Targeted combination therapy halts disease, extends life in advanced melanoma patients

September 29 2014

A world-first study in today's *New England Journal of Medicine* heralds the efficacy of a targeted combination drug therapy after reporting major declines in the risk of disease progression and death in people with metastatic melanoma.

The multi-centre, double-blind, randomised, phase 3 trial compared oral dabrafenib (150 mg twice daily) and oral trametinib (2 mg once daily) combination therapy with oral dabrafenib (150 mg twice daily) and placebo.

All trial patients had inoperable stage 3C or 4 metastatic melanoma that had a BRAF gene mutation V600E or V600K. Among cancer patients with metastatic melanoma, about 40 per cent have a BRAF gene mutation – an abnormality that assists some melanoma tumours to grow and spread.

Led by Associate Professor Georgina Long of Melanoma Institute Australia at the University of Sydney, the finding affirms accumulating evidence of the efficacy of targeted combination therapies in extending life and halting disease progression in patients with cancers that carry genetic mutations that resist monotherapies.

"We show a significant 25 per cent reduction in the risk of disease progression with the combination of dabrafenib and trametinib over single-agent dabrafenib," says A/Professor Long.

"We also report a significant 37 per cent relative reduction in the risk of death among people who received the combination drug therapy compared with monotherapy.

The research also reports that two in three patients (67%) treated with the combination therapy had a complete or partial response compared to one in two patients (51%) treated with monotherapy.

"This means that significantly more patients who received combination therapy experienced complete or partial tumour regression compared to patients who received monotherapy," says A/Professor Long.

"Unlike standard chemotherapy, so-called BRAF-targeted therapies are designed to interact with specific molecules that are part of the pathways and processes used by cancer cells to grow, divide, and spread in the body.

"Further, these new generation targeted drugs act on specific molecular targets in cancer cells that have been identified through research, while most standard chemotherapies act indiscriminately on all rapidly dividing cells.

"They're designed to target specific vulnerabilities in the cancer cell, while most standard chemotherapies were identified through trial and error. Also, targeted therapies tend to have fewer and less toxic side effects than standard chemotherapy, because they do less damage to normal cells."

"However, trials of BRAF-targeted monotherapies reveal that half the patients start to develop resistance about six to seven months after starting therapy. This is why researchers are conducting trials of combination therapies that target and interrupt the mechanisms that allow cancer cells to resist monotherapies.

"Our new report confirms the accumulating evidence that targeted combination therapies can extend life and halt disease progression among people with metastatic cancer who carry genetic mutations in their cancer that resist standard chemotherapy treatments and targeted monotherapies."

Provided by University of Sydney