

Adis Clinical Trials Insight: Presented at Meetings – Women's Health

The table below highlights some of the randomised trials presented during sessions at the meetings described.

Annual San Antonio Breast Cancer Symposium (32nd : December 2009 : San Antonio, Texas, USA)

Adis CTI Record	Drug(s)	Purpose	Study Results	Sponsor
1 803004486	Cyclophosphamide Doxorubicin Fluorouracil Paclitaxel	This study investigated the performance of a 30-gene predictor of pathological complete response (pCR) in patients who received either neoadjuvant paclitaxel then fluorouracil + doxorubicin + cyclophosphamide (FAC) or FAC alone in women with stage I-III breast cancer.	A 30-gene predictor of pathological complete response (pCR) successfully predicted the treatment response to neoadjuvant paclitaxel then fluorouracil + doxorubicin + cyclophosphamide (FAC) in women with stage I-III breast cancer. Patients who were predicted to achieve a pCR had a significantly higher pCR rate (38%) than unselected patients (19%). Paclitaxel + FAC resulted in a higher pCR rate than FAC alone (19% vs 9%; p<0.05).	
2 803005024	Anastrozole Tamoxifen	This study compared the cost effectiveness of anastrozole, tamoxifen and radiotherapy for the adjuvant treatment of elderly women with node-negative, estrogen receptor (ER)-positive, early breast cancer following lumpectomy in the USA.	Tamoxifen appeared to be cost effective compared with anastrozole and radiotherapy for the adjuvant (following lumpectomy) treatment of elderly women with node-negative, estrogen receptor-positive, early breast cancer in the USA. The treatment failure rates (recurrence of ipsilateral or contralateral breast cancer) were 5.32%, 3.41% and 5.25% in the radiotherapy, anastrozole and tamoxifen groups, respectively, and this resulted in total costs per patient of \$US12,252, \$US18,987, and \$US1,540, respectively.	
3 803005047	Capecitabine Docetaxel Epirubicin Trastuzumab	This study investigated the safety and efficacy of neoadjuvant epirubicin + docetaxel + capecitabine, compared with epirubicin and docetaxel alone, in patients with operable early breast cancer. Also, the efficacy of the addition of trastuzumab to the above regimens was investigated in patients with HER-2 positive early breast cancer. The primary endpoint was the complete pathological response rate (pCR) at the time of surgery.	Neoadjuvant epirubicin + docetaxel + capecitabine was associated with a similar incidence of adverse events to epirubicin + docetaxel alone, in patients with operable early breast cancer (26% vs 21%).; Neoadjuvant epirubicin + docetaxel + capecitabine was associated with significantly higher rates of complete pathological response than epirubicin + docetaxel alone (primary endpoint; 24% vs 15%; p	
4 803004892	Cyclophosphamide Epirubicin Fluorouracil Lapatinib Paclitaxel	The ongoing phase IIb CHER-LOB study examined the efficacy and tolerability of neoadjuvant paclitaxel followed by fluorouracil + epirubicin + cyclophosphamide (FEC) with trastuzumab and/or lapatinib in patients with	Neoadjuvant therapy with paclitaxel + fluorouracil + epirubicin + cyclophosphamide administered concurrently with trastuzumab and/or lapatinib appeared to be generally well tolerated, with respect to cardiac toxicity, in patients with HER2-positive stage IIa-III breast cancer.	GlaxoSmithKline

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	Trastuzumab	HER2-positive, stage II-III breast cancer. The primary endpoint of the study was the complete pathological response (pCR) rate. Tolerability results from the first 66 randomised and evaluable patients were reported, as were the pCR results from the 45 patients who underwent surgery.	The mean left ventricular ejection fraction was 61%-62% in all three groups. [CONT.]	
5 803004897	Cyclophosphamide Docetaxel Epirubicin Lapatinib Trastuzumab	This interim safety analysis of the GeparQuinto trial investigated the tolerability associated with lapatinib (L) compared to trastuzumab when administered with epirubicin, cyclophosphamide and docetaxel as neoadjuvant treatment of HER2-positive breast cancer.	Lapatinib and trastuzumab were both well tolerated when administered with epirubicin, cyclophosphamide and docetaxel as neoadjuvant treatment of HER2-positive breast cancer. Lapatinib was associated with more grade 1/2 skin rash (28% vs 7%), and less grade 1/2 anaemia (28% vs 52%).	
6 803005065	Bevacizumab Cyclophosphamide Docetaxel Epirubicin Everolimus Paclitaxel	The internal pilot phase for safety of this study investigated the tolerability of epirubicin + cyclophosphamide +/- bevacizumab, followed by paclitaxel + everolimus in non-responders (less than 50% decrease in tumour size), in patients with untreated breast cancer. This reports on a planned safety analysis of 60 patients with HER-2 negative disease.	Bevacizumab in combination with epirubicin + cyclophosphamide was associated with more grade 3-4 neutropenia (70% vs 41%; p	
7 803004501	Exemestane Tamoxifen	The TEAM study compared the efficacy and tolerability of adjuvant exemestane versus tamoxifen for the treatment of postmenopausal women with hormone receptor-positive early breast cancer. This analysis focused on the second primary endpoint of DFS at 5 years for exemestane versus tamoxifen then exemestane.	This study compared the efficacy of exemestane with tamoxifen followed by a switch to exemestane for the treatment of postmenopausal women with hormone receptor-positive early breast cancer. The primary endpoint of focus was the disease-free survival at 5 years. Results data were not presented.	Pfizer
8 803004867	Zoledronic-acid	This study compared the cost effectiveness of delayed and up-front zoledronic acid and no zoledronic acid for the prevention of osteoporotic fractures in postmenopausal women with hormone receptor-positive early breast cancer (EBC) with a bone mineral density (BMD) T-score of greater than or	Delayed and up-front zoledronic acid appeared to be cost effective compared with no zoledronic acid for the prevention of osteoporotic fractures in postmenopausal women with hormone receptor-positive early breast cancer with a baseline bone mineral density T-score of greater than or equal to -2 receiving adjuvant letrozole in the UK. Compared with no zoledronic acid, the up-front	Novartis Oncology

