TPS631 Poster Session

A randomized trial of trastuzumab deruxtecan and biology-driven selection of neoadjuvant treatment for HER2-positive breast cancer (ARIADNE).

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Background: Neoadjuvant therapy is the standard of care for the treatment of non-metastatic HER2-positive breast cancer. Studies on first generation antibody-drug conjugates (ADC) such as trastuzumab emtansine (T-DM1) showed equal or slightly lesser efficacy than chemotherapy combined with dual HER2 blockade. Trastuzumab deruxtecan (T-DXd) is a next generation ADC approved for the treatment of metastatic HER2-positive breast cancer, with greatly improved efficacy compared with T-DM1. **Methods:** ARIADNE is an academic, international, open label, randomized, comparative phase IIB trial, actively enrolling in Sweden (ten sites) and in Norway (seven sites), with sites in Belgium (three), Netherlands (one) and Italy (three) activating during Q2 2025. A total of 370 patients with non-metastatic HER2-positive primary breast cancer and an indication for neoadjuvant therapy will be offered inclusion and randomized 1:1 to receive either i) a taxane, carboplatin, trastuzumab and pertuzumab for three cycles or ii) T-DXd for three cycles. Further treatment is based on the PAM50-defined intrinsic molecular subtype from a pretreatment biopsy: HER2-enriched (approximately 65%) patients continue with the same treatment for three more cycles. Estrogen receptor (ER) positive and luminal (approximately 25%) patients receive trastuzumab and pertuzumab for three cycles, combined with letrozole and ribociclib for two cycles. Finally, ER-negative and luminal or basal-like (approximately 10%) patients either continue with the same treatment for three additional cycles in case of radiologic complete response, or they receive four cycles of dose-dense epirubicin and cyclophosphamide in case of lack of complete response. The primary endpoint of ARIADNE is locally assessed rate of pathologic complete response (pCR) in patients with molecularly HER2-enriched tumors, defined as ypT0/Tis, ypN0, as determined by a pathologist blinded to treatment assignment (intention-to-treat analysis). Key secondary endpoints are rates of complete radiologic response at three cycles; rates of pCR in the other two molecular groups and in the two groups of the initial randomization; event-free survival, defined as the time from randomization to disease progression, locoregional or distant recurrence, contralateral breast cancer, other cancer, or death due to any cause. Tissue and plasma samples are collected at baseline, during treatment and surgery, as well as during follow-up. The first patient was randomized on 26th October 2023; 46 patients had been enrolled to the study until January 2025. Clinical trial information: NCT05900206. Research Sponsor: None.