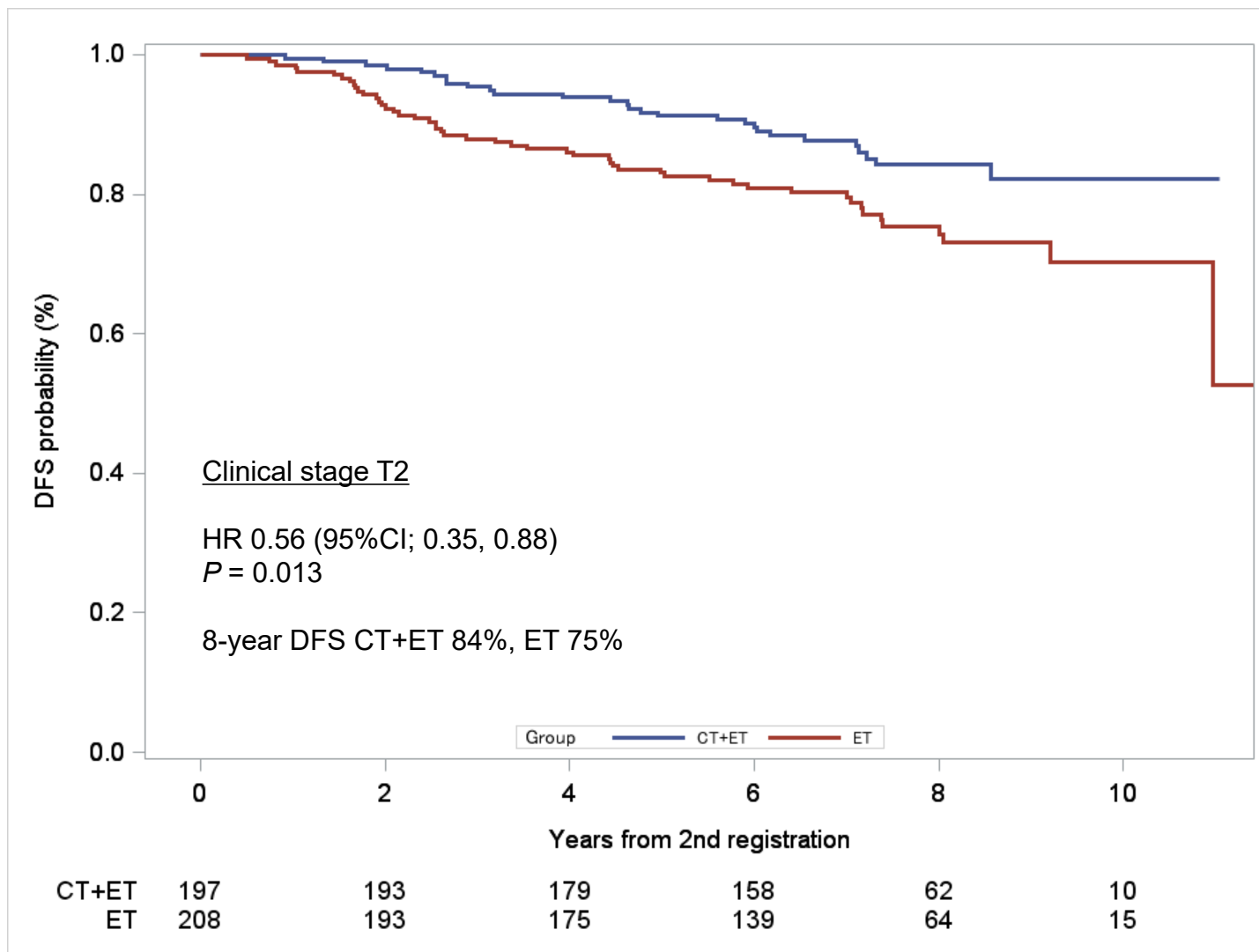
Correspondence to: Hiroji Iwata, Breast Oncology, Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan. Email: hiwata@aichi-cc.jp