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		equal to -2 at baseline receiving adjuvant letrozole in the UK.	and delayed zoledronic acid strategies had incremental costs per quality-adjusted life-year (QALY) gained of GBP16,069 and GBP21,973, respectively. [CONT.]	
9 803004490	Exemestane Tamoxifen	This study compared the efficacy and tolerability of switching to exemestane versus continuing tamoxifen in women with early breast cancer who had already received 2-3 years of adjuvant tamoxifen treatment. Here, long-term follow-up efficacy data were reported, with respect to disease-free and overall survival outcomes.	After a median of 91 months follow-up, switching to exemestane was associated with significantly improved long-term disease-free survival outcomes, compared with continuing tamoxifen (hazard ratio [HR] 0.81; 95% CI 0.71, 0.92; p=0.001), as well as improved overall survival outcomes (HR 0.86; 95% CI 0.75, 0.99; p	Pfizer, Pharmacia
10 803004575	Anastrozole Exemestane	This study investigated the effects of new vasomotor or joint symptoms on relapse-free survival (RFS) in postmenopausal women with hormone-receptor-positive early breast cancer (with no relapse in the first 3 months) receiving either adjuvant anastrozole or exemestane.	There was no correlation between the emergence of the emergence of new vasomotor or joint symptoms and an improvement in the relapse-free survival (RFS) in postmenopausal women with hormone-receptor-positive early breast cancer (with no relapse in the first 3 months of treatment) receiving either adjuvant anastrozole or exemestane. RFS was not statistically significant between the women with or without new symptoms (hazard ratio 1.129; 95% CI, 0.708, 1.800).	
11 803004205	Letrozole Zoledronic-acid	This study compared the biological effects of neoadjuvant zoledronic acid in addition to letrozole compared with letrozole alone or no treatment in postmenopausal women with early-invasive, hormone receptor-positive breast cancer. The primary study endpoint was the reduction in in Ki-67 levels between diagnosis and surgical excision.	Letrozole + zoledronic acid and letrozole alone had similar effects on Ki-67 levels (primary endpoint) when administered as neoadjuvant therapy in women with hormone receptor-positive, early-invasive, breast cancer. The reductions in the Ki-67 levels were +0.8, 8.6, and 12.9 in the placebo, letrozole, and letrozole + zoledronic acid groups, respectively (p	Novartis
12 803004198	Tamoxifen	This study investigated whether p21-activated kinase 1 (Pak1) and phosphorylation of the estrogen receptor (ER) alpha305 (pERalpha305) predicted the treatment response to tamoxifen in postmenopausal women with node-negative, ER-positive breast cancer.	Nuclear expression of p21-activated kinase 1 (Pak1) and phosphorylation of the estrogen receptor alpha305 predicted a reduced response to adjuvant tamoxifen (tamoxifen vs no tamoxifen, hazard ratio 1.33; 95% CI 0.42, 4.2) in postmenopausal women with node-negative, estrogen receptor-positive breast cancer; whereas, patients without this combination of protein expression benefited from tamoxifen (hazard ratio 2.02; 95% CI 1.16, 3.52; p<0.001).	

