

ADAPT: Adjuvant dynamic marker-adjusted personalized therapy trial optimizing risk assessment and therapy response prediction in early breast cancer.

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Background: Indication of (neo-)adjuvant therapy is based on risk profile, hormone receptor and HER2 status at time of primary diagnosis. Data indicate dynamic proliferation changes after short-term induction therapy are superior to static initial biopsy results in predicting outcome and tumor response following neoadjuvant CTx in distinct BC subtypes. First generation trials such as TAILORx, MINDACT, NNBC-3, WSG planB utilize information of new prognostic/predictive tests to reduce overtreatment by CTx. Results still pending. ADAPT is a second generation trial addressing individualization of adjuvant decision-making in early BC by utilizing optimized pre-therapeutic biomarker information and early biomarker changes in a second core biopsy after 3-week subtype specific induction therapy. It aims at reducing over-/undertreatment in luminal tumors and optimizing therapy in HER2+ (T-DM1, pertuzumab) / TNBC (nab-paclitaxel + platinum/gemcitabine). **Methods:** Design: ADAPT combines static prognosis assessment by conventional markers (nodal status) and Recurrence Score (HR+) with dynamic measurement of proliferation changes after a short 3-week induction therapy, using the baseline diagnostic and repeat core biopsy following induction. ADAPT is a prospective, multi-center, controlled, non-blinded, randomized phase II/III trial, comprising an umbrella trial and 4 sub-trials (HR+/HER2-, HR+/HER2+, HR-/HER2+, TNBC). Eligibility criteria: Pre-/postmenopausal women with histologically confirmed unilateral primary invasive BC. Pts requiring CTx/targeted therapy with no contraindications. Statistics: Assumption across sub-protocols: CTx spared in 1120 HR+/HER2-, pCR achieved in 170 HER2+/TNBC pts. Outcome of good-proliferation responders/pCR pts will be compared to reference group (n=640 HR+/HER2- pts: low RS, no CTx, 94% 5yr survival). One-sided test of non-inferiority (3.2% margin, 90.8%) with alpha=0.05 will have 80% power. Present/target accrual:By 01/2013: 16/35 sites initiated. ADAPT HR+/HER2-: 161/4000 pts recruited. ADAPT HER2+/HR+: 9/380 pts recruited. ADAPT HER2+/HR- or TNBC: start of recruitment planned for Q2 2013. Clinical trial information: NCT01781338.