Supplementary Figure S1

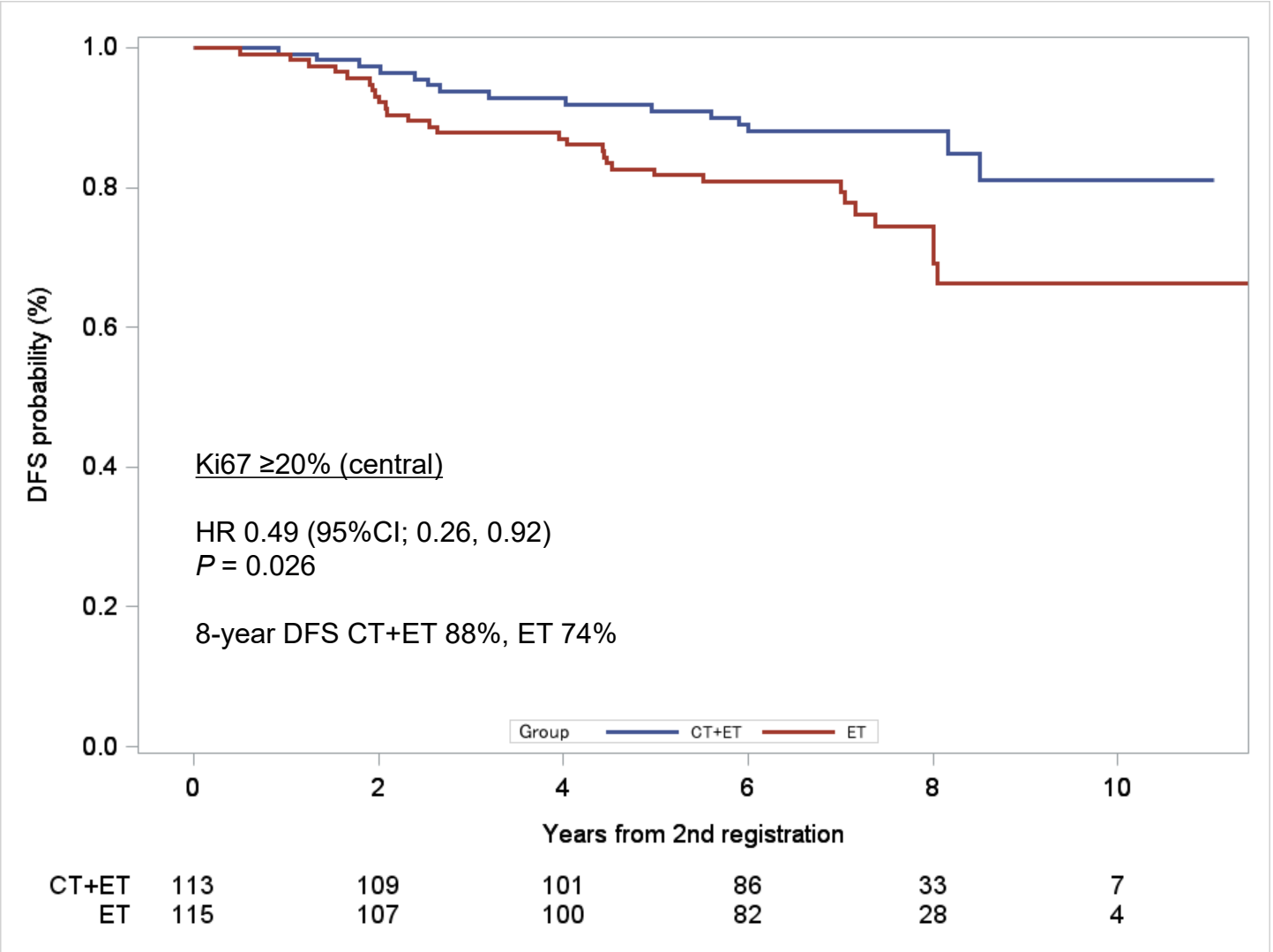
A



B

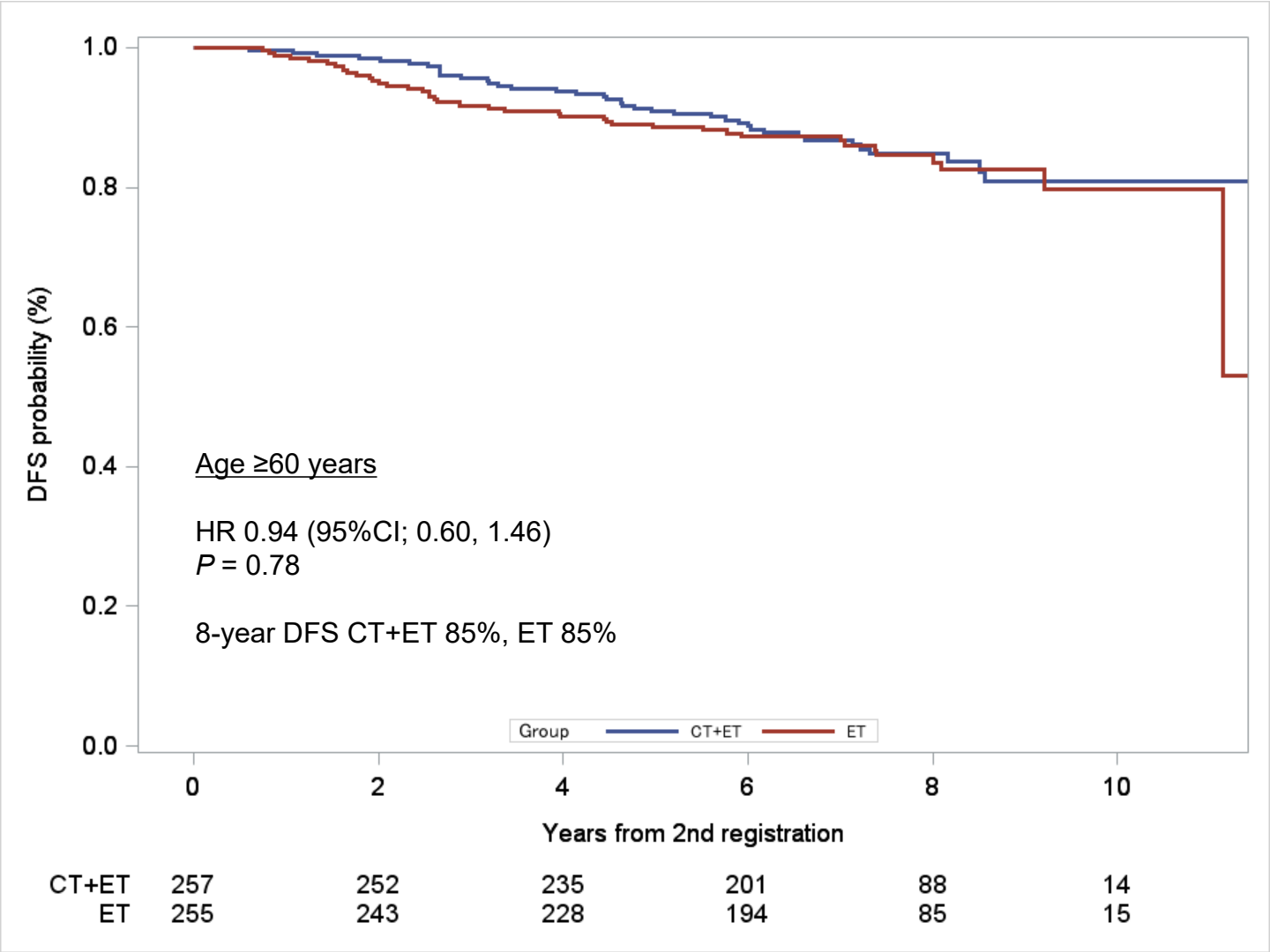


C

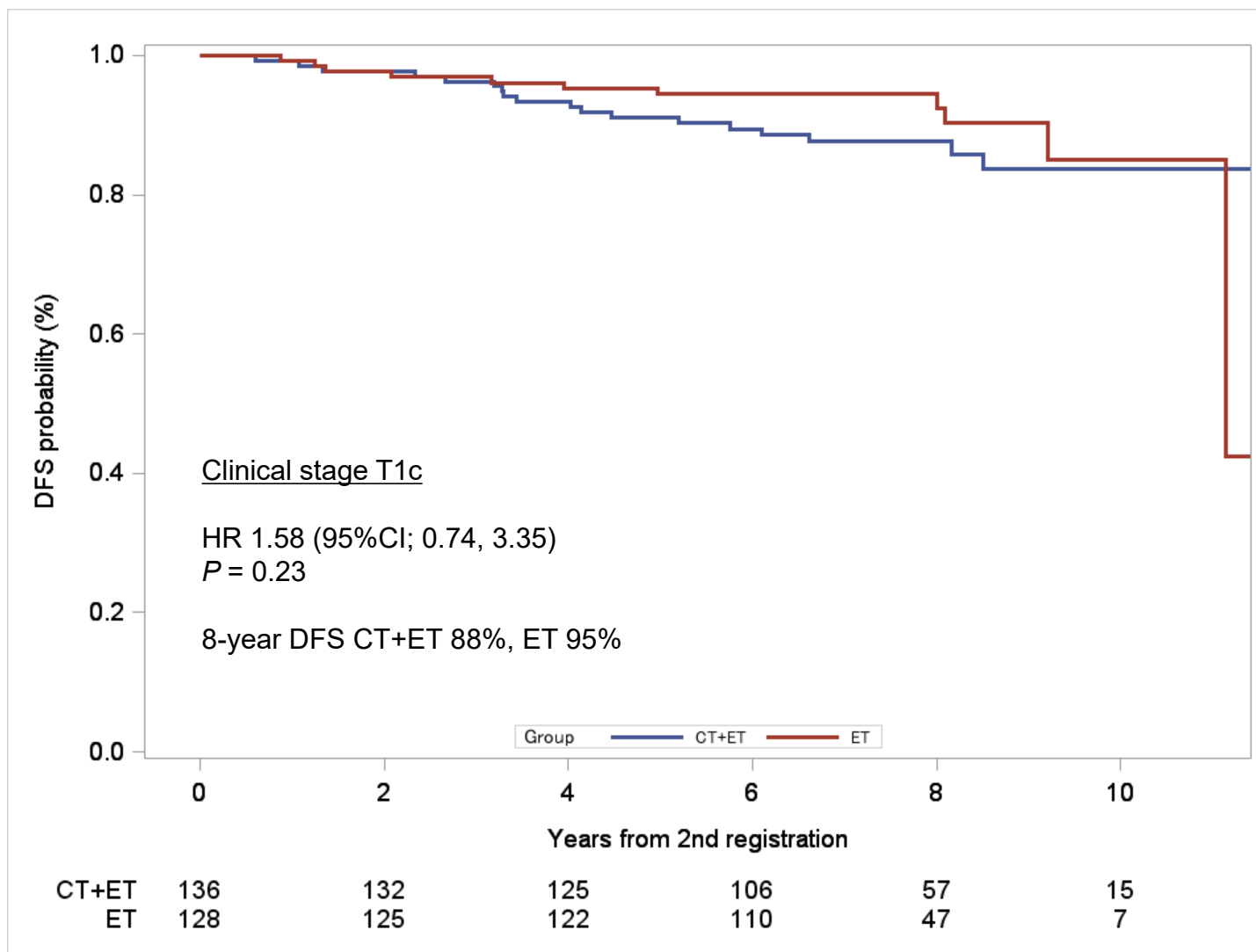


Supplementary Figure S2

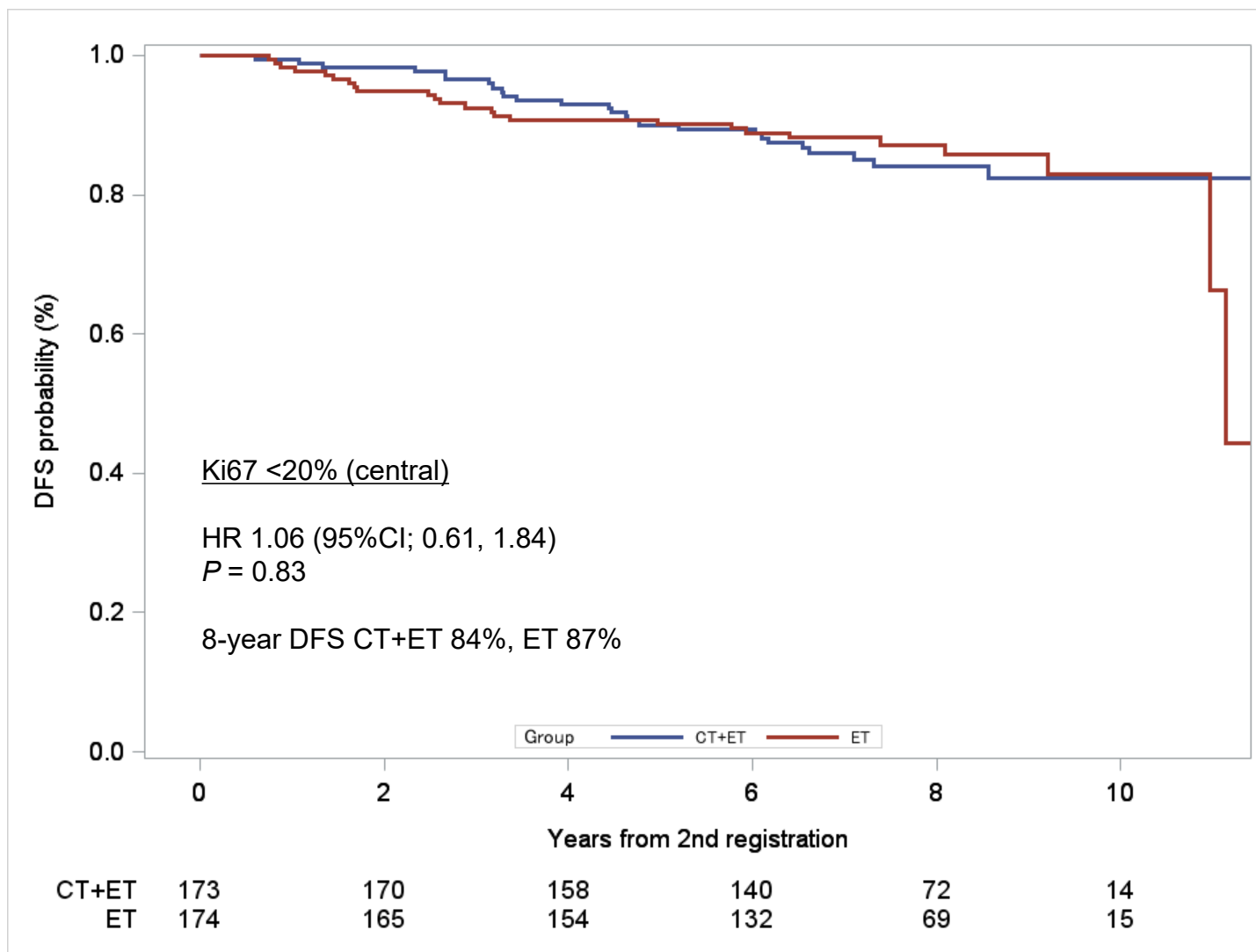
A



B