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13 803004196	Carboplatin Cetuximab	This trial evaluated the efficacy and associated predictive markers of cetuximab (C) +/- carboplatin in women with estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 negative, metastatic breast cancer (MBC).	Cetuximab +/- carboplatin improved progression-free survival, particularly in patients with high levels of epidermal growth factor receptor and phosphatase and tensin homolog expression and low levels of alpha basic crystallin and Kirsten rat sarcoma viral oncogene (in patients with basal-like breast cancer) expression, in women with estrogen receptor, progesterone receptor and human epidermal growth factor receptor negative, metastatic breast cancer.	Bristol-Myers Squibb
14 803004197	Carboplatin Cetuximab Irinotecan	This trial evaluated the efficacy and potential predictive markers of irinotecan + carboplatin +/- cetuximab (C), in women with triple negative (estrogen, progesterone and human epidermal growth factor receptors [ER, PR and HER2, respectively]) or ER+/HER-, metastatic breast cancer (MBC).	Addition of cetuximab to irinotecan + carboplatin improved objective response rate in patients who were estrogen receptor (ER), progesterone receptor and human epidermal growth factor receptor (HER2) negative but not in those who were ER+/HER2-, and further benefits were seen in patients who had high HER2, high phosphatase and tensin homolog and low alpha basic crystallin levels (all in those with nonbasal-like breast cancer) and who lack Kirsten rat sarcoma viral oncogene (in those with [CONT.]	Bristol-Myers Squibb
15 803005121	Cyclophosphamide Docetaxel Epirubicin Fluorouracil	This study compared the efficacy and tolerability of adjuvant fluorouracil + docetaxel versus no adjuvant therapy in women with inflammatory breast cancer who had received neoadjuvant epirubicin + cyclophosphamide then surgery then radiotherapy. The primary endpoint was disease-free survival.	Adjuvant fluorouracil + docetaxel was associated with a similar three-year disease-free survival rate to no adjuvant therapy (63% vs 60% of patients; primary endpoint) as well as a similarly high five-year survival rate (70% vs 70% of patients) in women with inflammatory breast cancer who had undergone neoadjuvant epirubicin + cyclophosphamide therapy then surgery then radiotherapy.; Neoadjuvant epirubicin + cyclophosphamide was associated with increased grade 3/4 vomiting, infection, fever and nausea (53%, 13%, 9% and [CONT.]	
16 803005089	Cyclophosphamide Doxorubicin Doxorubicin-liposomal Paclitaxel Trastuzumab	This trial compared the cardiovascular tolerability of doxorubicin liposomal [PLD; Caelyx] + cyclophosphamide (C) + trastuzumab [Herceptin; H] with doxorubicin + cyclophosphamide, both followed by paclitaxel + trastuzumab, when given for the adjuvant treatment of women with HER2-positive	No level 1 or 2 cardiovascular events (primary endpoint) were observed with doxorubicin liposomal + cyclophosphamide + trastuzumab nor doxorubicin + cyclophosphamide when both were followed by paclitaxel + trastuzumab for the adjuvant treatment of women with HER2-positive breast cancer. A significant reduction from baseline in left ventricular ejection fraction was observed	Schering-Plough

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		(HER2+) breast cancer. The primary outcomes were the overall incidence of level 1 and 2 cardiac events during eight courses of therapy.	with doxorubicin + cyclophosphamide (p	
17 803005061	Cyclophosphamide Docetaxel Doxorubicin Paclitaxel	This trial investigated the incidence of oedema and weight gain and the effects on patient quality-of-life associated with four taxane-containing regimens in women with node-positive breast cancer who have undergone surgery. Patients were randomised to doxorubicin + cyclophosphamide followed by paclitaxel (regimen 1), doxorubicin + cyclophosphamide followed by docetaxel (regimen 2), paclitaxel alone (regimen 3) or docetaxel alone (regimen 4).	Adjuvant docetaxel, alone or in combination with cyclophosphamide + doxorubicin, was associated with greater weight gain from baseline than paclitaxel and cyclophosphamide + doxorubicin + paclitaxel (p	
18 803005023	Cyclophosphamide Docetaxel Doxorubicin Fluorouracil	This study compared the cost effectiveness of docetaxel + doxorubicin + cyclophosphamide (TAC) and fluorouracil + doxorubicin + cyclophosphamide (FAC) for the adjuvant treatment of women with node-negative early breast cancer in the USA.	Docetaxel + doxorubicin + cyclophosphamide (TAC) appeared to be cost effective compared with fluorouracil + doxorubicin + cyclophosphamide (FAC) for the adjuvant treatment of women with node-negative early breast cancer in the USA. TAC had an incremental cost per quality-adjusted life-year gained of \$US26,654 compared with TAC.	sanofi-aventis
19 803005126	Capecitabine Docetaxel Epirubicin	This trial compared the efficacy and tolerability of docetaxel + capecitabine and docetaxel + epirubicin as first-line adjuvant therapy in patients with metastatic breast cancer (MBC). The primary endpoint was the progression-free rate 6 months after randomisation, however, slow accrual to the trial led to its early termination.	Docetaxel + capecitabine appeared to be slightly more effective than docetaxel + epirubicin for the first-line adjuvant treatment of women with metastatic breast cancer. The proportion of patients who were progression free at 6 months (primary endpoint) were 76% and 66% in the capecitabine and epirubicin groups, respectively. The median progression-free survival duration was longer in the capecitabine group compared with the epirubicin group (12 vs 7 months; p<0.01).	Roche
20 803004200	Anastrozole Tamoxifen	This study compared the effects of neoadjuvant tamoxifen and anastrozole on the expression of biomarkers (K1-67, Bcl2, Bax, Bak) and estrogen and progesterone receptor expression in postmenopausal women with palpable estrogen receptor-positive invasive	Neoadjuvant tamoxifen did not change the estrogen receptor (ER) status in postmenopausal women with ER-positive invasive ductal carcinoma. However, in anastrozole group, the ER status, originally 100%, was lowered to 89% (p>0.05), and the progesterone receptor (PR) expression rates were lowered from 56% to 28% in	

