BREAST CANCER

Utidelone: burden relief in pretreated women

The prevalence of breast cancer is rising in China and an increased use of anthracyclines and taxanes has led to a heavily pretreated and poor-prognostic drug-resistant metastatic breast cancer (MBC) population, with few treatment options. Thus, an urgent need exists for novel therapies for these women. The microtubule inhibitor ixabepilone is FDA-approved for women with MBC who fail to respond to taxane and anthracycline-based therapy. Ixabepilone, however, is expensive and treatment discontinuation is common owing to toxicities. Utidelone is a less costly epothilone analogue, produced using an engineered biosynthetic approach, and has shown promising efficacy and safety outcomes in phase I and phase II studies. This prompted Binghe Xu and co-authors to

initiate a multicentre, open-label, randomised, phase III trial to determine the efficacy and safety of utidelone plus capecitabine compared with capecitabine alone in women with MBC refractory to anthracycline and taxane therapy.

The utidelone plus capecitabine combination significantly improved progression-free survival (PFS; 8.44 months versus 4.27 months). Overall survival data were immature at the time of publication, although an interim analysis revealed a significantly longer overall survival for women receiving the utidelone combination (16.13 months versus 12.78 months). No significant between-group differences in safety outcomes were noted, although more women in the combination arm experienced grade 3 peripheral neuropathy. An earlier study of ixabepilone showed a 2-month PFS improvement but no overall survival advantage. Importantly, unlike ixabepilone, only mild myelosuppression and no liver toxicity was observed with utidelone.

Xu puts these results into context: “utidelone plus capecitabine not only substantially improved PFS, but this benefit was maintained consistently across subgroups irrespective of age, performance status, hormone and growth factor receptor status or the number of prior regimens”. He posits, “our study findings support utidelone as a novel chemotherapeutic option for MBC; since the mechanism of action of utidelone is different to taxanes, although both inhibit microtubule depolymerisation, it is a potential regimen for taxane-resistant MBC”.

In light of the favourable benefit–risk profile of the utidelone–capecitabine combination, these latest results indicate that “epothilone analogues remain good candidates for drug development, and we hope our findings promote further research and opportunities to optimize delivery to reduce peripheral neuropathy.”

Lisa Hutchinson

ORIGINAL ARTICLE Xu, B. et al. Utidelone plus capecitabine versus capecitabine alone for heavily pretreated metastatic breast cancer refractory to anthracyclines and taxanes: a multicentre, open-label, superiority, phase 3, randomised controlled trial. *Lancet Oncol.* [http://dx.doi.org/10.1016/S1470-2045\(17\)30088-8](http://dx.doi.org/10.1016/S1470-2045(17)30088-8) (2017)

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