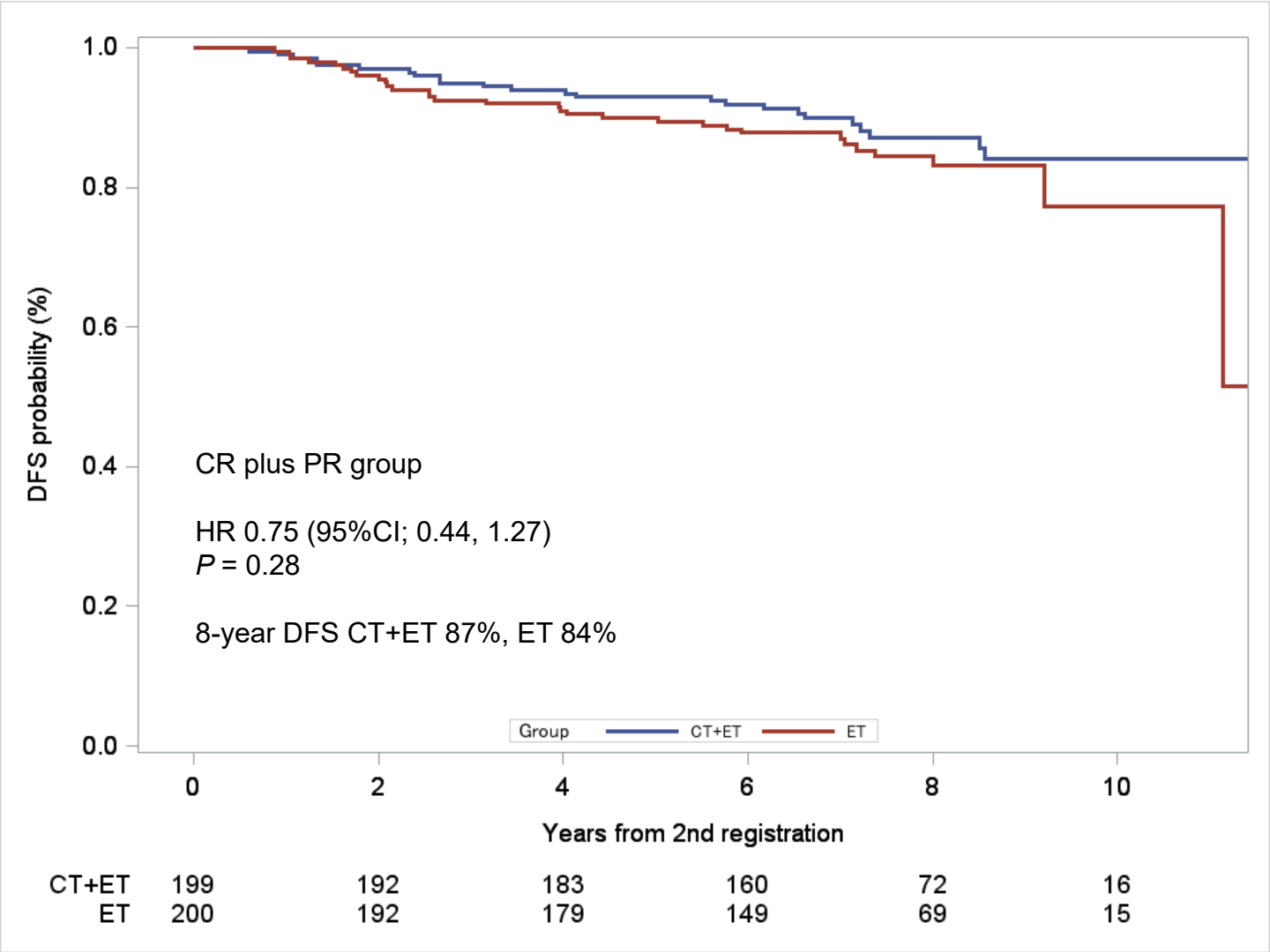


C

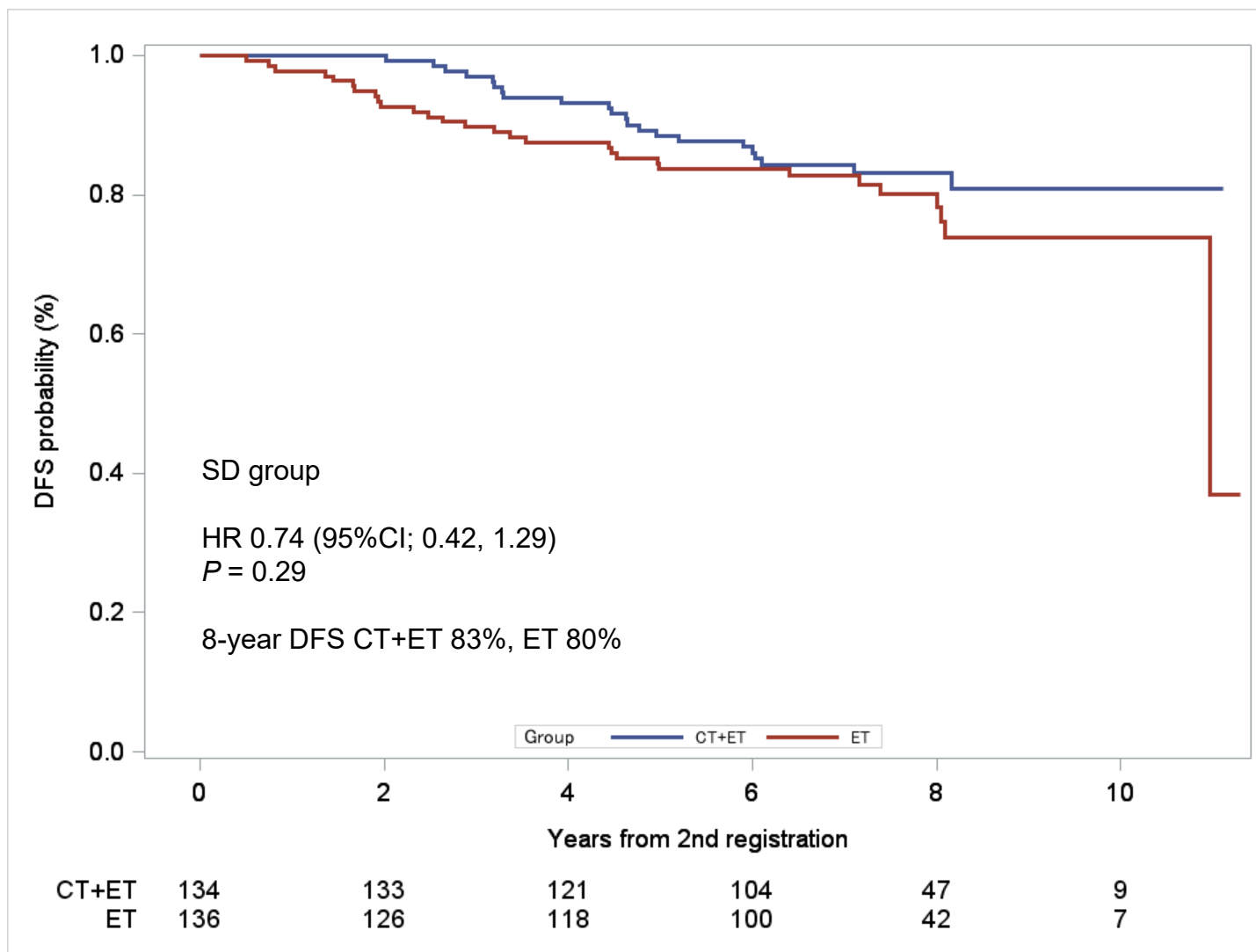


Supplementary Figure S3

A



B



Supplementary Table S1. Chemotherapy regimens in CT + ET group

	CT+ET (patients)
AC/EC	32
FAC/FEC	19
AC/EC/FEC-T	8
TC	144
CMF	63
No chemo	67