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21 803004577	Denosumab Zoledronic-acid	ductal carcinoma. This pivotal phase III trial compared the efficacy and tolerability of denosumab and zoledronic acid for the treatment of bone metastases in women with advanced breast cancer. The primary endpoint was the noninferiority of denosumab versus zoledronic acid with respect to time to first on-study skeletal-related event (including fractures, spinal cord compression, or need for radiotherapy or surgery on the bone). However, this analysis focused on the secondary endpoints.	post treatment (p Denosumab was more effective than zoledronic acid in delaying time to first radiation to bone (hazard ratio [HR] 0.74; 95% CI 0.59, 0.94; p=0.01) and first on-study skeletal-related event (SRE) or hypercalcaemia of malignancy (HR 0.82; 95% CI 0.70, 0.95; p	Amgen, Daiichi Sankyo Inc
22 803004435	Anastrozole Fulvestrant	This study compared the efficacy and tolerability of fulvestrant + anastrozole and anastrozole alone for the treatment of women with estrogen or progesterone receptor-positive advanced breast cancer after first relapse following primary treatment. The primary study endpoint was the time to progression.	Anastrozole + fulvestrant did not appear to be more effective than anastrozole alone for the treatment of women with estrogen or progesterone receptor-positive advanced breast cancer after first relapse following primary treatment. The disease progression rate was similar in the anastrozole + fulvestrant and anastrozole groups (both 78%).	AstraZeneca
23 803004440	Anastrozole Fulvestrant	This study compared the biological activity of fulvestrant [Faslodex] and anastrozole [Arimidex], used alone and in combination, when administered for the first-line neoadjuvant treatment of women with estrogen receptor (ER) positive primary breast cancer. The primary study endpoints were the changes in the estrogen and progesterone receptor status and the Ki67 index.	Fulvestrant, used alone or in combination with anastrozole, reduced the estrogen receptor (ER) index to a greater extent than anastrozole alone when administered as first-line neoadjuvant therapy in women with estrogen receptor-positive primary breast cancer. The mean pre-treatment ER index was reduced in all three treatment groups. There was a significant overall treatment effect between therapy arms (p=0.001). [CONT.]	AstraZeneca

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24 803004431	Fulvestrant	This study compared the efficacy and tolerability of fulvestrant [Faslodex] 250 and 500mg for the treatment of postmenopausal women with estrogen receptor-positive advanced breast cancer progressing or relapsing after prior endocrine therapy. The primary study endpoint was the time to progression (TTP).	Fulvestrant 500 mg/month appeared to be more effective than fulvestrant 250 mg/month for the treatment of postmenopausal women with estrogen receptor-positive advanced breast cancer progressing or relapsing after prior endocrine therapy. The time to disease progression (primary endpoint) was longer in the 500 mg/month group than in the 250 mg/month group (hazard ratio 0.80; 95% CI 0.68, 0.94; p<0.01).	AstraZeneca
25 803004130	Octreotide Tamoxifen	This trial evaluated the efficacy of adjuvant tamoxifen +/- octreotide and its association with tissue inhibitor of metalloproteinase-1 (TIMP-1) in postmenopausal women with breast cancer. Patients were stratified according to receiving no, concurrent or sequential chemotherapy. This analysis focused on relapse-free survival, divided into four types: all types, bone only, all types of bone and nonbone.	Adjuvant tamoxifen +/- octreotide increased nonbone and bone only relapse-free survival in patients who had prior chemotherapy (p	
26 803004123	Metformin	This study investigated the effects of neoadjuvant metformin on gene expression when administered in combination with chemotherapy in women with operable, invasive, primary breast cancer.	Neoadjuvant metformin resulted in an over-expression of the AMP-activated protein kinase (AMPK)-beta and phosphatidylinositol 3' kinase (PI3K), and a down regulation in AMPK-gamma and ADCY1, in women with operable, invasive, primary breast cancer.	
27 803004295	AE-37 Sargramostim	This trial is investigating the efficacy and tolerability of sargramostim [GM-CSF (Granulocyte Macrophage Colony Stimulating Factor) immunoadjuvant] with and without AE 37 vaccine in prevention of recurrent breast cancer (BCa) in disease-free patients. The primary endpoint is the rate of disease recurrence at 2 years. Results from an interim analysis are reported here.	Adjuvant therapy with sargramostim in combination with AE 37 vaccine was more effective than sargramostim alone in prevention of recurrent breast cancer in disease-free patients. At 13 months, disease recurrence (primary endpoint) was found in 0% of AE 37 recipients compared to 7% of sargramostim alone recipients (0.05<p	Antigen Express, Generex Biotechnology Corporation
28 803004574	Tamoxifen	This trial evaluated the efficacy of adjuvant tamoxifen and radiotherapy, either alone or in combination, in women with ductal carcinoma in situ (DCIS).	Adjuvant radiotherapy improved the overall recurrence rate of breast cancer compared with tamoxifen (59% vs 29%, respectively), although tamoxifen improved the rate of contralateral tumours compared with radiotherapy (hazard ratios=0.44 vs 0.84, respectively), in women with	

