1.5–61.4 months), the hazard ratio (HR) for DFS in the overall population was 0.58 (0.45–0.76, p = 0.00004) in favor of letrozole. Almost all patients (97.4%) had estrogen receptor (ER) and/or progesterone receptor (PgR) positive primary tumors.
Materials and Methods: Both ER and PgR values were known in 4653 patients and retrospective exploratory analyses were conducted to compare time to recurrence in the four receptor sub-groups by ER (±) and PgR (±) status. ER and PgR positivity was defined as ⩾10 fmol/mg protein, or positive by ERICA or PgRICA.
Results: The results are shown below. As indicated the benefit of letrozole was most pronounced in women with ER+PgR+ and ER-PgR+ tumors. The ER+PgR+ compared with the ER+PgR− group indicated a statistically significant difference in the treatment effect between them (p = 0.02) however this was not a pre-planned comparison. Adjustment for nodal status and prior adjuvant chemotherapy did not affect this result.

	n	Letrozole (L) events	Placebo (P) events	HR* L vs P (95%CI)
ER+ PgR+	3809	60 (3%)	117 (6%)	0.50 (0.36–0.68)
ER+ PgR−	636	19 (6%)	17 (5%)	1.19 (0.62–2.29)
ER7minus; PgR+	200	4 (4%)	5 (5%)	0.62 (0.17–2.31)
ER− PgR−	8	–	–	–

*Hazard ratios for event in DFS (HR less than one indicates value in favor of letrozole)

Conclusions: The effect of letrozole in this placebo-controlled trial appears most pronounced in women with the most hormone dependent, ER+ PgR+, tumors. Its apparent benefit in ER− PgR+ve tumors and lack thereof in ER+ PgR− implies activity of letrozole against disease with a functional ER. The results presented here should be interpreted with caution as it was an unplanned analysis, there is overlap between the HR's and the receptor levels were measured locally. A plan for central measurement and comparison of standard ER and PgR levels is now underway.

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Gynaecological adverse events and hysterectomies in the ATAC ('Arimidex', Tamoxifen, Alone or in Combination) trial

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Background: The Completed Treatment Analysis of the ATAC trial at a median follow-up of 68 months showed that anastrozole is a more effective and better tolerated treatment than tamoxifen as primary adjuvant treatment for postmenopausal women (n = 9366) with hormone-sensitive early breast cancer (EBC). Treatment with anastrozole was associated with significant reductions in the incidence of predefined gynaecological adverse events (AEs) compared with tamoxifen: vaginal bleeding 5.4% vs 10.2%, p < 0.0001; vaginal discharge 3.5% vs 13.2%, p < 0.0001; endometrial cancer 0.2% vs 0.8%, p = 0.02.
Methods: This retrospective analysis investigated all gynaecological AEs and hysterectomies recorded on the ATAC main trial database.

Diagnoses leading to hysterectomy in the ATAC trial

	Anastrozole (n = 2228)[a] n (%)	Tamoxifen (n = 2236)[a] n (%)
Hysterectomy all diagnoses	30 (1.3)	115 (5.1)
Malignancy	7 (0.3)	20 (0.9)
Benign	23 (1.0)	95 (4.2)
Prolapse	7 (0.3)	32 (1.4)
Fibroids	8 (0.4)	15 (0.7)
Polyps	1 (< 0.1)	14 (0.6)
Ovarian cysts	2 (0.1)	4 (0.2)
Other	5 (0.2)	30 (1.3)

[a]Patients with an intact uterus at baseline

Results: Overall, gynaecological AEs were significantly less common with anastrozole compared with tamoxifen (20.5% vs 34.2%, p < 0.0001). This difference was largely accounted for by lower incidences of endometrial hyperplasia (0.7% vs 6.1%*), endometrial neoplasia (1.0% vs 5.3%*), leucorrhoea (2.7% vs 9.2%), and vaginal haemorrhage (5.2% vs 8.3%*) with anastrozole compared with tamoxifen [*Percentages derived from patients with an intact uterus at baseline]. Treatment with anastrozole was also associated with an almost four-fold reduction in the incidence of hysterectomy due to both malignant and benign diagnoses in women with an intact uterus at baseline (Table). The majority of gynaecological AEs occurred during the first 2.5 years of treatment.
Conclusions: Not only is treatment with anastrozole associated with a significantly lower risk of gynaecological AEs compared with tamoxifen but the substantially higher hysterectomy rate in women treated with tamoxifen compared with those treated with anastrozole is a cause for concern. Thus, treatment with anastrozole rather than tamoxifen may avoid the psychological distress and associated costs of investigations and/or treatment for gynaecological side effects for many women. The findings of this analysis further support that anastrozole should now be considered the preferred primary adjuvant treatment for postmenopausal women with EBC.

Oral presentations (Wed, 2 Nov, 9.15–11.15)
Early breast cancer – issues related to locoregional therapy

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Lumpectomy plus tamoxifen or arimidex with or without whole breast irradiation in women with favourable early breast cancer

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Background: In women with favourable early breast cancer treated by lumpectomy plus tamoxifen or arimidex it remains unclear, whether breast irradiation is beneficial with regard to local control, disease-free and overall survival.
Methods: Between 1/1996 and 6/2004, the Austrian Breast and Colorectal Cancer Study Group (ABCSG) randomly assigned 875 women (24 ineligible, 25 excluded: total 826) within the clinical ABCSG trial 8 (Jakesz et al., SABCS 2004) to receive whole breast irradiation ± boost (group I, n = 410) or not (group II, n = 416) (ABCSG study 8A). Favourable early breast cancer was specified as tumour size <3 cm, negative lymph nodes, positive estrogen and/or progesteron receptor status, and manageable by breast conserving surgery. Breast radiotherapy was performed after lumpectomy with two tangential opposed breast fields with 50 Gy plus boost in 66% of patients with 10 Gy, median in 6 weeks.
Primary endpoint was local relapse. Further endpoints were contra-lateral breast cancer, distant metastases, disease-free and overall survival. The median follow-up was 42 months.
Results: Mean age was 66 years (±8). Overall, there were 14 local relapses (1.7%), with 1 local relapse in the irradiated group (I) (0.2%) versus 13 local events in the non-irradiated group (II) (3.1%) (p = 0.001). Contra-lateral breast cancer was 0 versus 4, respectively (p = 0.04). Overall, there were 9 pts. with distant metastases, 5 (1.2%) versus 4 (0.96%) in group I and II, respectively (p = 0.76). Overall recurrence was in 46 pts. with 18 events (4.4%) in group I versus 28 events (6.7%) in group II (p = 0.12). Overall survival was 97.2% (23 events) with 97.8% (9 events) in group I versus 96.6% (14 events) in group II (p = 0.28).
Conclusion: Whole breast radiotherapy ± boost in women with favourable early breast cancer after lumpectomy combined with tamoxifen/arimidex leads to a significant reduction in local relapse and contra-lateral breast cancer. After a median follow-up of 42 months, there is no significant impact on distant metastases, disease free and overall survival.