Background

- Triple-negative breast cancer (TNBC) is an aggressive type of breast cancer with high recurrence and mortality rates.
- Replication stress, caused by DNA damage, leads to genetic instability in cancer, which is the hallmark of cancer.
- Targeting ataxia telangiectasia and Rad3 proteins (ATR), a key sensor of DNA damage and replication stress, has emerged as an effective option for cancer treatment.
- Following DNA damage, several events driving TNBC pathogenesis increase reliance on ATR signaling.
- Targeting ATR can be a therapeutic option for TNBC.
- BAY 1895344 (BAY) exhibited antitumor efficacy in various cancer models by targeting ATR.

Objectives

- To evaluate the in vitro antitumor efficacy of ATR inhibitor BAY in TNBC cells.
- To investigate the action mechanism of BAY.

Hypothesis

BAY inhibits TNBC cell proliferation via inducing cell cycle arrest and apoptosis by specifically targeting ATR.

Methods

- The anti-proliferation effect of BAY was assessed using the CellTiter-Blue, sulforhodamine B, and clonogenic assays.
- The impact of BAY on target impression was assessed by Western blotting.
- The impacts of BAY on apoptosis and cell cycle progression were assessed by flow cytometry.

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Results

BAY inhibited proliferation of TNBC cells in vitro

BAY induced apoptotic cell death

BAY inhibited colony formation of TNBC cells in vitro

BAY induced G2/M and S phase arrest

Conclusion

- BAY suppressed TNBC cell growth by inducing cell cycle arrest and apoptosis.
- Targeting ATR can be an effective treatment strategy for TNBC.

Future studies

- Assess whether BAY inhibits TNBC cell growth by specifically targeting ATR.
- Evaluate the in vivo antitumor efficacy of BAY.
- Identify a potential partner whose inhibition potentiates BAY’s antitumor efficacy.

References

2. Ozawa PM, Breast Cancer Res Treatment, 2018; 172(3): 713-723
3. Wengner AM, ACR, 19(19)