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29 803005063	Anastrozole Exemestane Letrozole	This trial evaluated the effects of adjuvant anastrozole vs letrozole vs exemestane on lipid metabolism, in postmenopausal women with invasive, estrogen receptor positive breast cancer. Following four months of treatment patients were switched to tamoxifen for 12 months.	ductal carcinoma in situ. Adjuvant anastrozole and letrozole had similar effects on lipid metabolism, whereas exemestane significantly (p	Novartis
30 803005125	Anastrozole Tamoxifen	This trial evaluated the effects of adjuvant switching to anastrozole vs remaining on tamoxifen on endometrial thickness and uterine volume, in postmenopausal women with breast cancer with a thickened endometrium after 2-3 years of tamoxifen therapy. The primary endpoints were the change in double endometrial thickness (DET) and uterine volume (UV). [CONT.]	Adjuvant switching to anastrozole or remaining on tamoxifen were associated with similar rates of adverse events (54% and 51%, respectively), in postmenopausal women with breast cancer with a thickened endometrium after 2-3 years of tamoxifen therapy.; Adjuvant switching to anastrozole significantly (p	
31 803004028	Letrozole Trastuzumab	This study investigated the efficacy and tolerability of first-line letrozole + trastuzumab compared with letrozole alone in patients with HER2- and HR-positive advanced breast cancer. The primary endpoint was time to progression.	First-line letrozole + trastuzumab appeared to be more effective than letrozole alone in patients with HER2- and HR-positive advanced breast cancer. The median time to progression (primary endpoint) was 14.1 months compared with 3.3 months (hazard ratio 0.67).; First-line letrozole + trastuzumab had similar tolerability to letrozole alone in patients with HER2- and HR-positive advanced breast cancer. The incidence of adverse events was similar between treatments (10% vs 8%).	Novartis, Roche
32 803004022	Fulvestrant	This study compared the efficacy and tolerability of three fulvestrant dosing regimens in postmenopausal women with estrogen receptor-positive advanced breast cancer that has progressed or recurred on prior endocrine therapy. The primary endpoint was the objective response rate.	Fulvestrant 250 mg/day, 500 mg/day, and 500mg loading + 250 mg/day were associated with similar objective response rates (primary endpoint) in postmenopausal women with estrogen-receptor positive advanced breast cancer that had progressed or recurred following endocrine therapy (8.5%, 15.2% and 5.9%, respectively).	AstraZeneca
33 803004865	Bevacizumab Docetaxel	The AVADO study investigated the efficacy and tolerability of adding two dosages of bevacizumab to first-line therapy with docetaxel in patients with HER2-negative,	Docetaxel + bevacizumab 7.5 and 15 mg/kg/day had an acceptable toxicity profile compared with docetaxel alone as first-line therapy in patients with HER2-negative, locally-recurrent or metastatic breast cancer. Grade V	Roche

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locally recurrent or metastatic breast cancer. The primary endpoint was progression-free survival (PFS). Final overall survival (OS) and updated PFS results were presented.

adverse events were reported in 1.6% and 1.6% versus 2.6% of patients, respectively.; Docetaxel + bevacizumab was more effective than docetaxel alone as first-line therapy in patients with HER2-negative, locally-recurrent or metastatic breast cancer. [CONT.]

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34 803004429	Paclitaxel Sorafenib	This study (the second of four TIES studies) compared the efficacy and tolerability of paclitaxel + sorafenib and paclitaxel alone for the treatment of women with HER2-negative locally-advanced or metastatic breast cancer. The primary study endpoint was the progression-free survival (PFS) duration.	Paclitaxel + sorafenib appeared to be more effective than paclitaxel alone for the first-line treatment of women with HER2-negative locally-advanced or metastatic breast cancer. The progression-free survival duration (primary endpoint) was longer in the paclitaxel + sorafenib group than in the paclitaxel group (6.9 vs 5.6 months; hazard ratio 0.788; 95% CI 0.558, 1.112; 0.05<p<0.10).	Bayer HealthCare Pharmaceuticals, Onyx Pharmaceuticals
35 803004434	Capecitabine Sorafenib	This study compared the efficacy and tolerability of capecitabine + sorafenib and capecitabine alone for the second-line treatment of women with HER2-negative advanced or metastatic breast cancer. The primary study endpoint was the progression-free survival.	Capecitabine + sorafenib appeared to be more effective than capecitabine alone for the second-line treatment of women with HER2-negative advanced or metastatic breast cancer. The progression-free survival duration (primary endpoint) was longer in the capecitabine + sorafenib group than in the capecitabine group (p<0.001).	Bayer HealthCare Pharmaceuticals, Onyx Pharmaceuticals
36 803004580	Capecitabine Sunitinib	This study compared the efficacy and tolerability of sunitinib and capecitabine for the treatment of women with HER2-negative advanced breast cancer (ABC) who had previously failed taxane- and anthracycline-based therapy. The primary study endpoint was the progression-free survival (PFS) duration.	Sunitinib was not as effective as capecitabine for the treatment of women with HER2-negative advanced breast cancer who had previously failed taxane- and anthracycline-based therapy. The median progression-free survival (PFS; primary endpoint) was 2.8 months (95% CI 2.4, 3.9; 162 PFS events) compared with 4.2 months (95% CI 3.4, 5.0; 135 PFS events) for sunitinib and capecitabine, respectively (hazard ratio 1.473; 95% CI 1.167, 1.858; p<0.001).	Pfizer
37 803004573	Bevacizumab Motesanib Paclitaxel	This study compared the efficacy and tolerability of paclitaxel alone, paclitaxel + motesanib, and paclitaxel + bevacizumab for the first-line treatment of women with HER2-negative, metastatic breast cancer (MBC). The primary study endpoint was the objective response rate (ORR)	Motesanib + paclitaxel and bevacizumab + paclitaxel appeared to be slightly more effective than paclitaxel alone for the first-line treatment of women with HER2-negative metastatic breast cancer. [CONT.]	Amgen

