1163-92-840 **Avner Friedman** (nourridine@aims.ac.za) and **Nourridine Siewe*** (nourridine@aims.ac.za). *Overcoming Drug Resistance to BRAF Inhibitor.*

One of the most frequently found mutations in human melanomas is in the B-raf gene, making its protein BRAF a key target for therapy. However, in patients treated with BRAF-inhibitor (BRAFi), although the response is very good at first, relapse occurs within 6 months, on the average. In order to overcome this drug resistance to BRAFi, various combinations of BRAFi with other drugs have been explored, and some are being applied clinically, such as a combination of BRAF and MEK inhibitors. Experimental data for melanoma in mice show that under continuous treatment with BRAFi, the pro-cancer MDSCs and chemokine CCL2 initially decrease but eventually increase to above their original level, while the anti-cancer T cells continuously decrease. In this paper we develop a mathematical model that explains these experimental results. The model is used to explore the efficacy of combinations of BRAFi with anti-CCL2, anti-PD-1 and anti-CTLA-4, with the aim of eliminating or reducing drug resistance to BRAFi. (Received September 13, 2020)