

[13] Role of anthracycline-based therapy in the adjuvant treatment of breast cancer: efficacy analyses determined by molecular subtypes of the disease.

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**Background:** The use of anthracycline-based therapies for the adjuvant treatment of high-risk breast cancer has now become a common standard part of clinical practice. The evidence supporting this approach was initially controversial but finally thought to be resolved when the Oxford overview demonstrated a 4-5 % survival advantage in favor of anthracycline-based therapies over those that did not contain an anthracycline.

**Materials and Methods:** We performed a systematic review of published data from randomized, controlled adjuvant chemotherapy trials reporting HER2 subtype, i.e. HER2 positive vs. HER2 normal breast cancers. In addition, the analysis of two recent and separately conducted adjuvant trials of HER2 positive and HER2 normal breast cancers respectively, that were further sub-classified by whether or not they contained co-amplification of the topoisomerase II alpha (topo IIa) gene were included.

**Results:** The published data demonstrate a remarkably consistent finding. Specifically, the incremental efficacy benefit attributed to anthracycline-based therapies is restricted to the HER2 positive subgroup. A recent analysis of the BCIRG 006 (HER2+) and 005 (HER2-) studies reveals that topo IIa amplification is confined to cancers that contain the HER2 amplicon. In >1,600 HER2 FISH negative samples there is not a single topo IIa amplified case. Conversely, deletion of topo IIa was found in 5% of HER2+ and 3% of HER2- tumors respectively. An analysis of the impact of topo IIa co-amplification demonstrates that the improved efficacy imparted by an anthracycline vs. a non anthracycline-based regimen is restricted to the HER2/topo IIa co-amplified cancers. These constitute 35% of the HER2+ cancers. In these cancers the efficacy resulting from an anthracycline-based regimen alone was similar in magnitude to the addition of trastuzumab to adjuvant therapy.

**Conclusion:** The use of anthracyclines in the adjuvant treatment of all breast cancer is not supported by the existing data. Given the known long-term cardiac and leukemogenic/MDS toxicities of anthracyclines and the lack of an incremental benefit in non HER2/topoIIa co-amplified cancers (which is ~92% of the overall breast cancer population), other approaches to the adjuvant treatment of breast cancer should now be adopted.

General Session 1 (9:30 AM-10:30 AM)