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38 803004212	Cyclophosphamide Doxorubicin Fluorouracil Methotrexate	This study compared the quality of life (QOL) effects of standard chemotherapy (doxorubicin + cyclophosphamide [AC] or cyclophosphamide + methotrexate + fluorouracil [CMF]) with capecitabine when administered for the adjuvant treatment of elderly women with early breast cancer.	Capecitabine resulted in better quality of life than standard chemotherapy (doxorubicin + cyclophosphamide or cyclophosphamide + methotrexate + fluorouracil) when administered as adjuvant therapy in women with early breast cancer. The overall European Organisation for Research and Treatment of Cancer scores were better in the capecitabine group than in the standard chemotherapy group ($p < 0.001$).	
39 803004283	Estradiol Testosterone	This was a preliminary analysis of a phase II trial investigating the tolerability of estradiol [Estring] compared to testosterone cream [TEST] in treatment of vaginal dryness and decreased libido in patients [pts] with early stage breast cancer [BC] receiving aromatase inhibitors [AI].	Testosterone vaginal cream and estradiol vaginal ring were both well tolerated in treatment of vaginal dryness and decreased sexual libido in patients with early breast cancer receiving aromatase inhibitors. Reports of adverse events were rare, however, included grade I vaginal discharge, odour, burning, and hair growth.	
40 803004870	Anastrozole Exemestane Tamoxifen	This analysis of the N-SAS-BC04 study (substudy of TEAM) compared with effects of exemestane, tamoxifen and anastrozole on health-related quality of life (HRQOL) and psychological distress in Japanese postmenopausal women receiving adjuvant therapy for the treatment of hormone responsive early breast cancer.	Tamoxifen resulted in better quality of life scores than exemestane or anastrozole when administered for the adjuvant treatment of postmenopausal Japanese women with hormone responsive breast cancer. The Functional Assessment of Cancer Therapy (FACT) -G, -B and -ES scores were increased from baseline at 3 and 12 months in tamoxifen-treated women, but not in women treated with anastrozole or exemestane. There were no significant differences between groups in the Centre for Epidemiological Studies Depression scores.	
41 803005149	Celecoxib Cyclophosphamide Docetaxel Epirubicin Trastuzumab	This study compared the efficacy and tolerability of neoadjuvant epirubicin + cyclophosphamide followed by docetaxel (ECD) with or without celecoxib (HER2-negative patients) or trastuzumab (HER2-positive patients) in women with localised invasive breast cancer.	Neoadjuvant epirubicin + cyclophosphamide + docetaxel (ECD) with trastuzumab appeared to be effective in HER2-positive patients with localised invasive breast cancer, with a pathological complete response rate of 32%, compared with 19% among recipients of ECD alone. In HER2-negative patients, ECD + celecoxib was not associated with a significant difference in pathological complete response rate compared to ECD alone (13% vs 12%). Triple HER2-negative patients had a pathological complete response rate of 30%.	Pfizer, Roche, sanofi-aventis

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42 803005055	Letrozole PD-332991	This ongoing phase I trial investigated the tolerability and pharmacokinetics of PD 332991 in addition to letrozole as first-line therapy in post-menopausal women with oestrogen receptor positive and HER2-negative advanced breast cancer. Interim results are presented here.	PD 332991 in combination with letrozole was associated with no pharmacokinetic interactions as first-line therapy in post-menopausal women with oestrogen receptor positive and HER2-negative advanced breast cancer. Mean area under the plasma concentration curve of PD 332991 in the presence and absence of letrozole were similar (1904 vs 1893 ng.h/mL).; PD 332991 was well tolerated in combination with letrozole as first-line therapy in post-menopausal women with oestrogen receptor positive and HER2-negative advanced breast cancer. [CONT.]	Pfizer
43 803004495	Arzoxifene	This study investigated the efficacy and tolerability of arzoxifene when administered for the prevention of breast cancer and vertebral fractures in women with postmenopausal osteoporosis or low bone mass. The primary study endpoints were the incidence of radiographical vertebral fractures at 3 years in osteoporotic patients, and the incidence of invasive breast cancer in the entire population at 4 years.	Arzoxifene was effective for the prevention of invasive breast cancer and vertebral fractures in women with postmenopausal osteoporosis or low bone mass. [CONT.]	Eli Lilly
44 803004284	Exemestane Letrozole	This study investigated the effects of cytochrome P450 2A6 (CYP2A6) genetic variation on the pharmacokinetics of letrozole in postmenopausal women with early steroid hormone-receptor positive breast cancer.	Polymorphisms in the cytochrome P450 2A6 gene resulted in a significant variation (16.6 to 141.2 ng/mL) in the plasma concentrations of letrozole in postmenopausal women with early steroid hormone-receptor positive breast cancer. Plasma letrozole concentrations were higher in women with the slow or intermediate genotypes than in those women with the normal genotype (p<0.001).	Novartis, Pfizer
45 803004004	Cyclophosphamide Docetaxel Epirubicin Fluorouracil	This phase III trial examined the efficacy and tolerability of adjuvant epirubicin + cyclophosphamide with sequential docetaxel (E90C-D) compared with fluorouracil + epirubicin + cyclophosphamide (FE120C) in patients with advanced breast cancer with extensive lymph node metastases.	Epirubicin + cyclophosphamide + docetaxel appeared to be slightly better tolerated than fluorouracil + epirubicin + cyclophosphamide in patients with advanced breast cancer with extensive lymph node involvement. [CONT.]	

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Adis CTI Record	Drug(s)	Purpose	Study Results	Sponsor
46 803005048	Anthracyclines Bevacizumab Capecitabine Cyclophosphamide Docetaxel Doxorubicin Epirubicin Fluorouracil Paclitaxel	The RIBBON-1 study investigated the efficacy of adding bevacizumab to commonly used chemotherapy regimens as first-line therapy in women with HER2-negative metastatic or locally-recurrent breast cancer. The study comprised two independently powered study groups: in group one, bevacizumab + capecitabine was compared with capecitabine alone; and in the second group, bevacizumab in combination with either a taxane (paclitaxel or docetaxel) or anthracyclines was compared with taxanes or anthracyclines alone. [CONT.]	The addition of bevacizumab to first-line chemotherapy with either capecitabine, or taxanes or anthracycline-based therapy, significantly improved progression-free survival (primary endpoint), compared with capecitabine alone (hazard ratio 0.69; p	Genentech, Roche
47 803005062	Bevacizumab Docetaxel	The AVADO study investigated the efficacy of adding two dosages of bevacizumab [Avastatin] to first-line therapy with docetaxel in patients with human epidermal growth factor receptor-2 (HER2)-negative, locally recurrent or metastatic breast cancer. The primary endpoint was progression-free survival (PFS).	Docetaxel + bevacizumab 7.5 and 15 mg/kg/day were associated with significantly improved progression-free survival (primary endpoint) compared with docetaxel alone, as first-line therapy in patients with human epidermal growth factor receptor-2-negative, locally recurrent or metastatic breast cancer. The spread of metastatic lesions at disease progression was lower in patients receiving bevacizumab compared to placebo.	Roche
48 803004880	Ixabepilone	This trial investigated the efficacy and tolerability of weekly versus 3-weekly ixabepilone [Bristol-Myers Squibb] in the treatment of advanced breast cancer. The primary efficacy endpoint was the rate of progression free survival. Preliminary toxicity results are presented here.	Weekly ixabepilone (16 mg/m ²) was tolerated better than 3-weekly ixabepilone (40 mg/m ²) in treatment of advanced breast cancer. Grade 3-4 treatment-related adverse events were less common in weekly than 3-weekly recipients (22% vs 57%).	Bristol-Myers Squibb
49 803004437	Lapatinib Trastuzumab	This study compared the efficacy and tolerability of lapatinib + trastuzumab and lapatinib alone for the treatment of women with trastuzumab-refractory, HER2-positive, metastatic breast cancer (MBC).	Lapatinib + trastuzumab appeared to be more effective and lapatinib alone for the treatment of women with trastuzumab-refractory, HER2-positive metastatic breast cancer. The overall survival durations were 61 and 41 weeks in the lapatinib + trastuzumab and lapatinib groups, respectively (hazard ratio 0.74; 95% CI 0.57, 0.97; p<0.05).	GlaxoSmithKline
50 803004763	Sagopilone	This study investigated the efficacy and tolerability of a range of sagopilone [Bayer Schering Pharma] doses (12, 16, and 22 mg/	Sagopilone (12-22 mg/m ² /day) was not effective as a second-line or greater therapy in the treatment of advanced breast cancer. The co-primary endpoints, of a	Bayer, Bayer Schering Pharma

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51 803004444	Carboplatin Cyclophosphamide Docetaxel Doxorubicin Trastuzumab	m2/3h or 22 mg/m2/0.5h) as a second-line or greater therapy in patients with metastatic breast cancer (MBC). The co-primary endpoints were the rates of complete response, partial response, and overall response. This third, planned interim analysis (after 650 disease-related events) of the Breast Cancer International Research Group 006 (BCIRG 006) trial compared the efficacy and tolerability of adjuvant docetaxel [Taxotere] + carboplatin + trastuzumab [Herceptin] or doxorubicin + cyclophosphamide then docetaxel with or without trastuzumab in women with HER2-positive early breast cancer. The primary endpoint was disease-free survival.	complete or partial response to treatment of at least 37%, were not met at any dose of sagopilone. A partial response was reported in just 14% of recipients.; Sagopilone (12-22 mg/m2/day) was not well tolerated as second-line or greater therapy in the treatment of advanced breast cancer. [CONT.] Results data not available.	sanofi-aventis
52 803004815	Cyclophosphamide Doxorubicin Paclitaxel Trastuzumab	This study compared the efficacy and tolerability of adjuvant doxorubicin + cyclophosphamide then paclitaxel versus doxorubicin + cyclophosphamide then paclitaxel then trastuzumab versus doxorubicin + cyclophosphamide then paclitaxel + trastuzumab then trastuzumab alone in women with stage I-III human epidermal receptor-2 (HER2) positive breast cancer. The primary endpoint was disease-free survival (DFS). Here, the results of an interim analysis are presented.	Adjuvant doxorubicin + cyclophosphamide then paclitaxel then trastuzumab was associated with significantly improved disease-free survival (primary endpoint) outcomes, compared with doxorubicin + cyclophosphamide then paclitaxel alone (hazard ratio [HR] 0.70; 95% CI 0.57, 0.86; p	Genentech
53 803004583	Letrozole	This trial evaluated the safety of adjuvant letrozole administered either concurrently vs sequentially with radiotherapy, in postmenopausal women with early breast cancer.	Concurrent and sequential therapy with letrozole + radiotherapy were associated with low and similar rates of grade 3 skin dermatitis (4 and 6 patients, respectively) and grade 2 or more radiation-induced subcutaneous fibrosis (2 patients in each), in postmenopausal women with early breast cancer.	