AC/EC; adriamycin or epirubicin in combination with cyclophosphamide; CMF, cyclophosphamide, methotrexate, and 5-Fluorouracil; CT, chemotherapy; ET, endocrine therapy; FAC, 5-fluorouracil, adriamycin, and cyclophosphamide; FEC, 5-fluorouracil, epirubicin, and cyclophosphamide; FEC-T, Fluorouracil, epirubicin, cyclophosphamide and docetaxel; TC, docetaxel and cyclophosphamide.

Supplementary Table S2. Predictive markers of clinical response to letrozole

	Odds ratio	(95% CI)	<i>P</i> value
Age ≥65 vs. <65 years	0.72	(0.32–1.63)	0.43
BMI ≥25 vs. <25 kg/m ²	0.45	(0.17–1.20)	0.11
T2 vs. T1c	0.73	(0.31–1.73)	0.48
HG 2 vs. 1	1.98	(0.56–6.95)	0.29
HG 3 vs. 1	10.84	(2.23–52.72)	0.0031
Progesterone receptor positive vs. negative	0.23	(0.10–0.50)	0.0002
HER2 1+ vs. 0 (IHC, local)	0.70	(0.29–1.69)	0.43
HER2 2+ vs. 0 (IHC, local)	0.99	(0.35–2.79)	0.99
Ki67 ≥20% vs. <20% (central)	1.82	(0.79–4.18)	0.16

BMI, body mass index; CI, confidence interval; HG, histological grade; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry.