Results: 153 women were surveyed with a median age of 60. 51% had node-negative disease, 89% had prior radiation, 61% had prior chemotherapy and 59% had prior tamoxifen therapy. The mean duration of AI therapy was 31 months. 30% of women required a 5-year survival benefit of less than 1% and 27.5% needed a decrease in recurrence risk of less than 1% to continue an AI beyond 5 years. In contrast, none of the 40 MOs surveyed felt a survival benefit or decrease in recurrence risk of less than 1% was sufficient to prescribe an AI for an additional 5 years. There was a significant correlation between increased severity of menopausal/endocrine symptoms experienced on AIs and an increased minimum survival benefit required for women to continue therapy ($p = 0.036$).

Conclusions: While approximately one-third of patients are willing to continue AIs for a benefit of less than 1%, no physician surveyed is willing to prescribe an AI beyond 5 years for this benefit. Patients' willingness to continue AIs beyond 5 years correlates to the severity of the side effects they experienced while on AIs.

Patient & physician opinion of minimum benefit required to continue AIs beyond 5 years

	<1%	1–2%	2–5%	5–10%	10–15%	15–20%	>20%	Unknown
Patient opinion:								
Survival benefit	46 (30.1%)	22 (14.4%)	18 (11.8%)	19 (12.4%)	6 (3.9%)	6 (3.9%)	26 (17.0%)	10 (6.5%)
Decrease in recurrence	42 (27.5%)	22 (14.4%)	20 (13.1%)	22 (14.4%)	7 (4.6%)	9 (5.9%)	22 (14.4%)	9 (5.9%)
Physician opinion:								
Survival benefit	0 (0.0%)	18 (45.0%)	15 (37.5%)	5 (12.5%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (2.5%)
Decrease in recurrence	0 (0.0%)	1 (2.5%)	15 (37.5%)	14 (35.0%)	5 (12.5%)	0 (0.0%)	1 (2.5%)	4 (10.0%)

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Defining a numerical threshold for chemotherapy using Adjuvantonline

G. Wishart[1], L. Hughes-Davies[2]. [1]*Addenbrooke's Hospital, Breast Unit, Cambridge, United Kingdom;* [2]*Addenbrooke's Hospital, Oncology, Cambridge, United Kingdom*

Background: Adjuvantonline (Aol) is a decision support tool used by oncologists to compute the absolute benefit from adjuvant therapies including chemotherapy. It allows individualised discussion with the patient. This approach has supplanted more general consensus recommendations from the St Gallen and NIH Panels. However, both St Gallen and the NIH explicitly recognise a threshold for chemotherapy. We have found that one drawback to Aol is the absence of a clear threshold to begin chemotherapy discussions. In this study, we seek to evaluate such a threshold.

Methods: We used Aol to estimate the absolute benefit from chemotherapy in a group of 295 patients whose gene expression risk profile had been previously been determined with Mammaprint. We then varied the Aol numerical threshold for a decision to treat in order to examine the effect of this threshold on the accuracy of patient selection for chemotherapy.

Results: Aol's ability to select high risk patients and exclude low risk patients from chemotherapy is comparable to (but no better than) treatment decisions based on the NIH and the St Gallen recommendations. Its accuracy improves as the threshold is increased to 3%, and then plateaus (see table).

Effect of varying Aol threshold for a chemotherapy recommendation in 295 patients previously sorted into high risk and low risk groups by gene expression profiling. (A false positive decision would give chemotherapy to a low risk patient; false negative decision would withhold chemotherapy from a high risk patient).

AOL benefit (%)	false positive (%)	false negative (%)	accuracy (%)
1	83	2	58
2	66	10	62
3	48	14	69
4	41	23	68
5	23	33	72
6	20	41	70

Conclusions: This study allows oncologists to evaluate an Adjuvantonline numerical threshold below which chemotherapy need not be discussed. We suggest that it can be used to support a "3% discuss, 5% recommend" threshold. This quantitative Adjuvantonline threshold would be broadly compatible with those that had earlier been agreed at the St Gallen and NIH Consensus conferences, would standardise chemotherapy use between different breast units, and would allow patients to be spared the distress of an unnecessary chemotherapy discussion.