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Adis CTI Record	Drug(s)	Purpose	Study Results	Sponsor
54 803004915	Antineoplastics	This study investigated the cost effectiveness and effects on quality of life (QOL) of the addition of neoadjuvant radiotherapy following adjuvant endocrine therapy and surgery in elderly women with low-risk breast cancer in the UK.	The addition of neoadjuvant radiotherapy following adjuvant endocrine therapy and surgery did not appear to improve quality of life, or be cost effective, compared with no neoadjuvant radiotherapy, for the treatment of elderly women with low risk breast cancer in the UK. Overall the quality of life and quality-adjusted life-years were similar in both groups, and neoadjuvant radiotherapy cost and additional GBP2128 per patient.	

Adis Clinical Trials Insight: Ongoing Trials Status Tracking – January 2010

The table below outlines the clinical trial activity of randomized phase III & IV clinical trials identified whose status has changed during January 2010.

Adis CTI Record	Drug(s)	Study Status	Study Phase	Headline	Sponsor
1 700048947	Carbetocin Oxytocin	Recruiting	IV	Carbetocin vs oxytocin: pharmacodynamics Assessing haemodynamic response In pregnant women scheduled for elective Caesarean section	
2 700041704	Cisplatin Gemcitabine	Recruiting	III	Cisplatin +/- gemcitabine: therapeutic use Cervical cancer Phase III trial in combination with radiotherapy in patients with positron emission tomography/computed tomography defined poor-prognostic advanced disease	Eli Lilly
3 700019116	Cetrorelix Follitropin-alfa Lutropin-alfa	Completed	III	Lutropin alfa + cetrorelix +/- follitropin alfa: therapeutic use Female infertility Effects on ovarian response and pregnancy rates in women patients undergoing in vitro fertilisation/embryo transfer	
4 700039925	Bazedoxifene Conjugated-estrogens/bazedoxifene Conjugated-estrogens/medroxyprogesterone	Active, no longer recruiting	III	Bazedoxifene vs conjugated estrogens/medroxyprogesterone vs conjugated estrogens/bazedoxifene: therapeutic use Menopausal syndrome, prevention of postmenopausal osteoporosis	Wyeth

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Adis CTI Record	Drug(s)	Study Status	Study Phase	Headline	Sponsor
5 700045916	Mirabegron	Active, no longer recruiting	III	Mirabegron: therapeutic use Overactive bladder	Astellas Pharma, Astellas Pharma BV
6 700050238	Levonorgestrel	Recruiting	III	Levonorgestrel: therapeutic use Infertility Comparing levonorgestrel-releasing intrauterine system with Mirena intrauterine system	Medicines360
7 700037779	Ganirelix Nafarelin	Recruiting	IV	Ganirelix vs nafarelin: therapeutic use Female infertility In patients undergoing in vitro fertilisation/intracytoplasmic sperm injection treatment	
8 700020620	Goserelin	Active, no longer recruiting	III	Goserelin: therapeutic use Prevention of premature menopause In oestrogen non-responsive breast cancer patients receiving adjuvant chemotherapy	
9 700015329	Metformin	Completed	III	Metformin: therapeutic use Polycystic ovary syndrome Effects on fertility in women undergoing in vitro fertilisation	
10 700037297	Metronidazole Miconazole	Discontinued	III	Metronidazole +/- miconazole: therapeutic use Prevention of bacterial vaginosis In non-pregnant women	Embil Pharmaceutical
11 700021506	Indometacin	Active, no longer recruiting	III	Indomethacin: therapeutic use Female infertility	
12 700041727	Estradiol-valerate Nafarelin Progesterone	Recruiting	IV	Nafarelin + estradiol valerate + progesterone: therapeutic use Infertility Natural versus hormone replacement therapy cycles in patients with frozen embryo replacement in vitro fertilisation	
13 700051798	Chorionic-gonadotropin	Recruiting	IV	Chorionic gonadotropin: therapeutic use Infertility Intrauterine injection before embryo transfer in in-vitro fertilisation/intracytoplasmic sperm injection	
14 700014694	Dinoprostone Misoprostol	Completed	III	Misoprostol vs dinoprostone: therapeutic use Labour disorders	Alliance Pharmaceuticals

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Phase III trial for induction of labour in multiparous patients					
Adis CTI Record	Drug(s)	Study Status	Study Phase	Headline	Sponsor
15 700016938	Clomifene Infertility-therapies Urofollitropin	Active, no longer recruiting	IV	Infertility therapies: therapeutic use Female infertility Clomifene/IUI then IVF vs urofollitropin/IUI then IVF vs immediate IVF Efficacy and cost analysis in women aged 38-43 years: the FORT-T Trial	
16 700022612	Lapatinib Paclitaxel Trastuzumab	Recruiting	III	Lapatinib, trastuzumab, paclitaxel: therapeutic use Early breast cancer Phase III trial as neoadjuvant therapy with paclitaxel in combination with trastuzumab, lapatinib or both	
17 700004495	Alendronic-acid	Completed	III	Alendronic acid: therapeutic use Postmenopausal osteoporosis Phase III trial	Merck & Co

For further information, please call +44 (0) 20 7981 0765 or send an e-mail to clientsupport@wolterskluwer.com.