# GZD824 inhibits endometrial cancer cell migration and invasion via regulation in EMT

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Most endometrial cancer (EC) patients generally have a good outcome. However, for those diagnosed with aggressive subtypes or recurrent disease, prognosis remains poor. The standard first-line chemotherapy remains as the carboplatin-paclitaxel doublet, despite the fact that only patients harbouring TP53 mutations generally benefit from it[1]. Novel therapies are urgently warranted in these patients. GZD824 is a small molecule previously applied in clinical trials for chronic myeloid leukemia (CML) and Ph+ acute lymphoblastic leukemia (ALL) as a BCR-ABL inhibitor. Recently, GZD824 was reported to inhibit downstream signalling of ROR1[2]. ROR1 is a key receptor for non-canonical Wnt Signalling pathway that we have identified as a promising biomarker to target in endometrial cancer[3-4]. This study aimed to investigate the potential of the multi-kinase inhibitor GZD824 in treating endometrial cancer.

We selected Ishikawa and ARK1 cell lines to model Type I and II EC respectively. At first, the half maximal inhibitory concentration (IC50) for GZD824 in each cell line at 72h was determined using the IncuCyte S3 live imaging system. Next, the effects of GZD824 treatment on migration and invasion were estimated via wound healing migration and transwell invasion assay respectively. Last, we analysed the change in epithelial-mesenchymal transition (EMT) markers (E-cadherin and Vimentin) following GZD824 treatment.

Both cell lines were sensitive to the GZD824 with an IC50 of less than 0.5μM (Figure 1 A). GZD824 significantly inhibited cell migration ability of both Ishikawa and ARK1 (Figure 1 B) and prevented ARK1 invasion (Figure 1 C). Ishikawa and ARK1 showed distinct EMT phenotypes prior to treatment. ARK1 started to undergo MET following 0.1μM GZD824 treatment, even before proliferation became majorly impeded. This study showed the effect of GZD824 on reversing the EMT in EC cells and supports the potential of the drug in treating EC metastasis.

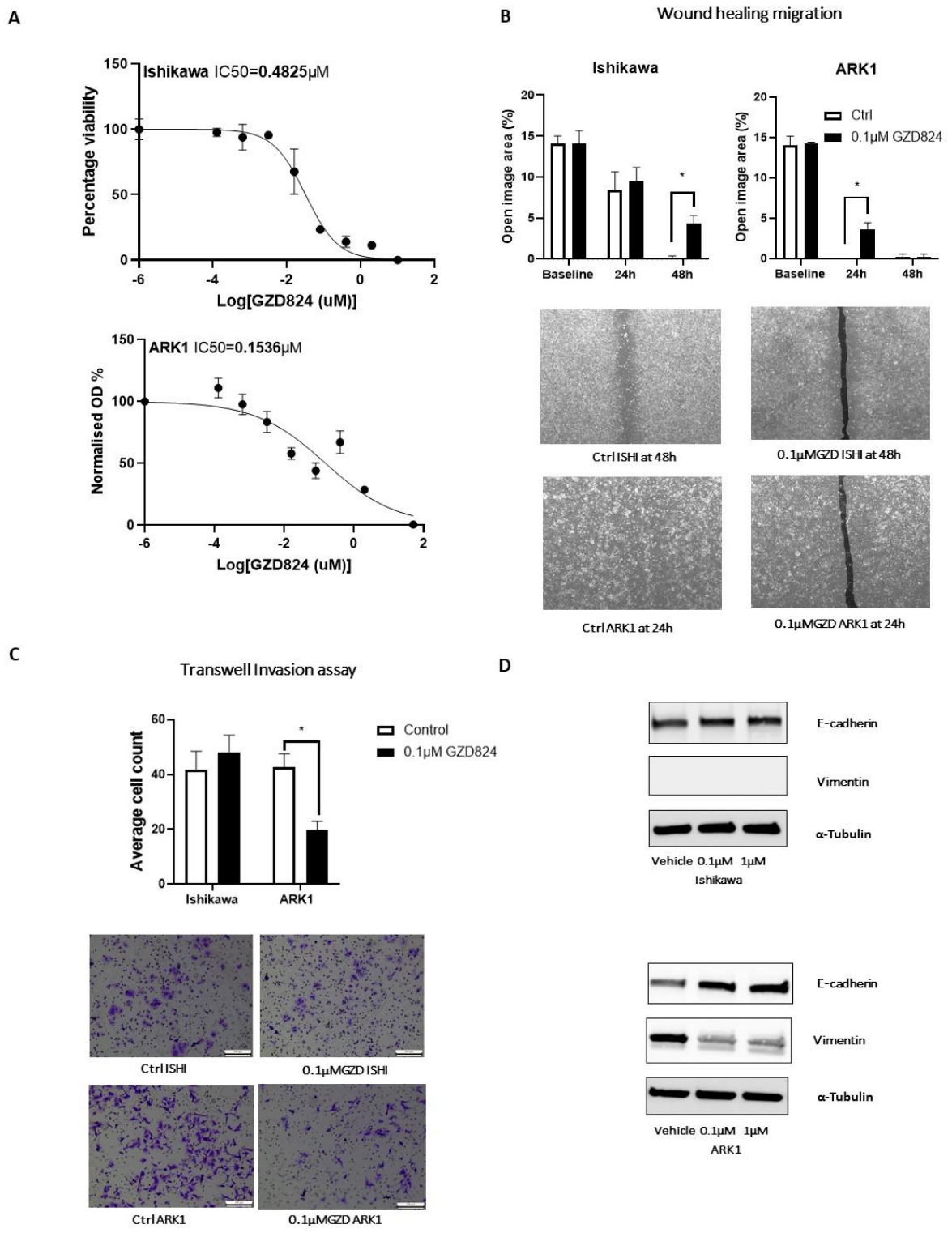


**Figure 1: GZD824 significantly decreased the migration and invasion ability of ARK1 high grade serous endometrial cell via reversing EMT)** A. Dose-response curves with IC50 indicated for GZD824 in Ishikawa and ARK1 cell lines. B. GZD824 at 0.1μM significantly inhibited Ishikawa cell migration at 48h and ARK1 cell migration at 24h. C. Treating ARK1 with 0.1μM GZD824 significantly inhibited its invasion potential. D. Western blot showing both doses (0.1 and 1μM) of GZD824 increased E-cadherin in Ishikawa and ARK1. *Significant at $p<0.05$ level.

**References**


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