MEBENDAZOLE and LEUKEMIA - potent inhibitor of T-cell ALL Leukemia cells and overcomes chemoresistance! Rare 2020 study shows Mebendazole outperforms chemo



2020 Wang et al - Mebendazole is a potent inhibitor to chemoresistant T cell acute lymphoblastic leukemia cells

- Mebendazole (MBZ) is a tubulin-suppressive antihelmintic agent with low toxicity, which has been repurposed to treat different types of tumors
- In recent years, multiple studies have demonstrated that MBZ and other benzimidazoles, such as **fenbendazole**, can suppress different types of malignant cells
- studies also showed that MBZ was able to enhance the effects of chemotherapeutic agents and radiation therapy on tumor cells

T-cell ALL Leukemia

- T cell acute lymphoblastic leukemia (T-ALL) represents 15% of acute lymphoblastic leukemia cases in children and 25% in adults, which is known for its inferior prognosis than B cell acute lymphoblastic leukemia
- Conventional chemotherapy agents, such as dexamethasone, doxorubicin, paclitaxel and vincristine, are often used in the treatment of T-ALL
- Rate of relapse in pediatric T-ALL cases is high & drug-resistance is common in relapsed T-ALL patients, which results in dismal chances of recovery
- Therefore, therapeutic agents that can overcome drug-resistance are needed for chemoresistant T-ALL



Fig. 1. Inhibition of cell proliferation and viability by MBZ in T-ALL cells. Vincristine VCR camptothecin (CPT)



Mebendazole drops cancer cell viability to 65% and chemo to 55% in chemosensitive leukemia cells.

Mebendazole drops cancer cell viability to 60% and chemo stays at 90% in chemoresistant leukemia cells.

MICE:



Fig. 5. T-ALL in murine models relieved by MBZ administration. BALB/c nu/nu mice were dosed

- murine T-ALL models were generated
- MBZ could inhibit the growth of CEM/C1 cells in vivo & could potentially be developed as a chemotherapeutic agent for chemoresistant T-ALLs

CONCLUSION:

- In summary, MBZ at nanomolar concentrations was found to suppress the growth and reduced the viability of the T-ALL cell line, CCRF, and its chemoresistant subclone, CEM/C1.
- The suppressive effects were found to be dose-dependent and not to be affected by the chemoresistance.
- Besides the effects of cell cycle arrest, caspase 3/7 activation and tubulin disruption, MBZ was also found, for the first time, to suppress the Notch1 signaling pathway.
- Experiments using T-ALL murine models further confirmed that MBZ administration could inhibit inoculated chemoresistant T-ALL cells in vivo.
- Collectively, these findings indicated that MBZ might be developed as a therapeutic agent to treat T-ALLs with chemoresistance.

My Take...

Fenbendazole and Mebendazole, which differ structurally by only one atom, are powerful anti-parasitic drugs being repurposed to treat CANCER.

There is a growing body of literature suggesting that Mebendazole is a powerful Leukemia treatment. Important to remember T-ALL is one of the most aggressive leukemias there is.

Very impressive that Mebendazole is able to overcome chemoresistance in T-ALL.

Once again, anti-parasitic drug outperforms chemotherapy!



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