

Abemaciclib plus fulvestrant for breast cancer

Results from the MONARCH 2 trial have shown that abemaciclib plus fulvestrant improves overall survival in patients with hormone receptor-positive, HER2-negative, advanced breast cancer whose disease has progressed on previous endocrine therapy.

In the randomised, placebo-controlled, double-blind phase 3 trial, 669 eligible women were randomly assigned (2:1) to receive either the CDK4/6 inhibitor abemaciclib plus fulvestrant (n=446) or placebo plus fulvestrant (n=223). Treatment consisted of 500 mg intramuscular fulvestrant on days 1 and 15 of the first 28-day cycle and day 1 of each subsequent cycle, combined with either 150 mg of abemaciclib orally once daily or matching placebo. The primary endpoint was progression-free survival, reported previously; overall survival was a key secondary endpoint.

Exploratory endpoints included time to second disease progression.

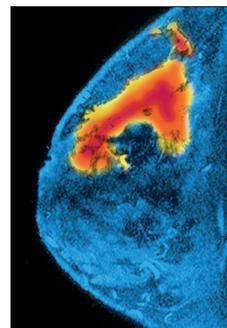
At a pre-specified interim analysis of overall survival (at approximately 77% maturity), in the intention-to-treat population 211 patients in the abemaciclib group and 127 in the placebo group had died. Median overall survival was 46.7 months in the abemaciclib group versus 37.3 months in the placebo group (hazard ratio [HR] 0.757 [95% CI 0.606–0.945]; p=0.01). The median time to second disease progression was 23.1 months in the abemaciclib group versus 20.6 months in the placebo group (HR 0.675; 95% CI 0.558–0.816).

Lead study author George W Sledge (Stanford University Medical Center, Stanford, CA, USA), said "This research was motivated by the recognition that the cyclin-CDK4/6 pathway was a crucial element of growth in oestrogen receptor-positive disease, which made

it a great target. The data from all three CDK4/6 inhibitors shows growing evidence of a positive effect on survival, pointing inevitably towards their study in the setting of micrometastatic disease, the place where cure is possible."

Hope Rugo (Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA) added, "Along with other trials demonstrating survival benefits with CDK4/6 inhibitors, we can feel confident that these agents prolong survival when added to endocrine therapy. Abemaciclib in general is well tolerated, but it causes diarrhoea which can make it hard to tolerate for some patients. Now we wait for additional data from the first-line trials with aromatase inhibitors, and the outcome of adjuvant trials with or without a CDK4/6 inhibitor combined with endocrine therapy."

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