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Breast conservation and long term survival after neo-adjuvant chemotherapy

M. Debled[1], L. Mauriac[1], I. de Mascarel[2], V. Brouste[3], F. Bonichon[4], A. Avril[5]. [1]*Institut Bergonié, Medical Oncology, Bordeaux, France;* [2]*Institut Bergonié, Pathology, Bordeaux, France;* [3]*Institut Bergonié, Biostatistics, Bordeaux, France;* [4]*Institut Bergonié, Nuclear Medicine, Bordeaux, France;* [5]*Institut Bergonié, Surgery, Bordeaux, France*

From 01.1985 to 04.1998, a randomised trial was conducted to compare first line mastectomy followed with adjuvant medical treatment (n = 138) to neo-adjuvant chemotherapy followed with adjusted loco-regional treatment (n = 134) for women with too big tumours to be treated with immediate conserving surgery.

After total mastectomy, patients received adjuvant chemotherapy (n = 110) in case of histological nodal involvement (n = 82) or absence of oestrogen and progesterone receptor (n = 28). Patients without these poor prognostic factors (n = 28) did not received adjuvant medical treatment. No irradiation was delivered in this group.

After neo-adjuvant treatment 63% of patients had conserving treatment: 33% had exclusive irradiation thanks to clinical complete response and 30% had conserving surgery followed with breast irradiation in case of residual tumour smaller than 2 cm. Remaining patients (37%) were treated with total mastectomy without irradiation because of residual tumour bigger than 2 cm.

With a 20 year median follow-up, overall survival and distant disease free survival are identical between the two groups, being both 55% at 15 year respectively.

As a stratification was done before randomisation between positive and negative steroid receptor, we can analyse distant disease free survival in these 2 subgroups: there is no difference between neo-adjuvant chemotherapy and first line mastectomy. But EPR negative tumours have earlier recurrences than positive tumours, whereas positive tumours have more frequently late recurrences.

Patients treated with neo-adjuvant chemotherapy had more often local recurrences (breast, chest wall, axillary or internal mammary nodes), due to exclusive irradiation given in case of clinical complete response. Nevertheless, in this subgroup of non-operated women, recurrences were more often localized in axilla (n = 10) than in breast (n = 4). Finally with this very long follow-up, one out of 4 breast-sparing patients had secondary salvage mastectomy because of local recurrence. A large majority of these local recurrences (80%) occurred within the first 5 years.

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A randomized feasibility/phase II study (SBG 2004-1) with dose-dense/tailored epirubicin, cyclophoshamide (EC) followed by docetaxel (T) or fixed dosed dose-dense EC/T versus T, doxorubicin and C (TAC) in node-positive breast cancer

S. Margolin[1], L. Carlsson[2], M. Hellström[1], P. Karlsson[3], E. Lidbrink[1], B. Linderholm[4], H. Lindman[5], P. Malmström[6], D. Sköld Pettersson[1], J. Bergh[1]. [1]*Karolinska University Hospital, Department of Oncology, Stockholm, Sweden;* [2]*Sundsvall hospital, Department of Oncology, Sundsvall, Sweden;* [3]*Sahlgrenska University Hospital, Department of Oncology, Gothenburg, Sweden;* [4]*Linköping University Hospital, Department of Oncology, Linköping, Sweden;* [5]*Uppsala University Hospital, Department of Oncology, Uppsala, Sweden;* [6]*Lund University Hospital, Department of Oncology, Lund, Sweden*

Background: The primary aim of the study was to evaluate the toxicity and feasibility of a both tailored (possibility of dose escalation) and dose-dense (biweekly) EC/T and of the same regimen given with fixed doses as adjuvant breast cancer therapy. The TAC regimen served as a standard arm.

Patients and Methods: Patients with node-positive breast cancer were randomized to either four cycles of biweekly and tailored EC (dose range: epirubicin 38–90–120 mg/m^2, cyclophosphamide 450–600–1200 mg/m^2) followed by four cycles of docetaxel (60–75–90 mg/m^2) (arm A) or to the same regimen with fixed doses (E90C600 x 4 $\rightarrow$ T75 x 4) (arm B) or to docetaxel, adriamycin and cyclophosphamide (T75A50C500 x 6) every third week (arm C). All regimens were given with G-CSF support and prophylactic ciprofloxacin. The toxicity was evaluated according to NCI, CTC, version 3.0.

Results: Between November 2005 and May 2006 124 patients were randomized. A total of 305 (arm A), 315 (arm B) and 222 (arm C) cycles